Aryne Chemistry. Part XVII.[1] The Reaction of Tetrahalogenobenzynes with Thioanisole

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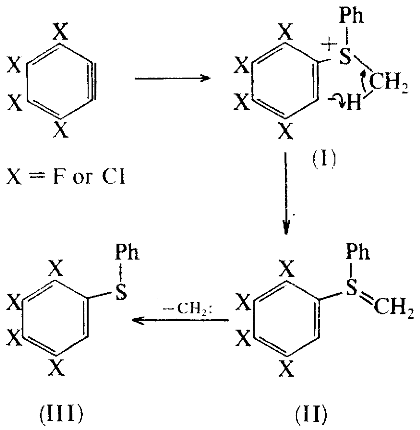
Tetrafluoro- and tetrachloro-benzyne react with thioanisole to yield 1,2,3,4-tetrahalogeno-5-phenylthiobenzenes (III) in 45 and 61% yield respectively. Labelling experiments show that intramolecular proton transfer occurs to give ylids (II) which break down to give the isolated products.

We have previously reported reactions of tetrachloro- and tetrafluoro-benzyne with aromatic compounds.[2] 1,4-Cycloaddition reactions occur in high yield with arenes including anisole. In view of these results, and the known cleavage of thioethers by benzyne,[3] we have studied the reactions of tetrachloro- and tetrafluoro-benzyne with thioanisole.

Pentafluorophenylmagnesium chloride, when heated with thioanisole, gave 1,2,3,4-tetrafluoro-5-phenylthiobenzene (III; X = F) (45%), identified by analysis and spectroscopy. A similar reaction occurred when tetrachloroanthranilic acid was added to 3-methylbutyl nitrite at 40° in the presence of thioanisole to give the tetrachloro-analogue (III; X = Cl) (61%).

The strongly nucleophilic character of sulphur apparently results in attack by lone-pair electrons on the sulphur on the aryne in preference to a cycloaddition reaction involving the benzene ring. Previous work[3] suggests the indicated mechanism.



When tetrachlorophthalic acid was added to the thioanisole in a repeat reaction with tetrachloroanthranilic acid we isolated dimethyl tetrachlorophthalate in addition to compound (III; X = Cl). This type of reaction of a sulphur ylid has been reported previously.[4] We therefore prepared [*Me*-^{3}H]thioanisole from diazomethane and thiophenol to which tritiated water had been added. This reaction is an extension of the known method for the deuteriation of anisole.[5] Reaction of tetrafluorobenzyne with the [^{3}H]thioanisole gave compound (III; X = F) with 7·39% of the activity of the labelled thioanisole. This value corresponds to an isotope effect of 4·5.

It remained to show whether the conversion of the intermediate betaine (I) into the ylid (II) proceeded by an inter- or an intra-molecular mechanism. We prepared [4-^{2}H]benzenethiol by the reaction of [4-^{2}H]-phenylmagnesium bromide with sulphur.[6] The reaction of potassium [4-^{2}H]benzenethiolate with [^{2}H$_3$]-methyl iodide in dimethyl sulphoxide[7] afforded [4-^{2}H]-phenyltrideuteriomethyl sulphide. A solution of pentafluorophenylmagnesium chloride when heated at 80° in the presence of an equimolar mixture of thioanisole and the tetradeuteriothioanisole gave compound (III; X = F) which was analysed by mass spectrometry. Comparison of the mass spectrum with that of the unlabelled compound (Table) showed that the proton-transfer step proceeds intramolecularly. The intensity values quoted were obtained from ion current measurements, and are the average of four readings normalised to 100%. The values calculated for an intramolecular mechanism were obtained by interpolation and assume that the molecular ion peak (M^+) in the labelled product does not arise in part by the loss of deuterium from the $M + 2$ ion. Apparently the two betaines produced do not form ylids equally easily, and this results in an apparent isotope effect of 1·6.

Mass spectral data

[ion]$^+$	(III) (%)	(III) (from labelling) (%)	Calc. (%)
$M - 2$	4·11	4·71	
$M - 1$	18·43	18·54	
M	100·0	100·0	100·0
$M + 1$	14·44	27·68	26·04
$M + 2$	5·20	67·73	67·73
$M + 3$		9·51	9·30
$M + 4$		3·36	3·45

The yield of (III, X = Cl) dropped to 15% when tetrachlorobenzyne was generated from pentachlorophenyllithium in the presence of thioanisole. This

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[2] (*a*) J. P. N. Brewer, I. F. Eckhard, H. Heaney, and B. A. Marples, *J. Chem. Soc.* (*C*), 1968, 664; (*b*) H. Heaney and J. M. Jablonski, *J. Chem. Soc.* (*C*), 1968, 1895.

[3] V. Franzen, H.-I. Joschek, and C. Mertz, *Annalen*, 1962, **654**, 82; H. Hellmann and D. Eberle, *Annalen*, 1963, **662**, 188.

[4] H. Metzger, H. König, and K. Seelert, *Tetrahedron Letters*, 1964, 867.

[5] K. J. van der Merwe, P. S. Steyn, and S. H. Eggers, *Tetrahedron Letters*, 1964, 3923.

[6] *E.g.* F. Taboury, *Compt. rend.*, 1904, **138**, 982.

[7] R. G. Gillis, *Tetrahedron Letters*, 1968, 1413.

agrees with the known stabilisation of sulphur ylids in the presence of organolithium compounds.[3]

EXPERIMENTAL

Reaction of Tetrafluorobenzyne with Thioanisole.—To a solution of pentafluorophenylmagnesium chloride [from chloropentafluorobenzene (10·1 g.)[2a]] was added thioanisole (62 g., 10 moles) and the ether was distilled off until the temperature of the vapour reached 80°. The mixture was then heated at 80° for a further 5 hr. and cooled, and 4N-hydrochloric acid (50 ml.), was added, followed by ether (100 ml.). The organic layer was washed with water and dried, and the solvent and excess of thioanisole were distilled off, finally under reduced pressure. Analytical g.l.c. showed the presence of only one major product in the residue. The crude product was placed on a column of alumina (75 g.) (activity I) and when eluted with light petroleum (b.p. 50—60°) gave 1,2,3,4-*tetrafluoro*-5-*phenylthiobenzene* (III; X = F) (5·8 g., 45%), m.p. 52° (from methanol), $\nu_{\text{max.}}$ 3062, 1641, 1582, 1510, 1478, and 1082 cm.$^{-1}$, τ 2·62 (5H, s) and 3·02—3·57 (1H, m) [Found C, 55·8; H, 2·45; F, 29·3%; *M* (mass spectroscopy), 258. $C_{12}H_6F_4S$ requires C, 55·8; H, 2·3; F, 29·45%; *M*, 258].

Reactions of Tetrachlorobenzyne with Thioanisole.—(a) *From pentachlorophenyllithium.* To an ethereal solution of pentachlorophenyllithium [from hexachlorobenzene (14·25 g.)[2b]] was added thioanisole (50 g.); the mixture was allowed to warm to room temperature and then heated under reflux (temperature of the mixture 55°) for 3·5 hr. Hydrolysis and work-up essentially as for the previous reaction gave 1,2,3,4-*tetrachloro*-5-*phenylthiobenzene* (III; X = Cl) (0·95 g., 15%), m.p. 90·5—91° (from ethanol), $\nu_{\text{max.}}$ 3096, 3070, 3050, 1555, 1520, 1470, 1442, 748, and 705 cm.$^{-1}$, τ 2·45 (5H, s) and 3·28 (1H, s) (Found: C, 44·6; H, 1·9. $C_{12}H_6Cl_4S$ requires C, 44·5; H, 1·85%).

(b) *From tetrachloroanthranilic acid.* A solution of tetrachloroanthranilic acid (13·8 g.) in dry acetone (50 ml.) was added during 1½ hr. to a stirred mixture of 3-methylbutyl nitrite (15 g.), thioanisole (50 g.), and dichloromethane (35 ml.), heated at 40° during the addition and for a further 1 hr. The mixture was set aside overnight and filtered to remove insoluble polymethylene (3·9 g.). The solvents, excess of thioanisole, and 3-methylbutanol were distilled off, finally under reduced pressure, and the residue was chromatographed on alumina (50 g.). Elution with light petroleum (b.p. 60—80°) gave compound (III; X = Cl) (61%), m.p. and mixed m.p. 90·5—91°.

(c) *From tetrachloroanthranilic acid in the presence of tetrachlorophthalic acid.* Tetrachlorophthalic acid (2 g.) was added to the reactants in a reaction similar to (b). Compound (III; X = Cl) (57%) was obtained, and further elution of the chromatogram with benzene gave dimethyl tetrachlorophthalate (2·3 g.), m.p. 92° (lit.,[8] 92°) (from ethanol) (Found: C, 36·5; H, 2·0. Calc. for $C_{10}H_6Cl_4O_4$: C, 36·2; H, 1·8%).

Preparation of Labelled Compounds.—*Phenyl* [^{3}H]*methyl sulphide.* Tritiated water (0·5 ml.; 100 mc) was added to benzenethiol (10 g.) in dry ether. Diazomethane (*ca.* 3 g.) in ether was then added. Normal work-up and dilution with inactive thioanisole gave, after three distillations, thioanisole with a constant activity (103·6 disintegrations sec.$^{-1}$ mmole^{-1}).

[4-^{2}H]*Phenyl* [^{2}H$_3$]*methyl sulphide.* [4-^{2}H]Benzenethiol was prepared (64%) by the reaction of sulphur with [4-^{2}H]-phenylmagnesium bromide. A reaction between potassium [4-^{2}H]benzenethiolate and [^{2}H$_3$]methyl iodide (1 mol.) gave [4-^{2}H]phenyl [^{2}H$_3$]methyl sulphide (92%) [100% $^2H_4$ by mass spectroscopy: *m/e* 130 (4·7), 129 (8·6), 128 (100), and 127 (8·15%)]. The mass spectrum of thioanisole showed *m/e*, 126 (4·65), 125 (8·6), 124 (100), and 123 (8·4%).

Reaction of Tetrafluorobenzyne with Tritiated Thioanisole.—With the above tritiated thioanisole this gave compound (III; X = F) which was recrystallised to constant activity (7·65 disintegrations sec.$^{-1}$ mmole^{-1}).

Reaction of Tetrafluorobenzyne with an Equimolar Mixture of Thioanisole and the Tetradeuteriothioanisole.—This gave a product which was analysed by mass spectroscopy (see Table).

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