Tetrahedron. Vol. 28, pp. 105–109. Pergamon Press 1972. Printed in Great Britain

AROMATIC POLYFLUORO-COMPOUNDS—LIII[1]

REACTIONS OF POLYFLUOROARENES WITH THIOUREAS

P. L. COE,* N. E. MILNER and J. C. TATLOW
Chemistry Department, University of Birmingham, P.O. Box 363, Birmingham. B15 2TT

and

R. T. WRAGG
Dunlop Research Centre, Kingsbury Road, Birmingham

(*Received in the UK* 4 *August* 1971; *Accepted for publication* 16 *September* 1971)

Abstract—Thioureas react with activated arylfluoroides to give the corresponding diaryl sulphides. Octafluorotoluene, pentafluoronitrobenzene and 2,3,4,5-tetrafluoronitrobenzene afforded diaryl sulphides substituted *para* to the activating groups in good yield, whilst decafluoro-*o*-xylene, with two molecules of thiourea, gave 1,4,6,9-tetrafluoro-2,3,7,8-tetrakis(trifluoromethyl)thianthren. No reaction was observed with hexafluorobenzene, pentafluorobenzene, bromopentafluorobenzene and pentafluorostyrene. Studies of the reaction with dialkyl thioureas gave an insight into the possible reaction mechanism.

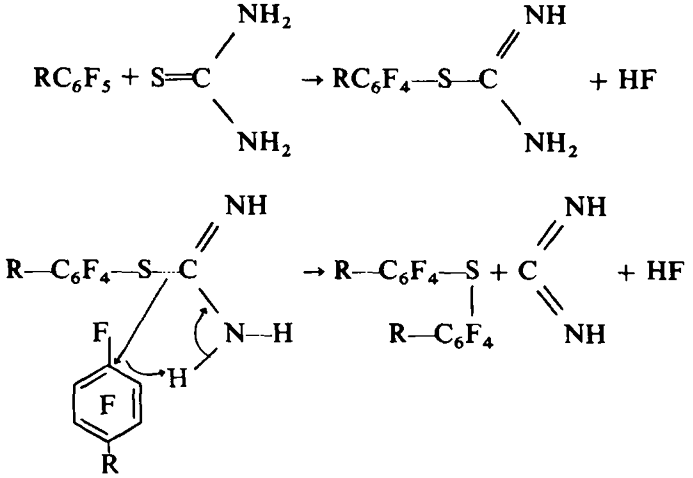
THE preparation of polyfluorodiaryl sulphides has been a difficult problem, conventional methods often leading to disulphide or polymer formation.[2] Methods using cuprous thiophenoxides[3] and reactions of sulphur with polyfluorodiaryl mercurials[4] are available but have limited use. Complementary to these processes, we now report a simple one-step reaction to sulphides derived from polyfluoroarenes containing groups which activate these compounds to nucleophilic substitution.

Although many reactions of alkyl halides with thiourea are known, there are few reports of aryl halides being involved in such processes. We have found that activated aryl polyfluorides react under mild conditions with thiourea in DMF. Thus, octafluorotoluene, pentafluoronitrobenzene and 2,3,4,5-tetrafluoronitrobenzene give fairly good yields of the corresponding diaryl sulphides having sulphur substituted *para* to the activating groups. The structures of these compounds were indicated by NMR spectroscopy, mass spectrometry, elemental analysis and comparison of IR spectra with compounds prepared by other routes.[5]

Decafluoro-*o*-xylene gave a product which had a very simple ^{19}F NMR spectrum indicating that the product was probably symmetrical and that CF_3-groups and F atoms were present in the ratio of 1:1. Mass spectrometry showed the product to contain two S atoms by isotope ratios and gave a parent ion peak at m/e 560. These data, along with elemental analysis, suggest the product to be 1,4,6,9-tetrafluoro-2,3,7,8-tetrakis(trifluoromethyl) thianthren, which is expected on the basis of previous work on nucleophilic substitution in this xylene.[6]

No reaction was observed between thiourea and hexafluorobenzene, pentafluorobenzene, bromopentafluorobenzene or pentafluorostyrene. Perfluoro-*m*-xylene and tetrafluoro-*o*-dinitrobenzene afforded only polymeric material under a variety of conditions, presumably due to substitution both *o*- and *p*- to the activating groups.

The mechanism of the reaction is interesting. Since most reactions of thiourea with halides appear to pass through isothiouronium salts, we looked (unsuccessfully) for such intermediates. Alternatively, base hydrolysis of this salt would yield a thiol which itself could attack the polyfluoroaromatic. In fact, the thiol derived from octafluorotoluene will react with more octafluorotoluene to give the sulphide, but only slowly and not in very good yield. Further, fairly strong base is usually needed to perform the hydrolysis and DMF itself is only a relatively weak base. This suggests that the isothiouronium derivative itself may be acting as a nucleophile without first being hydrolysed. Thus a possible mechanism could be:



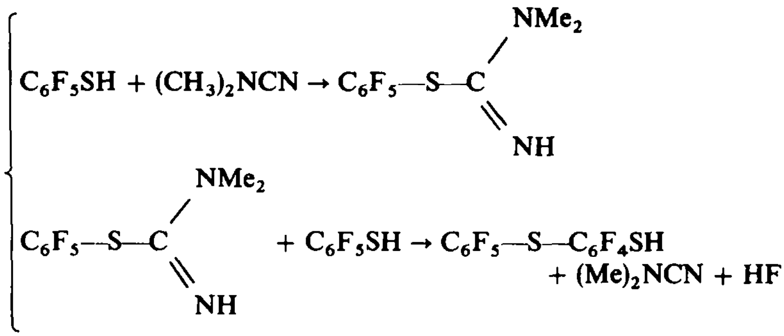
$$NH{=}C{=}NH \rightarrow NH_2CN \rightarrow \text{polymers of cyanamide}$$

The reactions of octafluorotoluene with NN′-dialkyl (alkyl = n-butyl, t-butyl, and dicyclohexyl), NN-dimethyl, and N-methylthioureas gave support to this idea. In each case bis(*p*-perfluorotolyl)sulphide was obtained. Examination of the mother liquors from the reactions involving NN′-dialkyl thioureas yielded carbodiimides (dialkylcarbo-diimides cannot rearrange to cyanamides), but N-methyl- and N,N-dimethylthiourea gave the corresponding cyanamides. These products correspond to the expected residues predicted by the above mechanism.

Further support comes from the reactions of polyfluoroaryl thiols with dimethyl cyanamide. Thus 4-trifluoromethyl tetrafluorothiophenol in DMF gives an intense yellow colour when the cyanamide is added, but on hydrolysis the colour is destroyed and the thiol recovered unchanged. If, however, the reaction is repeated using a mixture of the thiol and octafluorotoluene, the expected diaryl sulphide is obtained in good yield. Secondly, if a trace of dimethyl cyanamide is added to a solution of pentafluorothiophenol in DMF, rapid polymerisation to a polyaryl thioether occurs. Two mechanisms seem possible for this process:

$$(A)\begin{cases} C_6F_5SH + (CH_3)_2NCN \rightarrow C_6F_5S^- + (CH_3)_2\overset{+}{N}HCN \\ C_6F_5S^- + C_6F_5H \rightarrow C_6F_5{-}S{-}C_6F_4SH \rightarrow \text{polymer} \end{cases}$$

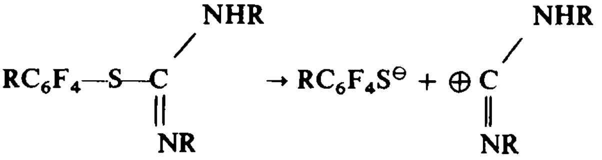
(B)



$$C_6F_5SH + (CH_3)_2NCN \rightarrow C_6F_5{-}S{-}C(NMe_2){=}NH$$

$$C_6F_5{-}S{-}C(NMe_2){=}NH + C_6F_5SH \rightarrow C_6F_5{-}S{-}C_6F_4SH + (Me)_2NCN + HF$$

In this, and in the proposed mechanism for diaryl sulphide formation, we cannot completely exclude dissociation of the isothiouronium salt, i.e.:



$$RC_6F_4{-}S{-}C(NHR){=}NR \rightarrow RC_6F_4S^{\ominus} + {}^{\oplus}C(NHR){=}NR$$

which corresponds to mechanism (A) above. We do not favour this idea since it requires cyanamides or carbodiimides to be relatively more basic than they appear to be. In support of this argument, it should be noted that under the same reaction conditions dimethylaniline only polymerises pentafluorothiophenol very slowly whereas triethylamine causes very rapid polymerisation, suggesting that here the formation of $C_6F_5S^-$ becomes the dominant process. This change in reaction follows the order of increasing basicity, i.e. triethylamine > dimethylaniline > dimethylcyanamide.[7]

We prefer therefore the postulate that an isothiouronium derivative is formed, probably reacting via the sulphur lone pair with expulsion of a carbodiimide as a good leaving group.

EXPERIMENTAL

Reaction of octafluorotoluene with thiourea

Octafluorotoluene (2·4 g), thiourea (3·1 g) and DMF (15 cm³) were heated and stirred together at 70° for 15 hr. The mixture was poured into water (100 cm³) and extracted with ether (3 × 50 cm³). The combined extracts were washed with water (3 × 100 cm³), dried ($MgSO_4$) and the ether distilled off. The pale yellow solid was semi-purified by sublimation (*ca* 120°) *in vacuo* to give crude product (1·8 g), crystallisation of which from aqueous EtOH afforded *4,4'-bis(trifluoromethyl)octafluorodiphenyl sulphide* (1·6 g), m.p. 74°. (Found: C, 35·75: F, 56·9. $C_{14}F_{14}S$ requires: C, 36·1: F, 57·1%).

Reaction of decafluoro-o-xylene with thiourea

Decafluoro-*o*-xylene (2·9 g), thiourea (1·6 g) and DMF (15 cm³) were heated and stirred together at 60° for 15 hr. After isolation as before, the pale yellow solid was semi-purified by sublimation (*ca* 130°) *in vacuo* to give crude product (2·6 g). Crystallisation from aqueous EtOH afforded *1,4,6,9-tetrafluoro-2,3,7,8-tetrakis-(trifluoromethyl)thianthren* (2·2 g), m.p. 112°. (Found: C, 34·6: H, 0·3: F, 54·0. $C_{16}F_{16}S_2$ requires: C, 34·3: H, 0·0: F, 54·3%).

When decafluoro-*m*-xylene (2·9 g), thiourea (1·6 g) and DMF (20 cm³) were stirred together at room temp for 15 hr, viscous oil (0·7 g) was obtained, sublimation of which *in vacuo* (120–170°) gave fractions becoming more viscous until a clear glass was obtained.

Reaction of pentafluoronitrobenzene with thiourea

Pentafluoronitrobenzene (2·2 g), thiourea (3·1 g) and DMF (15 cm^3) were stirred together at room temp for 1 hr. Extraction and sublimation (*ca* 160°) as before afforded crude product (1·6 g). Crystallisation from aqueous EtOH afforded *4,4'-dinitro-octafluorodiphenyl sulphide* (1·4 g), m.p. 94°. (Found: C, 34·3: H, 0·3: F, 36·6: N, 6·3. $C_{12}F_8N_2O_4S$ requires: C, 34·3: H, 0·0: F, 36·2: N, 6·66%).

When the reaction time was 15 hr, less product (0·2 g) was obtained together with an ether-insoluble polymer.

Reaction of 2,3,4,5-*tetrafluorobenzene with thiourea*

2,3,4,5-Tetrafluoronitrobenzene (2·0 g), thiourea (0·8 g) and DMF (15 cm^3) were stirred at room temp for 15 hr. Isolation as before afforded 3H,3'H-*4,4'-dinitrohexafluorodiphenyl sulphide*: (1·0 g from EtOH) m.p. 132°. (Found: C, 37·4: F, 29·8: N, 7·5. $C_{12}H_2F_6N_2O_4S$ requires: C, 37·5: F, 29·7: N, 7·3%).

Attempted reactions with thiourea

(a) o-*Dinitrotetrafluorobenzene. o*-Dinitrotetrafluorobenzene (2·0 g), thiourea (3·1 g) (excess) and DMF (10 cm^3) after 15 min at 15° gave only polymeric material.

(b) *Pentafluorobenzene.* Pentafluorobenzene (3·4 g), thiourea (3·1 g) and DMF (15 cm^3) were heated and stirred at 70° for 15 hr. Virtually pure pentafluorobenzene (by IR) (2·8 g) was isolated. Repetition at 70° for 72 hr and also at 150° for 15 hr gave similar results.

(c) *Pentafluorostyrene.* Pentafluorostyrene (2·0 g), thiourea (3·1 g) and DMF (15 cm^3) were heated and stirred at 70° for 15 hr. Virtually pure pentafluorostyrene (by IR) (1·7 g) was isolated. Reaction at 70° for 72 hr gave a similar result.

Attempt to isolate a thiouronium salt intermediate

Thiourea (1·0 g) dissolved in DMF (10 cm^3) was heated and stirred at 70°. Octafluorotoluene (2·4 g) was continuously added over a period of 48 hr by means of a gravity-fed fine capillary nozzle. The mixture was poured into ether (100 cm^3) which was saturated with HCl. An oil separated which was, however, completely miscible with conc HCl (10 cm^3). The ether soln was washed with water (3 × 100 cm^3), dried ($MgSO_4$) and the ether distilled off to give crude product (1·8 g).

Further purification by sublimation (*ca* 110°) *in vacuo* afforded 4,4'-bis(trifluoromethyl)octafluorodiphenyl sulphide (1·6 g) identified by IR.

Reaction of substituted thioureas with octafluorotoluene

(1) N,N'-*dibutyl.* A soln of the thiourea (1·88 g) and octafluorotoluene (4·72 g) in DMF (10 cm^3) was heated under vacuum in a sealed tube at 80–85° for 20 hr. Removal of the solvent in a rotary evaporator afforded a semi-solid residue which, after crystallization from EtOH, gave bis(*p*-perfluorotolyl) sulphide (3·7 g) in colourless needles m.p. 69–70°. (Found: C, 36·0: S, 9·1. Calc. for $C_{14}F_{14}S$: C, 36·1: S, 8·7%).

The distillate from the rotary evaporator and the EtOH used for crystallization were combined, poured into water and the organic layer extracted with ether. The solvent was removed from the dried ($MgSO_4$) extracts to leave an oily residue. This was subjected to preparative gas chromatography (Pye 105 instrument using a 12' × $\frac{3}{8}$" Apiezon L column at 160°). From the numerous fractions which were isolated N,N'-dibutyl carbodiimide (<0·1 g) was obtained, the IR spectrum of which was identical with that of the authentic compound. A trace amount of n-butyl isothiocyanate was also isolated.

(2) N,N-*dimethyl.* N,N-dimethylthiourea (1·04 g) and octafluorotoluene (4·72 g) were reacted in DMF as described. Rotary evaporation of the reaction mixture yielded a viscous semi-solid product which, upon trituration with EtOH, afforded bis(*p*-perfluorotolyl) sulphide (75%) m.p. and mixed m.p. 69–70°. The distillate, together with the EtOH extracts, were poured into an excess of water to afford a heavy, sweet-smelling organic layer which was then extracted with ether and dried ($MgSO_4$).

Distillation afforded unchanged perfluorotoluene (0·4 g) and a small amount of residue which could not be purified. Examination of the IR spectrum of the residue revealed an absorption at 2212 cm^{-1} (– C≡N) in good agreement with that obtained from dimethylcyanamide (authentic sample).

(3) N-*Methyl.* N-methylthiourea (0·90 g, 1 equiv) and octafluorotoluene (4·72 g, 2·0 equiv) were reacted in DMF as previously described. Rotary evaporation of the reaction product afforded a solid product which yielded bis(*p*-perfluorotolyl)sulphide (3·7 g, 80%) on crystallization from EtOH. The distillates and solvents from crystallization were combined and poured into water. The organic layer was extracted with ether, dried ($MgSO_4$) and distilled to afford unchanged perfluorotoluene. The distillation residue could not be

further purified. The IR spectrum of the residue revealed bands at 2212 cm^{-1} ($-C{\equiv}N$), 3330 cm^{-1} ($-NH$) and 1639 cm^{-1} ($-C{=}N$) in broad agreement with those expected for methyl cyanamide or its polymerisation products ( ).

(4) N,N'-*di-t-butyl*.N,N'-di-t-butylthiourea (1·88 g) and octafluorotoluene (4·72 g) were reacted in dry DMF soln as previously described. The mixture was filtered in order to remove a small amount of t-butylamine hydrofluoride and then subjected to rotary evaporation. The solid residue was crystallized from EtOH to afford bis(*p*-perfluorotolyl) sulphide (1·0 g, 21%) in needles m.p. 69–70°. The distillate was poured into an excess of cold water and the organic layer was extracted with ether and dried ($MgSO_4$). The solvent was removed and the residue was subjected to preparative scale gas chromatography (Pye 105 instrument using a 12' × ⅜" Apiezon T column at 154°/120 ml/min N_2).

The major components were: (i) unchanged perfluorotoluene (2·2 g): (ii) t-butyl isothiocyanate (1·1 g): (iii) bis (t-butyl) carbodiimide (0·1 g): (iv) t-butylamino-*p*-perfluorotoluene (0·1 g). Component (ii) was identified through its IR spectrum and its reaction with t-butylamine to form di-t-butylthiourea. Component (iv) was identified by comparison of its IR spectrum with that of an authentic sample prepared by the reaction of t-butylamine and perfluorotoluene.

(5) N,N'-*dicyclohexyl*. N,N'-dicyclohexylthiourea (2·28 g) and octafluorotoluene (4·72 g) were reacted together in DMF. Removal of the solvent by rotary evaporation afforded a semi-solid residue. Trituration of the residue with ether afforded a yellow solution (A) and a crystalline solid (B–0·4 g). B could be recrystallized from EtOH to afford dicyclohexyl urea m.p. 230–232°, undepressed on admixture with an authentic sample. The solution (A) upon evaporation, afforded a solid (2·7 g) which could be crystallized from EtOH to afford bis(perfluorotolyl) sulphide (2·1 g) m.p. 69·70°. Evaporation of the filtrate yielded a mixture of dicyclohexyl thiourea (0·2 g, m.p. 160–162°) and dicyclhexyl carbodiimide (*ca* 0·2 g)—identified by its IR spectrum.

The distillate from the rotary evaporator was poured into water and the organic layer was extracted with ether and dried ($MgSO_4$). After removing the solvent, the small amount of residue was shown, by gas chromatography, to consist of unchanged octafluorotoluene, bis(perfluorotolyl) sulphide and cyclohexyl isothiocyanate.

Reaction of p-*trifluoromethyl perfluorothiophenol with dimethyl cyanamide*

When the thiophenol (0·2 g) was dissolved in dry DMF (2·0 ml) containing 1 drop of dimethylcyanamide a deep yellow colouration was formed. After standing at room temp for 24 hr the mixture was poured into water, destroying the yellow colouration. From the organic layer, *p*-trifluoromethyl perfluorothiophenol was recovered in almost quantitative yield.

Reaction of p-*trifluoromethyl perfluorothiophenol with octafluorotoluene*

The thiol (0·25 g) and octafluorotoluene (0·24 g) were dissolved in dry DMF (2·0 ml) containing dimethylcyanamide (1 drop). An orange-yellow colour was formed and after standing for 2 hr at room temp the pungent odour of the thiophenol was no longer apparent. After 24 hr the product was poured into an excess of cold water to afford a colourless ppt. This was filtered off and crystallized from EtOH to yield bis(*p*-perfluorotolyl) sulphide (0·4 g) m.p. 69–70°, identical with an authentic sample.

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