Homolytic Reactions of Perfluoroaromatic Compounds. Part III.[1] Reactions of Benzoyl Peroxide with Hexafluorobenzene, Chloro-, Bromo-, and Nitro-pentafluorobenzene, and Pentafluoropyridine

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The reaction of benzoyl peroxide with hexafluorobenzene has been shown to give 2,3,4,5,6-pentafluorobiphenyl and a residue whose relative yields depend mainly on the conditions used for the distillation of the biaryl from the reaction mixtures. This supports the suggestion made previously that the biaryl is formed partly by defluorination of σ-complexes during reaction, and partly by thermal breakdown of dimers of the σ-complexes during the distillation. Analogous phenylation of chloro-, bromo-, and nitro-pentafluorobenzene and pentafluoropyridine gives mixtures of isomeric products. The ratios in which these isomers are formed with chloro- and bromo-pentafluorobenzene and pentafluoropyridine have been measured and are discussed.

REACTIONS of hexafluorobenzene with phenyl and substituted phenyl radicals have been reported,[2,3] and we now report the results of a more detailed study of the decomposition of benzoyl peroxide in hexafluorobenzene, chloro-, bromo-, and nitro-pentafluorobenzene, and pentafluoropyridine. 2,3,4,5,6-Pentafluorobiphenyl, a high-boiling residue, and a little benzoic acid have been isolated from the reaction in hexafluorobenzene. The results of a series of experiments in which the procedure for the conduct of this reaction was varied in several ways are given in Table 1.

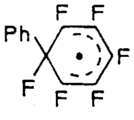
TABLE 1

Decomposition of benzoyl peroxide (1·21 g.) in hexafluorobenzene (9·3 g.)

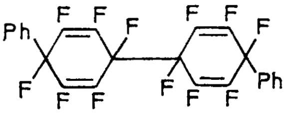
Special conditions or additives	Biaryl yield (g.) *	Residue yield (g.)
—	0·790 [a]	1·126
—	0·974 [b]	0·972
—	1·128 [c]	0·762
Water (0·12 g.)	0·804	—
Oxygen (10 ml./min.)	0·790	—
Nitrogen (10 ml./min.)	0·592	—
Nitrobenzene (0·18 g.)	0·692	—
Cu powder (0·24 g.)	0·447	—
Fe powder (0·21 g.)	1·000	—
Zn dust (0·21 g.)	0·625	—
CuCl (0·28 g.)	0·903	—
$CuCl_2$ (0·094 g.)	0·315	—
$FeCl_2,4H_2O$ (0·12 g.)	0·354	—
Quinol (0·07 g.)	0·193	—
Quinol (0·29 g.)	0	—

* Distillation conditions were 100—200 °C/0·01 mmHg in all cases except (*a*) 100—120 °C/15 mmHg, (*b*) 200 °C/ 15 mmHg, and (*c*) 300 °C/760 mmHg.

Even in the absence of added substances, the yields of the biaryl and of the residue vary considerably according to the manner in which the biaryls are distilled from the reaction mixture. The biaryl yield increases, and the residue yield decreases, with the temperature of this distillation, supporting the suggestion made in Part I[3] that the biaryls are formed partly during the reaction itself, by loss of fluorine from the σ-complexes (I) resulting from addition of phenyl radicals to the perfluoroaromatic nucleus, and partly during the subsequent distillation, by thermal decomposition of dimers of (I), such as (II). This is probably the main reason for the variability of the yield of biaryl in this reaction.



(I)



(II)

The biaryl yield was not appreciably increased by the presence of water or of oxygen or nitrobenzene which might by analogy with the phenylation of benzene[4,5] have been expected to have this result. Likewise the addition of reducing agents such as metals, copper(I) chloride, iron(II) chloride, and quinol, which might have been expected to assist the defluorination of the σ-complexes, had little beneficial effect. Iron powder and copper(I) chloride brought about small improvements in the biaryl yield, but the other additives resulted in a decrease in this yield. The best yield was obtained when no additive was used, but the products were distilled at 300°.

Reactions of benzoyl peroxide with chloro-, bromo-, and nitro-pentafluorobenzene and with pentafluoropyridine gave mixtures of isomeric phenylation products, and the results are consistent with the mechanism suggested in Part I[3] in which the rate-determining stage in the substitution process is the addition of phenyl radicals to the polyfluorinated nuclei to give σ-complexes leading to substitution at the various nuclear sites. In addition to the isomeric tetrafluoronitrobiphenyls, the reaction in pentafluoronitrobenzene also gave small quantities (*ca.* 5%) of phenyl benzoate and 2,3,4,5,6-pentafluorobiphenyl. The formation of the former product in reactions of benzoyl peroxide with aromatic substrates other than benzene and the mechanism of its formation, which does not involve the

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[1] Part II, P. H. Oldham and G. H. Williams, *J. Chem. Soc.* (*C*), 1970, 1260.

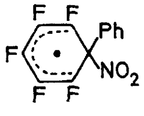
[2] P. A. Claret, Miss J. Coulson, and G. H. Williams, *Chem. and Ind.*, 1965, 228.

[3] P. A. Claret, G. H. Williams, and Judith Coulson, *J. Chem. Soc.* (*C*), 1968, 341.

[4] R. T. Morrison, J. Cazes, N. Samkoff, and C. A. Howe, *J. Amer. Chem. Soc.*, 1962, **84**, 4152.

[5] D. H. Hey, M. J. Perkins, and G. H. Williams, *Chem. and Ind.*, 1963, 83.

substrate, have been discussed.[6] The latter product must have been formed by addition of a phenyl radical to the 1-position of nitrobenzene to give the σ-complex (III) whose subsequent denitration would give the observed product. The formation of biphenyl in detectable quantities (as well as the isomeric phenyltetrafluoropyridines) in the reaction in pentafluoropyridine is somewhat unexpected, although a little biphenyl is often formed in phenylations with benzoyl peroxide. In this instance its formation must involve recombination of phenyl radicals, probably within the solvent cage.



(III)

The distribution of the isomeric binuclear products formed by phenylation of chloro- and bromo-pentafluorobenzene and pentafluoropyridine are given in Table 2, which also includes the corresponding results for the non-fluorinated analogues of these substrates for comparison. We were unable to measure the isomer distribution for the phenylation of pentafluoronitrobenzene because of the experimental difficulty of resolving the peaks corresponding to the 2-, 3-, and 4-isomers in the gas chromatogram.

TABLE 2

Distribution of isomers formed in phenylations with phenyl radicals at 80 °C (%)

Substrate	2-	3-	4-
PhCl [a]	50·1	31·6	18·3
PhBr [b]	49·3	33·3	17·4
C_5H_5N [c]	54	32	14
C_6F_5Cl	44·1	35·0	20·9
C_6F_5Br	43·6	39·0	17·4
C_5F_5N	47·7	22·1	30·3

[a] Chang Shih, D. H. Hey, and G. H. Williams, *J. Chem. Soc.*, 1958, 2600. [b] R. L. Dannley, E. C. Gregg, R. E. Phelps, and C. B. Coleman, *J. Amer. Chem. Soc.*, 1954, **76**, 445. [c] D. H. Hey, C. J. M. Stirling, and G. H. Williams, *J. Chem. Soc.*, 1955, 3963.

The distributions given in Table 2 may, of course, not be the same as the distributions of the isomeric σ-complexes, unless the diversion of σ-complexes by dimerisation to form residue is non-discriminatory as between the isomers. However there is substantial evidence [4,5] that in the analogous reaction in non-fluorinated substrates this is the case, and the distributions of isomeric binuclear products are valid as measures of the relative reactivities of the nuclear sites towards addition of phenyl radicals. If the situation is similar in the reactions with perfluoroaromatic compounds, the addition of phenyl radicals to such nuclei appears to be governed by factors similar to those which govern such additions to aromatic nuclei, namely, the relative stability of the isomeric σ-complexes,[7] since the patterns of the isomer distributions are essentially similar in both reactions.

Several new derivatives of 2,3,4,5,6-pentafluorobiphenyl have been prepared by independent routes for use as reference compounds in the measurement of the isomer distributions.

EXPERIMENTAL

Reactions of Benzoyl Peroxide with Polyfluoroaromatic Solvents.—The following general procedure was used. The peroxide (0·005 mole) was allowed to decompose in the solvent (0·05 mole) at 80 °C in a thermostat for 72 hr. When reaction was complete, two drops of the cooled solution were removed for g.l.c. Each experiment was carried out in duplicate. Products were isolated as follows. Acidic material was extracted with saturated aqueous sodium hydrogen carbonate (5 × 10 ml.) and these extracts were added to the bicarbonate solution. The latter was washed with ether (2 × 10 ml.) and these extracts were returned to the organic layer.

The aqueous phase was acidified with concentrated hydrochloric acid and the precipitated acid was extracted with ether (3 × 20 ml.). The combined extracts were washed with water until neutral. The dried ($CaCl_2$) ether solution was filtered, and the filtrate was allowed to evaporate at room temperature. Last traces of solvent and moisture were removed *in vacuo*.

The dried ($MgSO_4$) organic phase was filtered, and the ether and the bulk of the polyfluoroaromatic solvent were removed by simple distillation. The last traces of the latter were removed by distillation at 10 mm. The products were obtained by distillation *in vacuo* (0·01 mm.), and were collected in a weighed receiver at −80 °C.

Gas Chromatography.—This was carried out at 100—230 °C with an instrument fitted with a sensitive β-ray ionisation detector. The stationary phase was Apiezon L grease (15% w/w) on Celite 545 (72—85 mesh). The flow-rate of argon was appoximately 30 ml./min. The method of internal standardisation was used for quantitative determinations. In calculating the composition of the mixtures of isomeric chlorotetrafluorobiphenyls and phenyltetrafluoropyridines, it was assumed that the detector response was the same for all three isomers.

Hexafluorobenzene.—G.l.c. of the distillate showed the presence of one component. Crystallisation of the distillate gave 2,3,4,5,6-pentafluorobiphenyl, m.p. 111—112° (lit.,[8] 111—112°). The yields of this compound and of the high-boiling residue varied considerably from one run to another.

In separate experiments the effects on the yield of pentafluorobiphenyl and, in some cases, of the residue, of different conditions of distillation of the binuclear product, of conducting the reaction in a stream of nitrogen or oxygen, and of added water or various other additives were investigated.

Chloropentafluorobenzene.—The products were benzoic acid (0·135 g.), a binuclear fraction (0·653 g.), and a high-boiling residue (0·801 g.). G.l.c. of the binuclear fraction, which was obtained as a yellow crystalline solid (Found:

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[6] D. I. Davies, D. H. Hey, and G. H. Williams, *J. Chem. Soc.*, 1961, 562.

[7] G. H. Williams, *Chem. and Ind.*, 1961, 1286.

[8] J. M. Birchall, R. N. Haszeldine, and A. R. Parkinson, *J. Chem. Soc.*, 1962, 4966.

C, 55·7; H, 2·15; Cl, 13·6; F, 28·8. Calc. for $C_{12}H_5ClF_4$: C, 55·2; H, 1·92; Cl, 13·6; F, 29·1%) showed the presence of three components. Examination of the solution immediately after reaction also showed the same three components. A sample of 4-chloro-2,3,5,6-tetrafluorobiphenyl had the same retention time as the last of the peaks to be eluted from the reaction mixture. The i.r. absorption bands of the 4-chloro-compound also occurred in the i.r. spectrum of the mixture. Five large samples (0·250 g.) of the reaction mixture were subjected to preparative-scale g.l.c. (400 × 2·5 cm. column; stationary phase: 15% w/w Apiezon L grease on 40—60 mesh brick dust; column temperature: 190 °C; argon flow-rate: 240 ml./min.). In each case the first 0·05 g. of eluate was collected. These fractions were combined, chromatographed again under the same conditions, and the first 0·015 g. of eluate was collected. This was shown by analytical g.l.c. to be a pure substance, and to have the same retention time as the first peak in the gas chromatogram of the mixture (m.p. 74—75°) (Found: C, 55·3; H, 1·88; Cl, 13·6; F, 29·1. $C_{12}H_5ClF_4$ requires C, 55·2; H, 1·92; Cl, 13·6; F, 29·1%). In view of these results, and by analogy with the isomeric bromotetrafluorobiphenyls, all three isomers of which were independently synthesised, this compound is considered to be 2-*chloro*-3,4,5,6-*tetrafluorobiphenyl*, although its attempted synthesis by an unambiguous route failed. Since elementary analysis showed the mixture to consist only of chlorotetrafluorobiphenyls, and g.l.c. showed the presence of only three components, the third of these must have been 3-chloro-2,4,5,6-tetrafluorobiphenyl. The composition of this mixture of isomers was calculated from the gas chromatogram of the reaction mixture, and is given in Table 2.

Bromopentafluorobenzene.—The products were benzoic acid (0·190 g.), a binuclear fraction [0·725 g. (Found: C, 47·3; H, 1·87; Br, 26·0; F, 24·8. Calc. for $C_{12}H_5BrF_4$: C, 47·2; H, 1·64; Br, 26·2; F, 24·9%], and a residue (0·711 g.). G.l.c. of the binuclear fraction, and of the mixture immediately after reaction, showed the presence of three components.

Authentic specimens of the 2-, 3-, and 4-bromo-tetrafluorobiphenyls had the same retention times as the first, second, and third of the peaks eluted from the reaction mixture respectively. I.r. spectra of the distillate and of the authentic specimens were recorded. Absorption bands occurring in the spectra of the authentic specimens also occurred in the spectrum of the mixture. The composition of the mixture of isomers was calculated from the gas chromatogram of the solution after reaction, and is given in Table 2.

Pentafluoronitrobenzene.—The products were benzoic acid (0·134 g.), a binuclear fraction (0·330 g.), and a residue (0·856 g.). G.l.c. of the binuclear fraction, which was an orange solid, and of the solution after reaction showed four peaks. Two of these peaks occurred at retention times identical with those given by authentic specimens of 3,4,5,6-tetrafluoro-2-nitrobiphenyl and 2,3,5,6-tetrafluoro-4-nitrobiphenyl. These two peaks represented over 90% of the binuclear fraction, which gave the following elementary analysis: Found: C, 54·8; H, 1·92; F, 26·5; N, 4·8. (Calc. for $C_{12}H_5F_4NO_2$: C, 53·1; H, 1·85; F, 28·1; N, 5·2%). I.r. spectra of the distillate and of the 2- and 4-nitro-compounds were recorded. Absorption bands occurring in the spectra of the authentic specimens also occurred in the spectrum of the mixture. The 2- and 4-nitro-compounds were therefore present in the binuclear fraction, but the 3-nitro-compound may also have been present, if its retention time was similar to that of one of the other isomers. The nitrobiaryls together constituted more than 90% of the binuclear fraction. The two minor components in the distillate were identified by g.l.c. as phenyl benzoate and 2,3,4,5,6-pentafluorobiphenyl.

Pentafluoropyridine.—Benzoyl peroxide (0·005 mole) was allowed to decompose in pentafluoropyridine (0·025 mole). In other respects, the standard procedure was employed. G.l.c. of the binuclear fraction showed the presence of four components, one of which was shown to be biphenyl, and another (the last to be eluted), 4-phenyl-2,3,5,6-tetrafluoropyridine, by comparison with authentic specimens. The isomer distribution of the phenyltetrafluoropyridines (combined yield, 0·749 g.) was calculated on the assumption that the two remaining peaks were the 2-phenyl- and 3-phenyl-isomers, respectively, and is given in Table 2.

Reagents and Reference Compounds.—Hexafluorobenzene and chloro-, bromo-, and nitro-pentafluorobenzene (Imperial Smelting Corporation Ltd.) were dried ($MgSO_4$) and distilled. Their purity was checked by g.l.c. We are indebted to Professor W. K. R. Musgrave, of the University of Durham, for gifts of pentafluoropyridine and 4-phenyl-2,3,5,6-tetrafluoropyridine. The latter, recrystallised from methanol, had m.p. 106° (lit.,[9] 106—107°).

4-Chloro-2,3,5,6-tetrafluorobiphenyl was prepared by addition of sodium nitrite (0·4 g.) in water (5 ml.) during 20 min. to 4-amino-2,3,5,6-tetrafluorobiphenyl (I.S.C.) (0·55 g.) in hydrofluoric acid (25 ml. of 80% w/w) at 0 °C. The mixture was stirred in a Polythene bottle immersed in an ice–salt bath for a further 60 min. A solution of copper(I) chloride (1·5 g.) in concentrated hydrochloric acid (4 ml.) was then added during 20 min., the temperature still being kept at 0°. After being stirred for a further 2½ hr. at room temperature, the mixture was diluted with water and extracted with ether (2 × 100 ml.).

The combined ether extracts were washed until the washings were neutral, dried ($MgSO_4$), and the ether removed *in vacuo*. The residue was distilled *in vacuo* (0·01 mm./100—120°). Crystallisation of the distillate from aqueous methanol gave 4-*chloro*-2,3,5,6-*tetrafluorobiphenyl* (0·24 g., m.p. 106—107° (Found: C, 55·4; H, 1·82; Cl, 13·7; F, 29·2. $C_{12}H_5F_4Cl$ requires C, 55·2; H, 1·92; Cl, 13·6; F, 29·1%).

4-Bromo-2,3,5,6-tetrafluorobiphenyl was prepared in a similar way. The distillate was crystallised from aqueous methanol to give 4-*bromo*-2,3,5,6-*tetrafluorobiphenyl* (0·52 g., m.p. 104—105°) (Found: C, 47·4; H, 1·72; Br, 26·1; F, 24·9%. $C_{12}H_5F_4Br$ requires C, 47·2; H, 1·64; Br, 26·2; F, 24·9%).

3-Bromo-2,4,5,6-tetrafluorobiphenyl was prepared by means of the Ullmann reaction. A mixture of iodobenzene (1·53 g.), 1,3-dibromotetrafluorobenzene (I.S.C.) (2·21 g.), and copper bronze (2·1 g.) was heated for 2 hr. at 230—240 °C. The mixture was then thoroughly extracted with ether and after evaporation of the ether was distilled *in vacuo* (0·01 mm./100—120°) to give a white crystalline distillate, g.l.c. of which showed the presence of only two components. These were separated by chromatography on alumina and elution with light petroleum (b.p. 40—60°)–benzene (1 : 1 v/v). One component was identified as biphenyl by i.r. spectroscopy. The other was recrystallised

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[9] R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, Belg. Patent, 660,663,873 (1965).

from aqueous methanol and gave 3-*bromo*-2,4,5,6-*tetrafluorobiphenyl* (0·035 g., m.p. 89—90°) (Found: C, 47·5; H, 1·70; Br, 26·3%). The product was shown to be uncontaminated with other material by g.l.c.

2-Bromo-3,4,5,6-tetrafluorobiphenyl was prepared by boiling a mixture of 2-bromo-3,4,5,6-tetrafluoroaniline (I.S.C.) (2·44 g.), benzene (23 ml.), and pentyl nitrite (1·17 g.) under reflux for 2 hr. After distillation of the excess of solvent, distillation *in vacuo* (0·01 mm./100—120°) and crystallisation from light petroleum (b.p. 40—60°) gave 2-*bromo*-3,4,5,6-*tetrafluorobiphenyl* (1·2 g., m.p. 44—45°) (Found: C, 47·2; H, 1·53; Br, 26·4; F, 24·8%).

3,4,5,6-Tetrafluoro-2-nitrobiphenyl was prepared by boiling a mixture of 3,4,5,6-tetrafluoro-2-nitro-aniline (1 g.) [prepared from pentafluoro-2-nitrobenzene (I.S.C.) by Brooke, Burdon, and Tatlow's method [10]], benzene (7·48 g.), and pentyl nitrite (0·56 g.) under reflux for 2 hr. The excess of solvent was distilled off and the residue was distilled *in vacuo* (0·01 mm./120—140°). Crystallisation of the distillate from aqueous methanol gave 3,4,5,6-*tetrafluoro*-2-*nitrobiphenyl* (0·52 g., m.p. 70—71°) (Found: C, 53·3; H, 1·96; F, 27·8; N, 5·4. $C_{12}H_5F_4NO_2$ requires C, 53·1; H, 1·85; F, 28·1; N, 5·2%).

2,3,5,6-Tetrafluoro-4-nitrobiphenyl was obtained by oxidation of 4-amino-2,3,5,6-tetrafluorobiphenyl, which was prepared from 2,3,4,5,6-pentafluorobiphenyl by Chaudhry and Stephen's method.[11] Methylene dichloride (20 ml.), trifluoroacetic anhydride (5 ml.), and 86% hydrogen peroxide (2 ml.) were boiled under reflux for 15 min. with stirring. A solution of 4-amino-2,3,5,6-tetrafluorobiphenyl (1 g.) in methylene dichloride (10 ml.) was then added during 15 min., followed by 86% hydrogen peroxide (1 ml.) 1 hr. later, and finally by 86% hydrogen peroxide (1 ml.) and trifluoroacetic anhydride (1 ml.) after a further 2½ hr. The mixture was boiled under reflux with continuous stirring for 18 hr. in all. It was then cooled, washed with water (3 × 25 ml.), and dried ($MgSO_4$). The methylene dichloride was removed *in vacuo* and the residue distilled *in vacuo* (0·01 mm./120—130°). Crystallisation of the distillate from methanol gave 4-*nitro*-2,3,5,6-*tetrafluorobiphenyl* (1·0 g., m.p. 142—143°) (Found: C, 55·4; H, 1·70; F, 28·2; N, 5·1%).

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[10] G. M. Brooke, J. Burdon, and J. C. Tatlow, *J. Chem. Soc.*, 1961, 802.

[11] M. T. Chaudhry and R. Stephens, *J. Chem. Soc.*, 1963, 4281.