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THE THIOLATE ANION AS A NUCLEOPHILE

PART IX*. REACTIONS OF SOME FLUOROAROMATICS

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SUMMARY

The reactions of some halogenoaromatic compounds, mainly fluoroaromatics $C_6F_xH_{6-x}$ with the methanethiolate anion have been studied in DMF or an HMPA/THF mixture. Complete replacement of fluorine occurred forming $C_6(SMe)_xH_{6-x}$. Attempts to prepare $C_6(SET)_6$ and compounds such as $C_6(SET)_2(SMe)_4$ are described. Other new compounds isolated include $C_6(SMe)_5SH$ and $C_6F_2(SMe)_2(SET)_2$. Details of the spectra, particularly NMR, are given.

INTRODUCTION

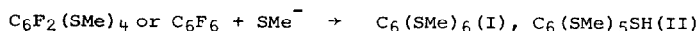
In previous parts of this series it has been found that in the reactions of the halogenated benzenes with the methanethiolate anion in ethylene glycol/pyridine mixture (volume ratio approximately 1:2) as solvent at least two halogen atoms usually remained on the aromatic ring and compounds such as $C_6(SMe)_4Hal_2$ (Hal = F, Cl, Br) have been isolated [2,3]. Only in the reaction of hexachlorobenzene could $C_6(SMe)_6$ be obtained by increasing the reaction time. In other solvent systems, such as HMPA/THF replacement of the fluorine atom in fluorobenzene by the SBU occurred [4]. The reactions of the fully halogenated benzenes, and other halogenated benzenes, were studied in solvent systems such as HMPA/THF and DMF to try and achieve complete replacement of the aromatic halogen atoms. These solvents are more polar than the ethylene glycol/pyridine mixture. Attempts were made to prepare mixed fully substituted thioethers, such as $p-(RS)_2C_6(SR')_4$, and hexakis(ethylthio)benzene, $C_6(SET)_6$.

*For Part VIII, see ref. 1

RESULTS AND DISCUSSION

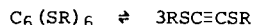
Hexakis(methylthio)benzene has very recently been prepared in excellent yields by the room temperature reaction of lithium methanethiolate in DMF with 1,3,4,5-tetrachloro-2,6-dinitrobenzene, 1,2,3,4-tetrachloro-5,6-dinitrobenzene, pentachloronitrobenzene or hexachlorobenzene [5]. It has also been obtained by the pyrolysis of cis $[\text{Cr}(\text{Co})_4\text{L}_3] \text{L}_3 =$ trimerized $\text{MeSC}\equiv\text{CSMe}$ (initially employed as ligand [6]). Hexakis(ethylthio)benzene has been reported in a patent, but no specific reaction conditions or physical properties of the product are given [7]. The reaction probably occurred in 2,4-lutidine as a solvent, using hexabromobenzene, sodium ethanethiolate and copper(I) bromide. Hexakis(phenylthio)benzene has been prepared from hexachloro- or hexabromobenzene and copper(I) thiophenolate [8]. The biphenyl compound $\text{C}_{12}(\text{SR})_{10}$ has also recently been prepared from $\text{C}_{12}\text{F}_{10}$ and the corresponding thiol in DMF containing potassium carbonate [9].

It has been found that it is possible to prepare $\text{C}_6(\text{SR})_6$ ($\text{R} = \text{Me}, \text{Et}$) from hexafluoro- or hexachlorobenzene or bis(methylthio)tetrafluorobenzene and the thiolate anion in HMPA/THF or DMF as solvent. If an excess of the methanethiolate nucleophile was employed some demethylation occurred and $\text{C}_6(\text{SMe})_5\text{SH}$ formed. The starting materials must be pure, particularly



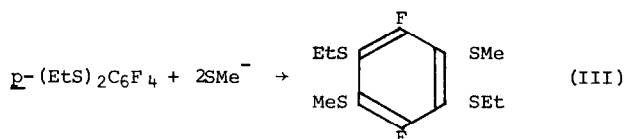
hexachlorobenzene. The mass spectrum of the crude reaction product from the hexachlorobenzene reaction showed clearly the presence of $\text{C}_6(\text{SMe})_5\text{Cl}$, but all attempts to isolate this failed and it presumably rearranged to $\text{C}_6(\text{SMe})_6$ and $\text{C}_6(\text{SMe})_4\text{Cl}_2$. Complete replacement of the chlorine atoms in C_6Cl_6 with SMe also occurred in the ethylene glycol/pyridine solvent if the reaction time was increased. The use of hexakis(methylthio)benzene(I) and various of aromatic ortho-bis(methylthio)ethers as chelating ligand has been studied [10].

The ethyl derivative $\text{C}_6(\text{SEt})_6$ could be detected in solution from its proton NMR spectrum. All attempts to isolate this showed that it was probably thermally unstable and the presence of an alkyne group was indicated in the infrared spectrum. This suggests that some sort of equilibrium may have been established



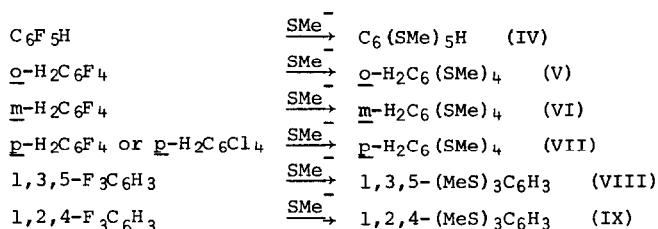
The alkyne compounds $RSC\equiv CSR$ are well known, and some reactions of the ethyl derivative $EtSC\equiv CSEt$ have been studied [11,12,13], although this could not be isolated in the attempted preparation of $C_6(SET)_6$.

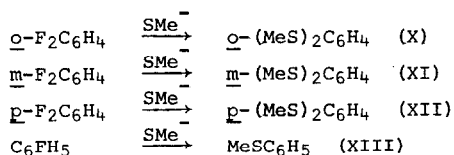
As an extension of these reactions the possibility of forming the mixed derivatives $C_6(SR)_2(SR')_4$ has been examined. The compounds $p\text{-}F_2C_6(SR)_4$ and $p\text{-}(RS)_2C_6F_4$ ($R = Me, Et$) are well known [2] and the reactions of these with corresponding thiolate anion were examined, i.e. $p\text{-}F_2C_6(SR)_4 + SR'^-$ and $p\text{-}(RS)_2C_6F_4 + SR'^-$. In these reactions it was not possible to prepare either $C_6(SMe)_4(SET)_2$ or $C_6(SMe)_2(SET)_4$. The reaction of $p\text{-}(EtS)_2C_6F_4$ with the methanethiolate anion gave $F_2C_6(SMe)_2(SET)_2$ rather than $C_6(SET)_2(SMe)_4$. By analogy with previous work the structure has been postulated as III [2.14].



The analogous compound $F_2C_6(SMe)_2(SPh)_2$ has been prepared from $F_4C_6(SMe)_2$ and the thiophenolate anion or $F_4C_6(SPh)_2$ and the methanethiolate anion [14]. In the reaction of $F_2C_6(SMe)_4$ with the ethanethiolate anion the NMR spectrum of the product while still in solution indicated the presence of $C_6(SET)_2(SMe)_4$, but this could not be isolated. These products appear to be somewhat thermally unstable at around room temperature.

As a continuation of these studies the reactions of various other fluorinated and some chlorinated benzenes with the methanethiolate anion in DMF have been examined. Complete replacement of the halogen occurred, whereas in ethylene glycol/pyridine mixture two fluorine atoms were not substituted [15]. These reactions can be summarized:





Some of the compounds have been prepared previously by other methods.

Thioanisole is well known, as are the ortho- meta- and para-bis (methylthio) benzenes and 1,3,5-tris(methylthio)benzene [16,17,18,19], although these have often been prepared by methylation of the parent thiol. Pentakis(methylthio)benzene has prepared from lithium methanethiolate and 1,3,5-trichloro-2,6-dinitrobenzene in DMF [5], whereas it was prepared from pentafluorobenzene and sodium methanethiolate in the present work.

The present method starting from the commercially available fluorobenzenes is an excellent method for preparing these methylthio ethers in a one step reaction.

The proton NMR spectra, infrared spectra and mass spectra of all the compounds isolated have been examined. The mass spectra were not studied in detail, but all confirmed the expected molecular weights of the products. Similarly the infrared spectra confirmed the presence of various functional groups.

The proton NMR spectra cannot always be used for unequivocal structural assignments, but assuming that no rearrangements had occurred during the reactions these spectra are consistent with the expected structures. In several cases the aromatic hydrogen spectra are complex, due to overlapping of the spectra of different hydrogens and some of the spectra being second order. Details of the NMR spectra are shown in Table 1. The structure III, $\text{p-F}_2\text{C}_6(\text{SMe})_2(\text{SEt})_2$, has been deduced from the 19-F and proton spectra. In $\text{p-F}_2\text{C}_6(\text{SMe})_4$, $\text{p-F}_2\text{C}_6(\text{SMe})_2(\text{SPh})_2$ and other similar compounds a singlet is observed in the fluorine NMR spectrum around 100 Hz and the SMe group is split into a triplet by coupling to fluorine [14].

TABLE 1

Proton NMR spectra*

Compound	Chemical shift/ppm and coupling constants/Hz
$C_6(SMe)_6$ (I)	2.25S 13-C 21.114S (Me), 146.851S (Ar)
$C_6(SMe)_5SH$ (II)	2.57S, 2.51S, 2.48S (intensity ratio 2:1:2) 6.77S (S-H)
$C_6(SET)_6^+$	1.15T (Me) J(H-H) 7.3 2.92Q (-CH ₂ -) J(H-H) 7.3
<u>p</u> - $(EtS)_2C_6(SMe)_4^+$	1.03T, 2.83Q (SEt) J(H-H) 7.0 Hz 2.41 (SMe) (intensity ratio Et:Me, 1:2)
$C_6(SMe)_2(SET)_2F_2$ (III)	3.00Q (-CH ₂ -) J(H-H) 7.5 F-19 99.96S 2.51T (SMe) J(H-Fo) 1.05 1.25T (CH ₃) J(H-H) 7.5
$C_6(SMe)_5H$ (IV)	2.42S, 2.45S, 2.54S (Me) (intensity ratio 2:2:1) 6.75S (ArH)
<u>o</u> - $H_2C_6(SMe)_4$ (V)	2.40S, 2.43S (Me) (intensity ratio 1:1) 7.06S (ArH)
<u>m</u> - $H_2C_6(SMe)_4$ (VI)	2.31S, 2.41S, 2.50S (Me) (intensity ratio 1:2:1) 6.70S (ArH)
<u>p</u> - $H_2C_6(SMe)_4$ (VII)	2.46S (Me) 7.09S (ArH)
1,3,5-(MeS) ₃ C ₆ H ₃ (VIII)	2.47S (Me) 6.88S (ArH)
1,2,4-(MeS) ₃ C ₆ H ₃ (IX)	2.44S, 2.47S, 2.48S (Me) (intensity ratio 1:1:1) 7.12M (ArH)
<u>o</u> -(MeS) ₂ C ₆ H ₄ (X)	2.42S (Me) 7.14M (ArH)
<u>m</u> -(MeS) ₂ C ₆ H ₄ (XI)	2.45S (Me) 7.06M (ArH)
<u>p</u> -(MeS) ₂ C ₆ H ₄ (XII)	2.44S (Me) 7.18S (ArH)
$C_6H_5(SMe)$ (XIII)	2.42S (Me) 7.16M (ArH)

*Measured in CDCl₃ solution with TMS as internal standard, or CCl₄,
CFCl₃ as internal standard for F-19

†Recorded in CCl₄ on a Perkin Elmer R24

s = Singlet, T = Triplet, Q = Quartet, M = Multiplet

EXPERIMENTAL

All the reagents were available commercially. Microanalyses were performed by Mikroanalytisches Laboratorium Beller, Göttingen, West Germany or the Butterworth Laboratories 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 on a Varian HA 100 (H-1 or F-19) or XL 100 (C-13). In the H and C-13 spectra CDCl_3 solutions were used with TMS as internal standard while the F-19 spectrum was recorded in CCl_4 , CFCl_3 solution using CFCl_3 as the internal standard. 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

Chemical analyses and physical properties of compounds isolated

Compound	M.p./°C	Calculated (%)			Found (%)			Yield (%)
		C	H	S	C	H	S	
$\text{C}_6(\text{SMe})_5\text{SH}$ (II)	93-94	38.8	4.7	56.5	38.8	4.8	56.6	50
$\text{C}_6(\text{SMe})_2(\text{SEt})_2\text{F}_2$ (III)	35-37	43.7	4.3	38.9	44.2	4.8	39.3	40
<i>o</i> - $\text{H}_2\text{C}_6(\text{SMe})_4$ (V)	104-06	45.8	5.4	48.9	45.6	5.3	48.4	54
<i>m</i> - $\text{H}_2\text{C}_6(\text{SMe})_4$ (VI)	129-30	45.8	5.4	48.9	45.6	5.3	48.7	29
<i>p</i> - $\text{H}_2\text{C}_6(\text{SMe})_4$ (VII)	124-26	45.8	5.4	48.9	45.8	5.4	48.9	45
1,2,4-(MeS) $_3\text{C}_6\text{H}_3$ (IX)	53-54	50.0	5.6	44.5	49.8	5.8	43.7	4

$\text{C}_6(\text{SMe})_6$ (I): 100 mmoles Na were dissolved in 250 mL DMF and MeSH added until it had all reacted. 15 mmoles C_6Cl_6 in 100 mL DMF was refluxed for 15 min and then added to the MeSH solution, which was refluxed for 0.5 h. After quenching on ice-acid the product was filtered off and recrystallized from EtOH. The mass spectrum of the crude product showed the presence of $\text{ClC}_6(\text{SMe})_5$, but this could not be isolated, decomposing to $\text{C}_6(\text{SMe})_6$ and $\text{Cl}_2\text{C}_6(\text{SMe})_4$. C_6F_6 could be used instead of C_6Cl_6 . 10 mmoles C_6F_6 in 5 mL HMPA and 5 mL THF was mixed with 10 mL THF containing an excess of MeSH and 66 mmoles Na and refluxed for 1.5 h. Yield of $\text{C}_6(\text{SMe})_6$ 97%. Similarly using a large excess of SMe^- with C_6Cl_6 in ethylene glycol/pyridine and an extended reaction time enabled $\text{C}_6(\text{SMe})_6$

to be prepared. M.p. 87-89°, lit. m.p. 88-90° [5]. Thermal gravimetric studies indicated that $C_6(SMe)_6$ was stable to >250°.

$C_6(SMe)_5SH(II)$: 5 mmoles $p-F_2C_6(SMe)_4$ (preparation ref. 2) were dissolved in 7.5 mL HMPA and 4.5 mL THF and added to a solution of 10 mmoles Na in 16.5 mL THF to which a considerable excess of MeSH had been added. The mixture was refluxed for 1 h, and then treated as for $C_6(SMe)_6$. $C_6(SMe)_5SH$ was isolated. Yield ~ 50%. The IR spectrum showed an S-H band at 2465 cm^{-1} .

$C_6(SET)_6$: 15 mmoles C_6Cl_6 were dissolved in 100 mL DMF and refluxed for 15 min. A solution of 10 mmoles Na and 100 mmoles of EtSH in 250 mL DMF was added and the mixture refluxed for 10 min. The mixture was quenched on ice-acid and extracted with Et_2O . TLC showed three components in the product. Distillation gave a yellow product b.p. 180-185°/0.003 mm which still showed three spots on TLC. The components were separated on a 40-140 mesh silica gel column using hexane as eluant. The third component was $C_6(SET)_6$, forming a solid, which decomposed to a tar within 12 h. The mass spectrum of the crude product clearly indicated the presence of $Cl_2C_6(SET)_4$. Similarly using C_6F_6 and HMPA/THF solvent mixture the only pure product isolated was $p-F_2C_6(SET)_4$, identified, inter alia, from its infrared spectrum.

$C_6(SMe)_2(SET)_2F_2(III)$: 6.5 mmoles $p-(EtS)_2C_6F_4$ in 7 mL HMPA and 7 mL THF was added to ~ 5 mmoles Na in 10 mL THF to which MeSH had been added and the mixture treated as in the preparation of $C_6(SMe)_6$. The main product was $C_6(SMe)_2(SET)_2F_2$, but the proton NMR spectrum of a second product, which was not studied further, showed it to be a complex mixture.

All the other products were obtained by methods analogous to that for $C_6(SMe)_6$, starting from the corresponding fluoroaromatic using DMF as the solvent. When $p-H_2C_6Cl_4$ was employed as the starting material the reaction was suited in the ethylene glycol/pyridine solvent system. Details of the yields are shown in Table 2.

The known products isolated were identified in most cases by chemical analysis and comparison of physical properties: $C(SMe)_5H(IV)$ m.p. 103-104.5°, lit. m.p. 103-05° [5], yield 48%; $o-(MeS)_2C_6H_4(X)$, m.p. 25-27°, lit. m.p. approx. room temp. [16], yield 61%; $m-(MeS)_2C_6H_4(XI)$, b.p. 21.5°/1 mm, lit. b.p. 149°/17 mm [17], yield 20%; $p-(MeS)_2C_6H_4(XII)$, m.p. 83-84.5°, lit. m.p. 85° [18], yield 12%; 1,3,5-(MeS) $_3C_6H_3(XIII)$, m.p. 61-63°, lit. m.p. 66-68° [19]; yield 37%; $C_6H_5SMe(XIII)$, b.p. 192°, lit. b.p. 193° [20], yield 44%.

In the reaction of $p\text{-F}_2\text{C}_6(\text{SMe})_4$ (preparation ref. 2) with EtS^- (1:1 molar ratio) in EMPA/THF , the TLC of the crude product showed 2 products. The NMR spectrum, taken immediately, was consistent with $\text{C}_6(\text{SMe})_4(\text{SEt})_2$, but this could not be isolated. Similar inconclusive results were obtained in the reactions of $p\text{-(EtS)}_2\text{C}_6\text{F}_4$ [2] and SMe^- in DMF, $p\text{-F}_2\text{C}_6(\text{SMe})_4$ and SPh^- .

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