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THE THIOLATE ANION AS A NUCLEOPHILE

PART VIII*. REACTIONS OF DIBROMOTETRAFLUOROBENZENES

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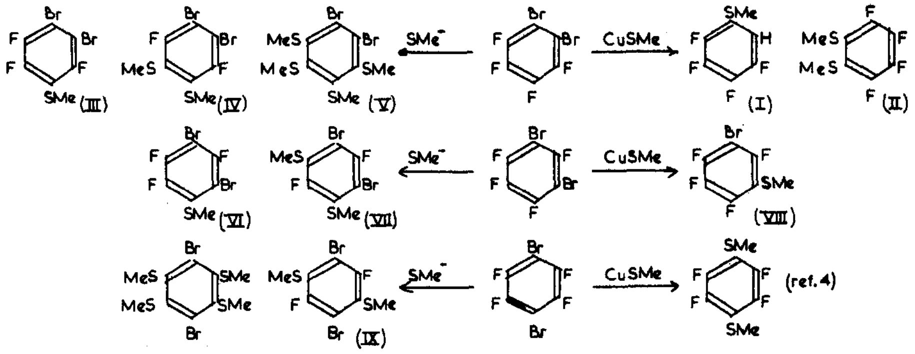
SUMMARY

The reactions of the isomeric dibromotetrafluorobenzenes with the methanethiolate anion and copper(I) methanethiolate have been examined. Using the thiolate anion replacement of fluorine by the SMe group occurred, but with copper(I) methanethiolate protodebromination and replacement of the bromine with the SMe group occurred. The new compounds isolated have been characterized and their spectra (NMR, IR, and mass) examined.

INTRODUCTION

In continuation of the study of the reactions of fluoroaromatics with thiolate anions [1], the reactions of the three isomeric dibromotetrafluorobenzenes with the methanethiolate anion and copper(I) methanethiolate have been examined. The reactions observed in this study are summarized below.



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*For Part VII, see ref. 1

The ortho dithiols or their derivatives can act as bidentate ligands and the properties of tetrafluorobenzene-1,2-dithiol and tetrachlorobenzene-1,2-dithiol as chelating agents have been examined [2,3]. Tetrafluorobenzene-1,2-dithiol can only be prepared in relatively small yield by a multistep procedure [4]. One of the objectives of this research was to examine whether ortho-bis (methylthio)tetrafluorobenzene(II) could be prepared in reasonable yields directly from ortho-dibromotetrafluorobenzene so that its properties as a ligand could be examined. This was extended to an examination of the reactions of all the isomeric dibromotetrafluorobenzenes.

RESULTS AND DISCUSSION

Bromopentafluorobenzene reacted with the thiolate anion in solution giving protodebromination and nucleophilic replacement of fluorine [5] and in the

$$BrC_6F_5 + SMe^- \rightarrow C_6F_4(SMe)H + C_6F_2(SMe)_3H$$

reactions of hexabromobenzene protodebromination as well as nucleophilic replacement of the bromine atoms occurred [6]. In the reactions of the dibromotetrafluorobenzenes with the thiolate anion in solution it would be expected that the fluorine atoms would be replaced preferentially and that some protodebromination might occur. The extent of the replacement of the fluorine atoms by the thiolate anions depends on the solvent employed [7]. In the present study using DMF as a solvent complete replacement of the fluorine atoms could occur and the actual products isolated depended on the stoichiometry of the reactants. In comparison using pyridine-ethylene glycol as a solvent, two fluorine atoms remained on the aromatic ring, which is consistent with previous observations using this solvent system [5]. Although the reaction times were approximately the same in each solvent system, the difference may be accounted for by the differences in polarity of the solvent, DMF being more polar, or the higher boiling and hence reaction temperature, of the solvent (DMF b.p. 149-150°, pyridine-ethylene glycol mixture b.p. 116°). No protodebromination was observed using the methanethiolate anion, MeS^-, as a nucleophile.

When copper(I) thiolate is used as a nucleophile [8,9,10] or when the reaction occurs in the presence of copper [8], under suitable conditions preferential replacement of the halogen other than fluorine was observed.

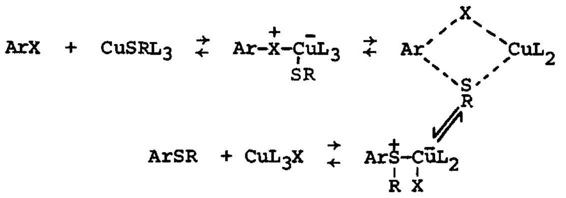
$$C_6F_5Br + CuSC_6F_5 \rightarrow C_6F_5SC_6F_5 \qquad \text{[ref. 9]}$$

The reaction p-dibromotetrafluorobenzene with copper(I) methanethiolate gave para-bis(methylthio)tetrafluorobenzene [4],

$$p\text{-}Br_2C_6F_4 + CuSMe \rightarrow p\text{-}(MeS)_2C_6F_4 \qquad \text{[ref. 4]}$$

a product which can readily be obtained from hexafluorobenzene and the methamethiolate anion [11]. In the reactions of the ortho- and meta-dibromotetrafluorobenzenes with copper(I) methanethiolate replacement of the bromine and protodebromination occurred. In analogous reactions of copper(I) pentafluorothiophenolate, $CuSC_6F_5$, with the dibromotetrafluorobenzenes only replacement of the bromine by the SC_6F_5 group was observed [12]. The yields of the products from the copper(I) methanethiolate reactions were relatively low, particularly of II. In the reaction of ortho-dibromotetrafluorobenzene with CuSMe I was the major product and II the minor product. If ortho-diiotetrafluorobenzene was used instead of ortho-dibromotetrafluorobenzene only II was isolated in low yield. The yield from this reaction could probably be improved. Purification of II by gas chromotography was tedious, so that this reaction has little synthetic value for the preparation of II. The procedure affords a reasonable method of preparation of I. The isomer of I with the hydrogen and methylthio group para to each other can readily be prepared by the reaction of the methanethiolate anion with pentafluorobenzene [13], but I has not been isolated in the reaction of methanethiolate anion with pentafluorobenzene.

A reaction mechanism is postulated below



X = Halogen

This mechanism implies that both the copper salt and the solvent are important in the formation of the products. The least electronegative halogen, bromine or iodine, is most likely to be involved in the formation of the intermediate. When thiourea is added or a more highly coordinating ligand is used as a solvent, an ion pair $CuL_3{}^+SR^-$ is formed and the SR^- anion replaces the aromatic fluorine atoms [8].

The structures of the new products were deducted from their N.M.R. spectra, both ^1H and ^{19}F. Details of the spectra are shown in Table 1. In most cases the structures could be derived from observations of combinations of the fluorine-fluorine and fluorine-aromatic hydrogen coupling constants and comparison with literature values. The splitting of the methyl protons by fluorine atoms ortho to the SMe group and corresponding splitting of the fluorine peaks [14] further assisted assignments of the structures. In all cases first order proton spectra were observed and in most cases first order fluorine spectra. A second order fluorine spectra, A_2X_2, was observed for

TABLE 1

Summary of N.M.R. Data

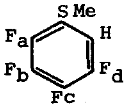
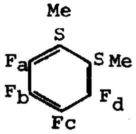
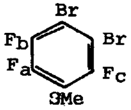
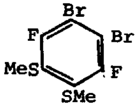
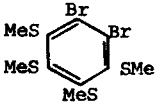
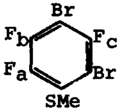
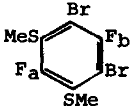
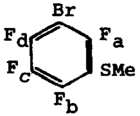
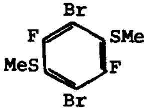
Compound		Chemical Shifts/p.p.m.	Coupling Constants/Hz
	(I)	H(ArH) 6.50 M	J(H-F_o) 10.2(H), 10.2(F_a) : J(H-F_p) 2.6(H) 2.5(F_b)
		H(Me) 2.46 S	J(H-F_m) 7.7(H), 7.6(F_c) : 6.3(H), 6.4(F_a)
		F_a 136.8 M	J(F_a-F_c) 20.3(F_a), 20.3(F_b) : J(F_a-F_c) 2.5(F_a), 2.5(F_c)
		F_b 155.7 M	J(F_a-F_d) 11.4(F_a), 11.2(F_d) : J(F_b-F_c) 19.1(F_b), 19.1(F_c)
		F_c 159.2 M	J(F_b-F_d) 2.5(F_b), 2.5(F_d) : J(F_c-F_d) 20.3(F_c), 20.3(F_d)
		F_d 139.9 M	
	(II)	H(Me) 2.49 T	J(Me-F_o) 0.8(H)
		$F_{a,d}$ 130.9 M	J(F_a-F_b) 24.0 : J(F_b-F_c) 20.7
		$F_{b,c}$ 155.3 M	J(F_a-F_d) 11.0 : J(F_a-F_c) 3.9
	(III)	H(Me) 2.51 T	J(Me-F_o) 1.0(H), 0.8(F_a) 0.8(F_b)
		F_a 127.1 M	J(F_a-F_b) 23.2(F_a), 23.2(F_b)
		F_b 128.1 M	J(F_a-F_c) 2.6(F_a), 2.6(F_c)
		F_c 97.4 M	J(F_b-F_c) 10.4(F_b), 10.4(F_c)
	(IV)	H(Me) 2.51 T	J(Me-F_o) 1.0(H) 0.4(F)
		F 96.0 Q	J(F-F) 1.4
	(V)	H(Me) 2.49 S	Intensity Ratio 1 : 1
		H(Me) 2.51 S	

TABLE 1 (continued)

Summary of N.M.R. Data

Compound		Chemical Shifts/p.p.m.			Coupling Constants/Hz
	(VI)	H(Me)	2.56	D	J(Me-F_o) 1.9(H) 1.8(F)
		F_a	130.3	M	J(F_a-F_b) 22.6(F_a) 22.6(F_b)
		F_b	127.0	D	J(F_a-F_c) 11.0(F_a) 11.0(F_c)
		F_c	97.8	D	J(F_b-F_c) ∿0
	(VII)	H(Me)	2.51		J(Me-F_o) 1.5(H) 1.5(F)
		F_a	96.1	M	J(F-F) 13.0(F_a) 13.0(F_b)
		F_b	93.8	D	
	(VIII)	H(Me)	2.467		J(Me-F_o) 0.8(H)
		F_a	97.29	D	J(F_a-F_b) 0(F_a) 0(F_b)
		F_b	117.94	M	J(F_a-F_c) 9.6(F_a) 9.5(F_c)
		F_c	151.95	M	J(F_a-F_d) 0(F_a) 0(F_d)
					J(F_b-F_c) 21.2(F_b) 21.5(F_c)
					J(F_b-F_d) 6.2(F_b) 6.3(F_d)
					J(F_c-F_d) 22.4(F_c) 22.4(F_d)
	(IX)	H(Me)	2.51	T	J(Me-F_o) 0.5(H)
		F	95.5	S	(½ peak width ∿4 Hz)

S = singlet

D = doublet

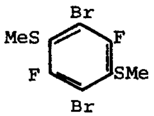
T = triplet

Q = quartet

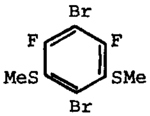
M = multiplet

$\underline{o}$-$(MeS)_2C_6F_4$ (II). The chemical shifts observed for the fluorine atoms were consistent with the literature values for analogous fluorine atoms [11,13].

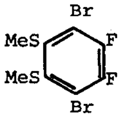
From the data available the structure of IX cannot be unambiguously assigned. The structures X and XI are also possible. The low fluorine-fluorine coupling constant would indicate F-F_m or F-F_p coupling, i.e. structures IX or



IX



X



XI

X. The origin of the splitting of the methyl proton into a quartet is unexplained. It is possible that a mixture of isomers was present that was not separated on TLC or GLC. The structure IX is probable. Previous experience has shown that the two fluorine atoms left on the ring in nucleophilic substitution of fluoroaromatics with the thiolate anion are always <u>para</u> to each other [11,13].

The infrared spectra of all the new compounds prepared have been examined. The spectra could not be used for structural determinations, but confirmed the presence of the various structural groups.

Similarly the identity of all the new products was confirmed by their mass spectra. In some cases products such as $C_6F_3HBrSMe$ (M/e 257) could be detected in the crude product from the reaction of $\underline{m}$-$Br_2C_6F_4$ with CuSMe, but could not be isolated. Some differences in the primary ion spectra of the isomers of $Br_2C_6F_2(SCH_3)_2$ were observed. The initial fragmentation of VII and IX showed loss of a methyl group, which was not observed in IV. Loss of bromine atoms occurred from the molecular ion in IV and IX but not from VII.

$$C_8H_6Br_2F_2S_2\rceil^{+\cdot} \rightarrow C_7H_3Br_2F_2S_2\rceil^{+} + CH_3^{\cdot} \qquad \text{(VII, IX)}$$

$$C_8H_6Br_2F_2S_2\rceil^{+\cdot} \rightarrow C_8H_6BrF_2S_2\rceil^{+} + Br^{\cdot} \qquad \text{(IV, IX)}$$

The primary ion spectra of the isomers of $Br_2C_6F_3SCH_3$, III and VI, were very similar.

EXPERIMENTAL

All the reagents were available commercially. Microanalyses were performed by Mikroanalytisches Laboratorium Beller, Göttingen, West Germany or the Butterworth Microanalytical Consultancy Ltd., Teddington, England. The analytical data and physical properties of the new compounds are shown in Table 2. Mass spectra (70 eV) were recorded on a Du Pont/C.E.C. Model 21-491 mass spectrometer using direct introduction techniques. NMR spectra were recorded in $CDC\ell_3$ solution using TMS or $CFC\ell_3$ as internal standards on a Varian A 56/60, HA 100 or XL 100. Infrared spectra were recorded on a Perkin Elmer model 457 spectrophotometer as thin films, as mulls with Nujol or hexachlorobutadiene, or as KBr discs.

TABLE 2

Reaction stoichiometry and products

Substrate	Molar Ratio $Br_2C_6F_4$: SMe^-	Solvent*	Major Products	Yield (%)	Purification†
o-$Br_2C_6F_4$	1 : 1	DMF	III	38	1,2
			IV	15	4,3
			V	11	4,3
	1 : 2	DMF	IV	20	4,3
			V	20	4,3
	1 : 2	P-E	IV	53	2
	1 : 5 CuSMe	DMF	I	23	1,2 or 5
			II	4	1,2 or 5
o-$I_2C_6F_4$	1 : 5 CuSMe	DMF	II	5	1,2
m-$Br_2C_6F_4$	1 : 1	DMF	VI	35	1,2
			VII	28	1,3
	1 : 2	DMF	VII	39	1
	1 : 2	P-E	VII	26	2
			VI	40	1
	1 : 5 CuSMe	DMF	X	32	1,2
p-$Br_2C_6F_4$	1 : 1	DMF	IX	12	1
	1 : 2	DMF	IX	21	1
			p-$Br_2C_6(SMe)_4$	3	1
	1 : 2	P-E	IX	83	2

* Solvent P-E = Pyridine-ethylene glycol

† Purification 1 = distillation
2 = gas chromatography
3 = TLC
4 = recrystallization
5 = sublimation

The experimental procedures followed using the thiolate anion as a nucleophilic have been described previously [1]. In those reactions using DMF the procedure was the same as that using ethyleneglycol-pyridine mixture [1]. Copper(I) methanethiolate was prepared by bubbling MeSH through an acetone solution of $Cu(OAc)_2$ and yellow CuSMe precipitated. The CuSMe was air dried and used immediately. In a typical experiment CuSMe (100 mmol) was refluxed with $Br_2C_6F_6$ (20 mmol) in 100 mL DMF for 24 h. The mixture was poured on an ice-acid mixture (250 mL 12 M HCl and 100 g of ice) and the product extracted with ether. Considerable difficulty was encountered in the separation of the reaction products. In some cases the crude products were cleaned up by column chromatography (silica gel) and finally separated by preparative gas chromatography (silicone rubber gum SE 30 column, He carrier gas). The latter technique was not suitable for non volatile compounds and thermally sensitive compounds. Details of the reactant stoichiometry and products are shown in Table 2 and analytical data in Table 3.

TABLE 3

Chemical analyses and physical properties of new compounds

Compound		m.p./°C or b.p./°C	Calculated (%)			Found (%)		
			C	H	S	C	H	S
$C_7H_4F_4S$	(I)	32-8/0.87 Torr	42.9	2.1	16.8	43.0	2.1	16.4
$C_8H_6F_4S_2$	(II)	58.3-58.9	39.7	2.5	26.5	39.6	2.5	26.4
$C_7H_3Br_2F_3S_2$	(III)	86-89/0.2 Torr	25.0	0.9	9.5	25.6	1.1	9.8
$C_8H_6Br_2F_2S_2$	(IV)	94.5-95.5	26.4	1.7	17.6	26.1	1.2	18.2
$C_{10}H_{12}Br_2S_4$	(V)	92.0-93.0	28.6	2.9		28.7	2.9	
$C_7H_3Br_2F_3S$	(VI)	120-122/10 Torr	25.0	0.9	9.5	25.0	1.0	9.6
$C_8H_6Br_2F_2S_2$	(VII)	123.0-124.0	26.4	1.7	17.6	26.1	1.2	17.7
$C_7H_3BrF_4S$	(VIII)	34-5/43 Torr	30.6	1.1	11.7	30.8	1.1	11.8
$C_8H_6Br_2F_2S_2$	(IX)	137.5-138.5	26.4	1.7	17.6	26.2	1.7	17.4

ACKNOWLEDGEMENTS

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