Aromatic Polyfluoro-compounds. Part LIV.[1] Copper-assisted Nucleophilic Displacement Reactions of Pentafluorohalogenobenzenes

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Copper-assisted nucleophilic displacement reactions of pentafluorohalogenobenzenes have been investigated; in some cases exclusive halogen replacement occurs, and in others fluorine displacement and halogen reduction are observed. The effects of solvent and added ligands, notably thiourea, on the course of the reaction have been studied and a theory developed to explain the results observed.

THERE has been considerable recent interest in reactions involving copper(I) derivatives in general organic synthesis.[2] Further, the Ullmann reaction [3] and related processes involving olefins [4] are valuable in fluorocarbon chemistry. Some work concerning the displacement of halogen (*i.e.* other than fluorine) from halogenopolyfluorobenzenes has been reported, while the present study was in progress.[5] These results were obtained using dimethylformamide as solvent and led to exclusive halogen replacement. Apart from synthetic utility, we were interested in establishing the roles of solvents and of the various cuprous salts in these processes and,

and probably take place within the co-ordination sphere of the metal atom.

In the first series of experiments the effects of using various dipolar aprotic solvents on standard nucleophilic displacements, involving NaOMe and Me_2NH, of bromo- and iodo-pentafluorobenzenes, were investigated. The results obtained are shown in Tables 1 and 2. The reactions all resulted in exclusive fluorine replacement to give halogenotetrafluorophenyl derivative with isomer ratios essentially the same as those we have previously reported for reactions in alcoholic medi^ [7] Thus, we may conclude that variation of the solv

TABLE 1

Reactions of C_6F_5X with MeO^- to yield *o*- and *p*-$MeOC_6F_4X$

| | C_6F_5Br | | | | C_6F_5I | | | |
| | 20° | | 120° | | 20° | | 120° | |
Solvent/ substrate	% *ortho* Isomer	Yield %	% *ortho* Isomer	Yield %	% *ortho* Isomer	Yield %	% *ortho* Isomer	Yield %
DMF	12·5	73	20	65	5	75	11	63
NMP	10·5	65		55	5	70		
HMP	11	78	19	70	3	79		
Sulpholan	12·5	72	14·5	66	7	70		

TABLE 2

Reaction of C_6F_5X with Me_2NH to yield *o*- and *p*-$Me_2NC_6F_4X$

| | C_6F_5Br | | C_6F_5I | |
Solvent/substrate	% *ortho* Isomer	Yield %	% *ortho* Isomer	Yield %
DMF	2	70	0	80
NMP	2	65	0	73

further, to establish more precisely conditions for the replacement of halogen and/or of fluorine itself. The results reported by Bacon and Hill [6] suggest that in the case of halogenonaphthalenes particularly, cuprous derivatives are involved but that certain added species, *e.g.* pyridine, inhibit the reaction.

With these results in mind, we have investigated the effects of solvents and of the addition of thiourea on copper-assisted nucleophilic displacement (c.a.n.d.) reactions of pentafluorohalogenobenzenes, *i.e.* those reactions which take place under the influence of cuprous species

alone, whilst it may affect the rate of reaction, does not significantly alter the type of reaction which occurs.

In a second and third series of experiments cupric ions in the form of cupric acetate and cuprous ions in the form of cuprous bromide were added to similar reaction systems to those just described, the results of these experiments are shown in Table 3 and 4.

In the case of cupric acetate, a largely unchanged pattern of substitution to that described above was observed. Thus, cupric ions do not appear to affect the course of these reactions significantly.

In the case of cuprous bromide, however, there appeared to be another reaction taking place. When the

[1] Part LIII, P. L. Coe, N. E. Milner, J. C. Tatlow, and R. J. Wragg, submitted to *Tetrahedron.*

[2] R. D. Stephens and C. E. Castro, *J. Org. Chem.,* 1963, **28,** 3313.

[3] E. Nield, R. Stephens, and J. C. Tatlow, *J. Chem. Soc.,* 1959, 166.

[4] G. Cammaggi, S. F. Campbell, D. R. A. Perry, R. Stephens, and J. C. Tatlow, *Tetrahedron,* 1966, **22,** 1755.

[5] L. J. Belf, M. W. Buxton, and G. Fuller, *J. Chem. Soc.,* 1965, 3372.

[6] (*a*) R. G. R. Bacon and H. A. O. Hill, *J. Chem. Soc.,* 1964, 1097; (*b*) 1108; (*c*) 1112.

[7] J. Burdon, P. L. Coe, C. R. Marsh, and J. C. Tatlow, *Tetrahedron,* 1966, **22,** 1183.

nucleophile was methoxide ion the expected fluorine substitution occurred, but with dimethylamine this substitution was accompanied by reductive debromination, to yield 2,3,5,6- and 2,3,4,5-tetrafluorodimethylaminobenzenes as the isolated products. This suggested

cess. Subsequent to our experiments (some of our results are mentioned in ref. 8) a note has appeared [9a] describing this method of preparation pentafluorophenyl(phenyl)acetylene in rather poorer yield than we now report.

TABLE 3

Reaction of C_6F_5Br with (a) MeO⁻, (b) Me₂NH in the presence of cupric acetate to yield o- and p-MeOC₆F₄X and o- and p-Me₂NC₆F₄X

	Solvent									
	MeOH		Py		DMF		NMP		HMP	
Nucleophile	% ortho Isomer	% Yield	% ortho Isomer	% Yield	% ortho Isomer	% Yield	% ortho Isomer	% Yield	% ortho Isomer	% Yield
MeO⁻	10 [a]	95	7 [b]	75	21 [b]	80	20 [b]	73	14·5 [b]	75
Me₂NH			5 [c]	65						

[a] At boiling point of the solvent. [b] At 120°. [c] At 100°, sealed tube.

TABLE 4

Reaction of C_6F_5Br with MeO⁻ and Me₂NH in the presence of cuprous bromide to give o- and p-MeOC₆F₄Br and Me₂NC₆F₄H

	Solvent							
	MeOH		Py		DMF		MeCN	
Nucleophile	% ortho Isomer	% Yield	% ortho Isomer	% Yield	% ortho Isomer	% Yield	% ortho Isomer	% Yield
MeO⁻	13 [a]	75	8·5	63	19·5 [b]	70		
Me₂NH			20 [a]	63			19 [a]	58

[a] Sealed tube at 120°. The product was a mixture of 2,3,5,6-tetrafluorodimethylamino- and 2,3,4,5-tetrafluorodimethylaminobenzenes, i.e. reductive debromination occurred. [b] At the boiling point of the solvent.

that cuprous species play a major part in reactions in which they are present. The results obtained can be rationalised readily in the light of later work (see below). In a similar series of experiments, but using cuprous chloride, a complex mixture was obtained, which was not further investigated, but this can be explained in terms of exchange between chlorine and bromine.[5]

It appeared that cuprous species were important in the reactions, though probably not as ions, but as cuprous salts. Thus, CuBr–MeOH would not, under our reaction conditions, effect significant replacement of bromine by methoxy– in bromopentafluorobenzene, and it seemed necessary to prepare the actual cuprous derivatives to carry out each replacement. Thus, the reactions were copper assisted and not copper catalysed. The fine distinction between these modes of action of copper will be more fully discussed below.

In order to test these ideas various copper(I) derivatives were prepared and treated with pentafluorohalogenobenzenes.

A convenient copper(I) derivative to prepare was phenylethynyl copper(I) which with pentafluoroiodobenzene and 1,2,3,4-tetrafluoro-5,6-di-iodobenzene gave pentafluorophenyl(phenyl)acetylene and 1,2,3,4-tetrafluoro-5,6-bis(phenylethynyl)benzene respectively. It should be noted that phenylethynyl-lithium and hexafluorobenzene gave the 1,4-isomer of the last-named compound [8] a result typical of a simple nucleophilic pro-

Cuprous thiobutoxide was readily prepared and has been useful in illustrating some interesting solvent and ligand effects. It was used under a variety of conditions, in various solvents, and the results are shown in

TABLE 5

Reaction of C_6F_5Br with CuSBu in various solvents

Solvent	Volume (cm³)	Temperature °C	% Br substitution [a]	% F substitution [b]
DMF	25	120	100	0
Benzyl cyanide	25	200	90	10
NMP	50	185	72	28
† Quinoline/pyridine	25	170	50	50
† Quinoline/pyridine	50	170	30	70
† Quinoline/pyridine	150	170	25	75
Succinonitrile	10	200	13	87
DMF/3 eq thiourea	50	150	21	79
DMF/4 eq thiourea	50	110	0	100
DMAC/4 eq thiourea	50	110	0	100
NMP/4 eq thiourea	50	110	0	100
Pyridine/4 eq thiourea	50	110	0	100

[a] Product C_6F_5SBu. [b] Product $BuSC_6F_4H$.
† Quinoline–pyridine 10/1.

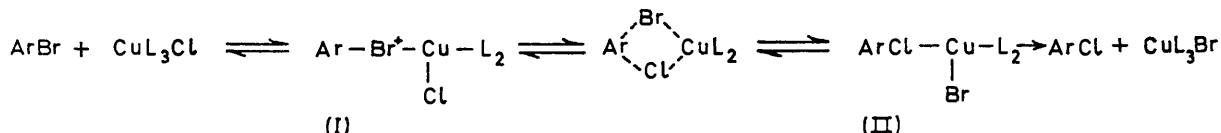Table 5. The reactions gave two products according to the scheme:

$$C_6F_5Br + CuSBu \longrightarrow C_6F_5SBu + BuSC_6F_4H$$
$$\quad\quad\quad\quad\quad\quad\quad\quad\quad A \quad\quad\quad B$$
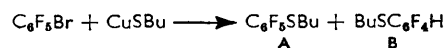
It can be seen from Table 5 that the product distribution

8 P. L. Coe, J. C. Tatlow, and R. C. Terrell, J. Chem. Soc. (C), 1967, 2626.

9 (a) M. D. Rausch, A. Siegel, and L. P. Klemann, J. Org. Chem., 1969, 34, 468; (b) R. Filler and E. W. Heffern, ibid., 1967, 32, 3249.

varies from exclusive bromine replacement (product A) (see ref. 5 also) when dimethylformamide (DMF) was the solvent to exclusive fluorine replacement and halogen reduction (product B) in experiments when thiourea was present; subsequently, it has been shown that under the reaction conditions thiourea alone does not react with bromopentafluorobenzene.[10] Product B was identified as n-butyl 2,3,5,6-tetrafluorophenyl sulphide with only trace amounts of other isomers. Both products (A and B) were further characterised by oxidation to sulphones.

Pentafluorobenzene was treated with cuprous thiobutoxide in *N*-methyl-2-pyrrolidone then in a similar

may be solvents, such as DMF, only halogen is replaced, a result quite different from the usual nucleophilic substitutions.[7] In the presence of strong ligands, however, it appears that ' normal ' nucleophilic species are formed (although they may still be associated in a copper complex) which cause replacement of fluorine. Any rationalisation of these results must account for these features. The reduction step may be separated from these effects and will be considered later.

A theory of c.a.n.d. reactions has been recently put forward by Bacon and Hill[6a] based on their own results and similar to an earlier idea of Castro.[2]

Bacon and Hill suggested the scheme shown below:

$$\text{ArBr} + \text{CuL}_3\text{Cl} \rightleftharpoons \text{Ar-Br}^+\text{-Cu-L}_2 \rightleftharpoons \text{Ar}\underset{\text{Cl}}{\overset{\text{Br}}{\diagdown}}\text{CuL}_2 \rightleftharpoons \text{ArCl-Cu-L}_2 \rightarrow \text{ArCl} + \text{CuL}_3\text{Br}$$

$$\underset{\text{(I)}}{\overset{\text{Cl}}{}} \qquad\qquad \underset{\text{(II)}}{\overset{\text{Br}}{}}$$

SCHEME 1

reaction with thiourea added. In the presence of thiourea, 4-substitution readily occurred to give product B above identical to that obtained from the reaction of sodium thiobutoxide and pentafluorobenzene. In the absence of thiourea only a small amount of reaction occurred with a reasonable recovery of pentafluorobenzene.

In similar experiments, but using chloropentafluorobenzene, no reaction occurred in the absence of thiourea, but when thiourea was added exclusive fluorine substitution occurred without chlorine reduction: a similar result was obtained using cuprous thiophenoxide as the attacking reagent. When the substrate was pentafluoroiodobenzene, cuprous thiophenoxide and thiourea caused rapid reduction and multiple fluorine displacement to occur, even at room temperature, the product being 2,4-difluoro-1,3,5-tris(thiophenoxy)benzene; pentafluorobenzene gave the same compound under essentially the same conditions.

Phenylcopper(I) was also treated with pentafluoroiodobenzene in pyridine to give a mixture of biphenyl and 2,3,4,5,6-pentafluorobiphenyl in amounts comparable to those obtained in a mixed Ullmann reaction. This result, although it may be significant in the mechanism of the Ullmann reaction, mainly suggests that even ligands like phenyl may be able to take part in c.a.n.d. reactions.

Attempted reactions using the *in situ* preparation of cuprous methoxide and cuprous phenoxide resulted in extensive bromine reduction and, in the case of the phenoxide, in a little fluorine substitution. This type of behaviour has recently been extensively studied in the hydrocarbon field and our results are in accord with those published.[11]

From the above results there seem to be two types of reaction occurring between fluorohalogenobenzenes and cuprous species, apart from reduction of halogen other than fluorine. In the presence of weak ligands, which
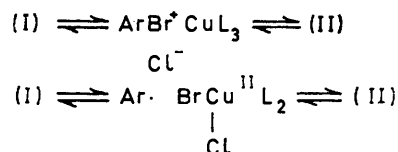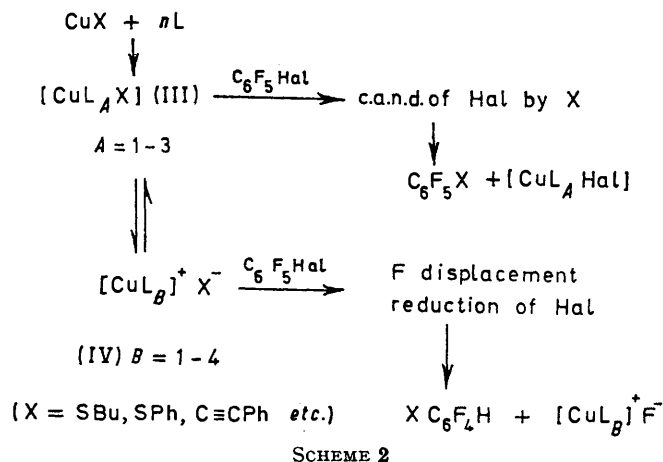
with the additional possibilities:

$$\text{(I)} \rightleftharpoons \text{ArBr}^+\text{CuL}_3 \rightleftharpoons \text{(II)}$$

$$\text{Cl}^-$$

$$\text{(I)} \rightleftharpoons \text{Ar}\cdot\text{ BrCu}^{\text{II}}\text{L}_2 \rightleftharpoons \text{(II)}$$

$$\text{Cl}$$

Although application of these ideas does not completely explain our results, we propose to use them as a framework, but with extensions, which we feel will both explain our results and overcome the problem found by Bacon and Hill[6a] of the effect of solvents such as pyridine on their reaction rates (such an effect cannot readily be accommodated by their basic premises).

In Scheme 2 is shown a possible situation of solvent/ ligand and cuprous species which could be obtained in our

$$\text{CuX} + n\text{L}$$

$$\downarrow$$

$$[\text{CuL}_A\text{X}] \text{ (III)} \xrightarrow{\text{C}_6\text{F}_5\text{Hal}} \text{c.a.n.d. of Hal by X}$$

$$A = 1-3 \qquad\qquad \downarrow$$

$$\updownarrow \qquad\qquad \text{C}_6\text{F}_5\text{X} + [\text{CuL}_A\text{Hal}]$$

$$[\text{CuL}_B]^+ \text{X}^- \xrightarrow{\text{C}_6\text{F}_5\text{Hal}} \text{F displacement reduction of Hal}$$

$$\text{(IV)} \; B = 1-4 \qquad\qquad \downarrow$$

$$\text{(X = SBu, SPh, C}\equiv\text{CPh } \textit{etc.)} \qquad \text{X C}_6\text{F}_4\text{H} + [\text{CuL}_B]^+\text{F}^-$$

SCHEME 2

system. In this scheme species (III) is designated as a contact ion-pair (*i.e.* X may not act independently of Cu^{I} and may still be strongly bonded to Cu^{I}) and species

[10] P. L. Coe, N. E. Milner, and J. C. Tatlow, submitted to *Tetrahedron*.

[11] R. G. R. Bacon and O. J. Stewart, *J. Chem. Soc.* (C), 1969, 301; R. G. R. Bacon and S. C. Rennison, *ibid.*, p. 312.

(IV) as a dissociated ion-pair in which X^- may act partly or wholly independently of the copper complex. The equilibrium constant of (III) $\rightleftharpoons$ (IV) will depend on the nature and quantity of the ligands present; there has been some evidence presented that such equilibra exist in copper complexes.[12] Thus, in our reactions one can envisage the presence of both (III) and (IV) in solution and the nature of the products obtained depends on the amount of each present. It is suggested that in the case where $L = DMF$, a weak ligand, a tetrahedral arrangement of ligands occurs, as is well documented in the literature [13] with X remaining co-ordinated to the copper atom. This species [(III) in the scheme] is then attacked by the stronger-bonding polyfluorohalogenobenzene with displacement of the weaker solvent ligand. This has the effect of weakening the Cu–X bond, since X now has less share of the d_π electrons of the copper atom and hence X is labilised. At the same time donation of one of the pairs of p electrons of the halogen tends to weaken the C–Hal bond thus making the carbon atoms slightly more positive; this facilitates attack of X on carbon leading, probably via a four-centre transition state, to exchange of X for halogen (see Scheme 3). It should be pointed

$$[CuL_3X] + ArHal \rightleftharpoons [CuL_2ArHalX]$$

$$ArX + [CuHal \cdot L_3] \longleftarrow [CuL_2ArXHal]$$
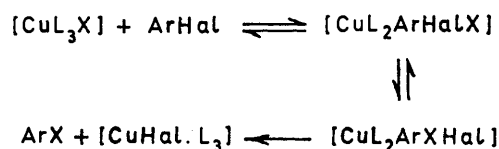
SCHEME 3

out here that this exchange can only take place by co-ordination to the copper of the substrate aryl halide and, as we have shown, it does not occur in the absence of copper(I). Thus, c.a.n.d. reactions basically consist of a competition between ligand displacements at the central metal copper(I) atom, the substrate displacing a solvent ligand in the first step (i.e. neutral vs. neutral ligand displacement) followed by a nucleophilic displacement of halide by X while the halide is co-ordinated to the cuprous ion; this results in the indirect exchange of halogen for X in the second step.

In the case when species (IV) predominates, i.e. when a strong ligand such as thiourea is present, a more complex situation arises since two sequences can occur. The fluoroaryl halide could first be substituted by the ' free ' X^- to give XC_6F_4Hal, i.e. fluorine replacement, and this product could then be reduced to give the compound isolated, namely (XC_6F_4H). Alternatively, reduction might precede the substitution stage. The sequence of these events is difficult to determine absolutely. If the first postulate is correct, i.e. that substitution occurs first, then it might have been expected that more ortho-substituted product would be formed, in accord with our earlier results,[7] unless X^- is not en-

tirely ' free ' and is, as is probably the case, in the co-ordination sphere of the copper(I) atom. The aryl halide might also be co-ordinated to the copper when it is substituted. These factors could well lead to altered orientations being observed. If the second sequence (i.e. reduction first) is correct, then the reactions of pentafluorobenzene with cuprous thiobutoxide in the presence and absence of thiourea are significant, since one might expect the usual pentafluorobenzene substitution pattern to be followed. To some extent this is true, but the rate of reaction of pentafluorobenzene with cuprous thiobutoxide in the absence of thiourea is rather slow (note that $NaSBu$ reacts at room temperature) to account for some of the results obtained with bromopentafluorobenzene and strong ligands. The absence of any 1,4-bis-(n-butyl)sulphide derivatives in all our experiments even when a large excess of $CuSBu$ is present does suggest that X^- is not entirely free, since if some $BuSC_6F_5$ were formed it would rapidly be attacked by BuS^-, as it has been shown that the RS group is quite activating towards nucleophilic substitution.[14] Further to this point, the absence of disubstituted products might lend support to the idea that any species capable of liganding to copper, e.g. $BrC_6F_5SC_4H_9$, is held out of solution so that any further attack might be prevented. This would be in accord with the formation of $BuSC_6F_4H$ and $BuSC_6F_4Cl$ from pentafluoro- and chloropentafluoro-benzenes in the $CuSBu$–thiourea system, since neither of the substrates are good ligands for Cu^I.

A possible alternative would be the formation of a copper compound which was then hydrolysed on the work up. To test this, reactions were carried out as before with bromopentafluorobenzene and cuprous thiobutoxide with addition in one case of iodine and in the second ease of deuterium oxide; in both reactions however only $BuSC_6F_4H$ was obtained.

The only certain conclusion about the order of the two reactions described above is that if substitution occurs first then the reduction must be very rapid; this follows from the complete absence of halogen-containing products.

The mechanism of the reduction is of interest. There have been several observations of such reductions [6] and recently possible mechanisms have been put forward.[11b] The first, and the one favoured by Bacon and Rennison, is a free-radical type using the copper as an electron transfer agent, and the second, which they discount, involves hydride transfer using the copper as a holding site for the reaction.

The fact that chloropentafluorobenzene reacts, with para-fluorine replacement, under conditions which normally lead to reduction, but with chlorine retention, leads us to suggest that co-ordination with the copper must be important, since bromo- and iodo-compounds,
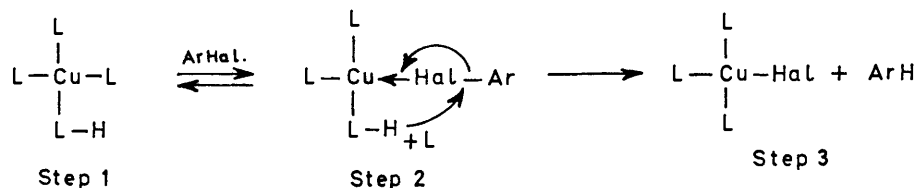
[12] V. Gutmann, Angew. Chem. Internat. Edn., 1967, 6, 271; F. A. Bolth, W. M. Whaley and E. B. Starkey, J. Amer. Chem. Soc., 1943, 65, 1456.

[13] W. I. O'Sullivan, F. W. Swamer, W. J. Humphlett, and C. R. Hauser, J. Org. Chem., 1961, 26, 2306.
[14] P. Robson, T. A. Smith, R. Stephens, and J. C. Tatlow, J. Chem. Soc., 1963, 3692.

which are stronger ligands, are apparently rapidly reduced. That reduction only occurs in the presence of strong ligands (*e.g.* thiourea, quinoline, and pyridine, which usually contain labile hydrogen) also strongly suggests that the reaction sphere of the copper is involved.

Accepting the view that the copper is involved then leads to the question of a free-radical *versus* an ionic mechanism. Our results give no definite evidence to support or reject either possibility except that if free radicals were involved some fluorobiphenyls might have been formed; none were, in fact, detected. If reduction does occur on the copper a feasible reaction scheme could be:

mixtures and by integration of the peak areas in ^{1}H and ^{19}F n.m.r. spectra. A similar set of experiments were carried out using pentafluoroiodobenzene.

The results of these experiments are shown in Tables 1 and 2 and are based on the average of duplicate experiments. They are expressed as percentages of *ortho*-isomer, the remainder in all cases being the *para*-derivative.

Reaction in the Presence of Added Cupric and Cuprous Ions.—The above reactions with C_6F_5Br were repeated but in one series cupric acetate was added and in the second cuprous bromide. The results (Tables 3 and 4) are expressed as percentages of *ortho*-isomer, the remainder being *para*.

Copper-assisted Nucleophilic Displacements.—(1) *Reaction of bromopentafluorobenzene with cuprous oxide–methanol.*

SCHEME 4

Such a mechanism, as was pointed out by Bacon,[11] would be in agreement with the more ready reduction observed in the presence of compounds with labile hydrogen atoms. It is suggested that co-ordination of the halogen with the copper labilises the Ar–Hal bond, thus facilitating the transfer of hydride ion, the whole process taking place under the influence of the central copper atom.

An objection to this idea is the replacement of a strong ligand, *e.g.* thiourea, by a weaker ArHal ligand. This may be overcome by the fact that whereas Step 1–Step 2 is reversible Step 2–Step 3 is irreversible since ArH once formed cannot now co-ordinate with the copper, thus pulling the reaction over to Step 3.

These results we feel demonstrate the usefulness of organo-copper compounds in synthesis, and the detailed studies on solvents illustrate the unusual nature of the reaction.

EXPERIMENTAL

Solvents.—Dimethylformamide (DMF), pyridine (Py), sulpholan, *N*-methyl-2-pyrrolidone (NMP), hexamethylphosphoramide (HMP), and dimethylacetamide (DMA) were purified and dried by standard procedures and stored over calcium hydride.

Nucleophilic Substitution in Dipolar Aprotic Solvents. General Procedure.—The nucleophile (3 mmol) in the dipolar aprotic solvent (4 cm^3) was added to a solution of bromopentafluorobenzene (1 g, 4 mmol) in the same solvent (10 cm^3) at room temperature. The mixture was stirred (30 min) and then poured into water (100 cm^3). The aqueous layer was extracted with ether (3 × 25 cm^3), and the combined ethereal extracts were dried (MgSO$_4$) and the solvents removed by evaporation. The residues were examined by g.l.c. and the isomer ratios determined by comparison of the peak heights with those of standard

A stirred suspension of cuprous oxide (10 g) and bromopentafluorobenzene (2·5 g) in methanol (5 cm^3) and DMF (20 cm^3) was heated at 120° for 24 h. Steam distillation of the reaction mixture yielded pentafluorobenzene (0·8 g, 45%) identified by comparison of i.r. spectra. No other products were isolated from the aqueous layer.

(2) *Reaction of bromopentafluorobenzene with cuprous oxide and phenol.* In a similar experiment to that above but using phenol (2 g) instead of methanol an oil (0·4 g) was obtained, which on distillation *in vacuo* afforded phenyl 3,5,6-*tetrafluorophenyl ether* (0·3 g), b.p. 125°/22 mmMg, m.p. 29—31° (Found: C, 59·6; H, 2·3. $C_{12}H_6F_4O$ requires C, 59·5; H, 2·5%).

Preparation of Pentafluorophenyl(phenyl)acetylene.—A suspension of phenylethynylcopper(I) (1·7 g) in dry pyridine (50 cm^3) and pentafluoroiodobenzene (3 g) were stirred at 15° under nitrogen for 6 h (the suspended solid slowly dissolved to give a red-brown solution after *ca.* 3 h). The reaction mixture was poured onto a concentrated hydrochloric acid–ice mixture (1 : 1) and the resulting mixture was steam distilled to give white crystals in the distillate. The condenser and distillate were washed with ether (3 × 50 cm^3). The combined washings were washed with 4N-sodium hydroxide and water, dried (MgSO$_4$), and the solvent evaporated to yield pentafluorophenyl(phenyl)-acetylene (1·7 g), m.p. 105—106° (cited ^{9b} 108·5—109·5°) (from light petroleum, b.p. 80—100°) (Found: C, 62·8; H, 2·1. Calc. for $C_{14}H_5F_5$: C, 62·7; H, 1·9%), $\lambda_{max.}$ (EtOH) 296 (ε 26,200), 279 (29,600), and 208 nm (17,700).

Preparation of 1,2,3,4-Tetrafluoro-5,6-bis(phenylethynyl)-benzene.—Phenylethynylcopper(I) 3·4 g and 1,2,3,4-tetrafluoro-5,6-di-iodobenzene (4 g) in dry pyridine (50 cm^3) were stirred at 70° for 10 h. The resulting red-brown solution was cooled and acidified with concentrated hydrochloric acid. The solids and aqueous layer were extracted with ether (3 × 50 cm^3) and the ether extracts dried (MgSO$_4$) and distilled to yield a brown solid; sublimation at 15 mmHg/120° and recrystallisation from light petroleum gave 1,2,3,4-tetrafluoro-5,6-bis(phenylethynyl)benzene (1·5

g), m.p. 104—105° (Found: C, 75·6; H, 2·7. $C_{22}H_{12}F_4$ requires C, 75·4; H, 2·9%). [19]F N.m.r. peaks at 135·4 and 155·1 p.p.m. (CCl$_3$F) comprising an A_2X_2 system (J_{AA}, 19·7 Hz; $J_{AX} = J_{A'X'}$, 21 Hz; $J_{AX'} = J_{A'X}$, 3·7 Hz; J_{AX}, 10·5 Hz); λ_{max} (EtOH) 312 (ε 22,600), 270 (47,100), 262 (17,800), and 215 mm (16,700).

Reaction of Bromopentafluorobenzene with Cuprous Thiobutoxide. Typical Reaction.—Bromopentafluorobenzene (5 g, 0·02 mol) and cuprous thiobutoxide (3 g, 0·02 mol) were heated in a mixture of dry quinoline and pyridine (25 cm³; 10 : 1) under an atmosphere of nitrogen. At 160° the suspended solid dissolved to give a red solution which was maintained at 160° for 5 h. The cool solution was poured onto concentrated hydrochloric acid–ice (1 : 1) and the product was steam distilled. Ether extraction of the distillate followed by evaporation of the ether gave an oil (2·3 g). Analytical g.l.c. showed two major peaks. Separation by preparative g.l.c. (silicone gum/Celite 1 : 3 20 ft × ⅜ in column (180°) gave (i) *n-butyl pentafluorophenyl sulphide* (1·2 g), b.p. 211—212°/760 mmHg (Found: C, 46·9; H, 3·7; S, 12·6. $C_{10}H_9F_5S$ requires C, 46·9; H, 3·5; S, 12·5%); (ii) *n-butyl 2,3,5,6-tetrafluorophenyl sulphide* (0·8 g), b.p. 222°/760 mmHg (Found: C, 50·2; H, 4·4; S, 14·1. $C_{10}H_{10}F_4S$ requires C, 50·4; H, 4·2; S, 14·1%). The former compound (i) (0·6 g) on oxidation with 90% hydrogen peroxide (2 cm³) in water (4 cm³) and glacial acetic acid (10 cm³) afforded *n-butyl pentafluorophenyl sulphone* (0·5 g), m.p. 55—56° (Found: C, 41·7; H, 3·3; S, 11·1. $C_{10}H_9F_5O_2S$ requires C, 41·7; H, 3·1; S, 11·4%). The latter sulphide (ii) on similar oxidation gave *n-butyl 2,3,5,6-tetrafluorophenyl sulphone* (0·4 g), m.p. 56—57° (Found: C, 44·1; H, 3·7; S, 12·2. $C_{10}H_{10}F_4O_2S$ requires C, 44·4; H, 4·0; S, 11·9%). [1]H and [19]F N.m.r. spectra were consistent with both these structures.

Similar reactions were carried out in other solvents and the products were estimated both by g.l.c. analysis of the mixture and by isolation of the products as described above. In all cases the yields were of the same order as in the above experiment.

In reactions when thiourea was added, a typical experiment was as follows: cuprous thiobutoxide (3·0 g, 0·02 mol) was heated with thiourea (6 g, 0·08 mol) in *N*-methyl-2-pyrrolidone (50 cm³) under nitrogen at 110°. Dissolution occurred and bromopentafluorobenzene (5 g, 0·02 mol) was added slowly; after further heating for 1·5 h the reaction mixture was worked up as above to yield n-butyl 2,3,5,6-tetrafluorophenyl sulphide (3·2 g) identical to an authentic sample, containing less than 0·5% of the *ortho*-isomer.

In a similar experiment but using more thiourea (12 g, 0·16 mol) there was obtained n-butyl 2,3,5,6-tetrafluorophenyl sulphide (2·9 g) with no other isolable products.

The results of a series of similar experiments carried out under various reaction conditions and in different solvents are shown in Table 5.

Reaction of Pentafluorobenzene with Sodium Thiobutoxide.—Sodium thiobutoxide (5·6 g) (from sodium hydride and butanethiol) and pentafluorobenzene (8·4 g) were stirred together at 15° for 12 h in NMP (50 cm³). The mixture was steam distilled and the distillate extracted with ether (3 × 25 cm³). The combined ether layers were dried (MgSO$_4$) and the ether removed to yield a malodorous oil which on distillation afforded n-butyl 2,3,5,6-tetrafluorophenyl sulphide (4·8 g), b.p. 223°, identical to an authentic sample.

Reaction of Cuprous Thiobutoxide with Pentafluoro-

benzene.—(a) *Alone.* Pentafluorobenzene (5 g) was heated at 135° in *N*-methyl-2-pyrrolidone (50 cm³) with cuprous thiobutoxide (4·5 g) for 2 h. Work-up as above revealed that little reaction had occurred and pentafluorobenzene (4·0 g) containing a trace of n-butyl 2,3,5,6-tetrafluorophenyl sulphide was recovered.

(b) *In the presence of thiourea.* Pentafluorobenzene (3·4 g) was heated with cuprous thiobutoxide (3 g) and thiourea (6 g) in NMP (60 cm³) at 130° for 2 h. Steam distillation and then vacuum distillation of the organic layer afforded n-butyl 2,3,5,6-tetrafluorophenyl sulphide (2·4 g) identical with an authentic sample.

Reaction of Cuprous Thiobutoxide with Chloropentafluorobenzene.—Chloropentafluorobenzene (5 g) cuprous thiobutoxide (4 g), and thiourea (8 g) were heated in NMP at 160° for 16 h. The colourless oil (3·1 g) obtained from the steam distillation showed two components by g.l.c. All attempts at separation failed. [19]F N.m.r. spectroscopy indicated a 90 : 10 mixture of *p*- and *o*-chlorotetrafluorophenyl n-butyl sulphides. Oxidation of the mixture from the reaction (3·1 g) as described above for n-butyl pentafluorophenyl sulphide gave *4-chloro-2,3,5,6-tetrafluorophenyl n-butyl sulphone* (2·2 g), m.p. 86—87° (Found: C, 39·2; H, 3·0; Cl, 11·6. $C_{10}H_9ClF_4O_2S$ requires C, 39·4; H, 3·0; Cl, 11·7%). Without thiourea, starting material only was recovered. In a similar experiment using cuprous thiophenoxide instead of thiobutoxide, *4-chloro-2,3,5,6-tetrafluorophenyl phenyl sulphide*, m.p. 40—42°, b.p. 296° (Found: C, 50·6; H, 1·6; S, 11·3; Cl, 12·7. $C_{12}H_5ClF_4S$ requires C, 50·9; H, 1·8; S, 11·3; Cl, 12·6%), 82% yield, was obtained.

Reaction of Cuprous Thiophenoxide and Pentafluoroidobenzene.—Pentafluoroiodobenzene (6 g) in NMP (30 cm³) was added slowly to a stirred solution of cuprous thiophenoxide (3·45 g) and thiourea (6 g) at 18°. After 12 h the mixture was poured into water and extracted with ether (3 × 50 cm³); the ether extract was dried (MgSO$_4$) and distilled to give *2,4-difluoro-1,3,5-tris(thiophenoxy)-benzene* (2·7 g), m.p. 59—60° (from light petroleum, b.p. 60—80°) (Found: C, 65·8; H, 3·9. $C_{24}H_{16}F_2S_3$ requires C, 65·7; H, 3·7%). [19]F N.m.r. was not inconsistent with the structure.

In a similar experiment, but using pentafluorobenzene (4 g, 0·02 mol) instead of the iodo-compound, the same compound as above (2 g) was formed.

Reaction of Phenylcopper(I) and Pentafluoroidobenzene.—Phenylcopper(I) was prepared *in situ* from bromobenzene (1·6 g) in ether (25 cm³); the ether layer was decanted and the cuprousphenyl was washed with ether, under nitrogen, by decantation. Pentafluoroiodobenzene (3 g) in dry pyridine (50 cm³) was then added to the mixture which was heated to 100° to give a red-brown solution. After 1 h at 100° the mixture was poured onto ice–concentrated hydrochloric acid 1 : 1 and the mixture extracted (2 × 25 ml) with ether; evaporation of the dried (MgSO$_4$) ether layers afforded a light brown solid (2·1 g). Recrystallisation from light petroleum afforded 2,3,4,5,6-pentafluorobiphenyl (0·4 g) [m.p. 85—87° identical to an authentic sample (i.r. and n.m.r.)] and biphenyl (0·3 g), m.p. and mixed m.p. 60°.

Reaction of Bromopentafluorobenzene with Cuprous Thiobutoxide and (a) Iodine, (b) Deuterium Oxide.—(a) Cuprous thiobutoxide (3 g) was stirred with bromopentafluorobenzene (5 g) and thiourea (6 g) in NMP (50 cm³) under nitrogen at 110° for 1·5 h. Iodine (2 g) in NMP (20 cm³)

was added to the mixture which was then stirred for 1 h. Work-up as previously described afforded n-butyl 2,3,5,6-tetrafluorophenyl sulphide (2·4 g) and no iodine-containing product.

(b) In a similar experiment deuterium oxide (2 cm³) was added instead of iodine; the product (2·1 g) was shown to be n-butyl 2,3,5,6-tetrafluorophenyl sulphide with no significant deuterium incorporation.