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Homolytic Arylation of Aromatic and Polyfluoroaromatic Compounds

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1 Introduction

Homolytic arylation involves the replacement of substituents in aromatic systems by aryl fragments generated by processes in which the attacking reagent appears to be a radical ($Ar^{\bullet}$). Evidence supporting this can come from consideration of the nature of the various products, or the sensitivity of the reaction towards environmental changes (*e.g.* solvent or substituent effects), or the detection of particular trapping products or, in some cases, of radical intermediates (ESR, CIDNP). Kinetic studies can also support a particular reaction mechanism, though rarely unequivocally; in most instances the agreement between the kinetic form and the mechanistic interpretation confirms or supports the mechanism rather than offering unambiguous evidence. This review consists, in its first part, of a general consideration of attack upon arenes by aryl radicals in which the postulate of such radicals and possible competing processes are discussed. Earlier reviews[1–3] were comprehensive; more recent ones[4,5] were less so, and this review is therefore concerned mainly with more recent work. In the second part, reactions involving polyfluoroaromatic radicals and polyfluoroarenes are reviewed in somewhat more detail since the subject, which has latterly aroused considerable interest, has advanced considerably since the previous publications.[6,7]

2 Evidence for Aryl Radicals

The intermediacy of phenyl radicals in the formation of biaryls from the thermolysis of derivatives of aryldiazonium ions or of aroyl peroxides was suggested[1–5] by the lack of orientational selectivity shown when monosubstituted arenes such as chlorobenzene were attacked. Both electron-withdrawing and -attracting groups apparently activated the aromatic ring towards attack, and an unexpectedly large amount of *o*-substituted biaryl was found. The postulated

[1] G. H. Williams, 'Homolytic Aromatic Substitution', Pergamon, Oxford, 1960.
[2] G. H. Williams, in 'Essays on Free Radical Chemistry', Special Publication No. 24, The Chemical Society, London, 1970, p. 25.
[3] M. J. Perkins, in 'Free Radicals', ed. J. K. Kochi, Wiley, New York, 1973, Vol. II, p. 231.
[4] D. H. Hey and G. H. Williams, in 'Rodd's Chemistry of Carbon Compounds', Elsevier, Amsterdam, 2nd Edition, 1971, Vol. IIIA, p. 113.
[5] G. H. Williams, in 'Rodd's Chemistry of Carbon Compounds', Elsevier, Amsterdam, Supplement to 2nd Edition, 1983, Vol. IIIA, p. 33.
[6] R. Bolton and G. H. Williams, in 'Advances in Free Radical Chemistry', Elek Science, London, 1975, Vol. V, p. 1.
[7] L. S. Kobrina, *Usp. Khim.*, 1977, **46**, 660.

phenyl radical has since been identified in a number of conditions, and has been observed directly (i) after photolysis of an argon–benzene matrix,[8] (ii) in the products of radiolysis of aqueous PhX (X = F, Cl, or Br) where it was identified by its absorption spectrum,[9] (iii) during ESR studies of the products of photolysis of $Ph{\cdot}CO{\cdot}O{\cdot}O{\cdot}CMe_3$[10] and of benzoyl peroxide,[11] and (iv) as the trapping product with $Ph{\cdot}CH{=}N(O)CMe_3$ after the radiochemical oxidation of toluene[12] and also after the $CuCl_2$-induced decomposition of aryldiazonium tetrafluoroborates.[13] Phenyl radicals are also proposed to occur during the pyrolysis of benzene at 1 200—1 900 K[14] and of bromobenzene at 1 300—1 600 K[15] from which studies, as well as from variable time photoelectron–photoion coincidence mass spectrometry of bromobenzene[16] and earlier kinetic studies[17] a heat of formation (ΔH_f^0) for $Ph^{\cdot}$ of 340 kJ mol^{-1} has been obtained.

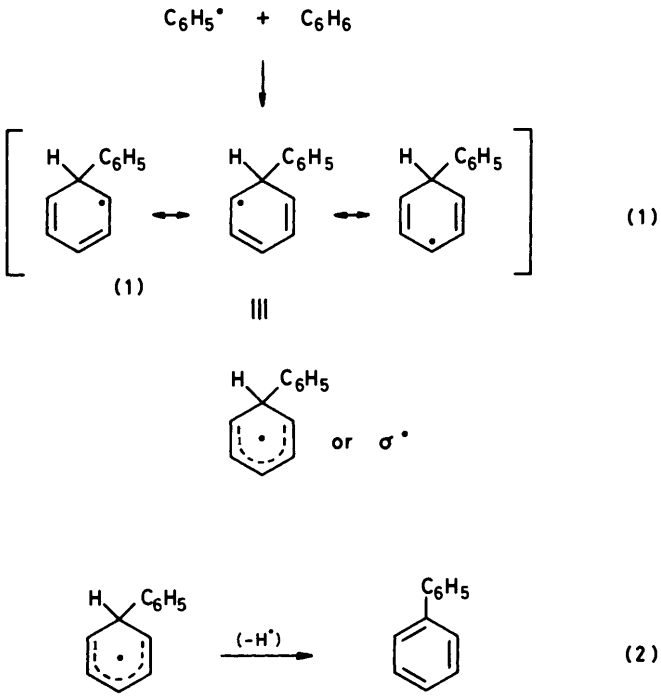
Arylation to arenes involves[1–5] the addition of the radical to the nucleus to give a sigma (σ) complex (1) which is dehydrogenated to give the substitution product [*e.g.* equations (1) and (2)]. The mechanism of the dehydrogenation (oxidation) process (2) depends mainly upon the source of the aryl radicals, and the efficiency with which it occurs determines the extent to which side-reactions (largely dimerization and disproportionation) of the σ-complex are avoided. Thus, (1) may be trapped by radicals generated in the reaction (*e.g.* $Ph_3C^{\cdot}$),[18] including those generated from other arenes (*e.g.* $PhCH_2^{\cdot}$)[19] arising from hydrogen abstraction from the side chain.

Phenyl radical arises from a number of sources; detailed mechanistic studies however have been made within relatively few systems.

3 Thermolysis of Aroyl Peroxides

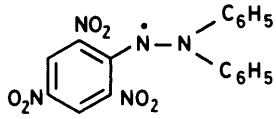
The pyrolysis of benzoyl peroxide in aromatic solvents provides the isomeric biaryls (Scheme 2), benzoic acid, high-boiling material, and, at low initial concentrations of peroxide, 1,2- and 1,4-dihydrobiaryls.[20] Kinetic studies of the decomposition of benzoyl peroxide in benzene and some substituted benzenes

[8] J. H. Miller, L. Andrews, P. A. Lund, and P. N. Schatz, *J. Chem. Phys.*, 1980, **73**, 4932.
[9] J. Lichtscheidl and N. Getoff, *Monatsh. Chem.*, 1979, **110**, 1367.
[10] L. V. Luk'yanenko, A. A. Turovskii, and N. A. Turovskii, *Zh. Obshch. Khim.*, 1979, **49**, 1391; *Chem. Abstr.*, 1979, **91**, 123124e.
[11] J. M. McBride, M. W. Vary, and B. L. Whitsel, in 'Organic Free Radicals', ACS Symposium No. 69, p. 208; *Chem. Abstr.*, 1978, **89**, 5661p.
[12] V. E. Zubarev, V. N. Belevskii, A. L. Zarazilov, and A. A. Aliev, *Vestn. Mosk. Univ., Ser. 2: Khim.* 1979, **20**, 446.
[13] R. G. Gasanov, B. V. Kopylova, L. V. Yashkina, and R. Kh. Freidlina, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1982, 1915.
[14] N. Fujii and T. Asaba, *J. Fac. Eng., Univ. Tokyo, Ser. B.*, 1977, **34** (1), 189—224; *Chem. Abstr.*, 1977, **87**, 167164.
[15] N. Fujii and T. Asaba, *Nippon Kagaku Kaishi*, 1977, 599.
[16] H. M. Rosenstock, R. Stockbauer, and A. C. Parr, *J. Chem. Phys.*, 1980, **73**, 773.
[17] G. A. Chamberlain and E. Whittle, *Trans. Faraday Soc.*, 1971, **67**, 2077.
[18] D. H. Hey, M. J. Perkins, and G. H. Williams, *J. Chem. Soc.*, 1965, 110.
[19] K. S. Jandu, M. Nicolopoulou, and M. J. Perkins, *J. Chem. Res. (S)*, 1985, 88.
[20] D. F. DeTar, R. A. J. Long, J. Rendleman, J. Bradley, and P. Duncan, *J. Am. Chem. Soc.*, 1967, **89**, 4051.



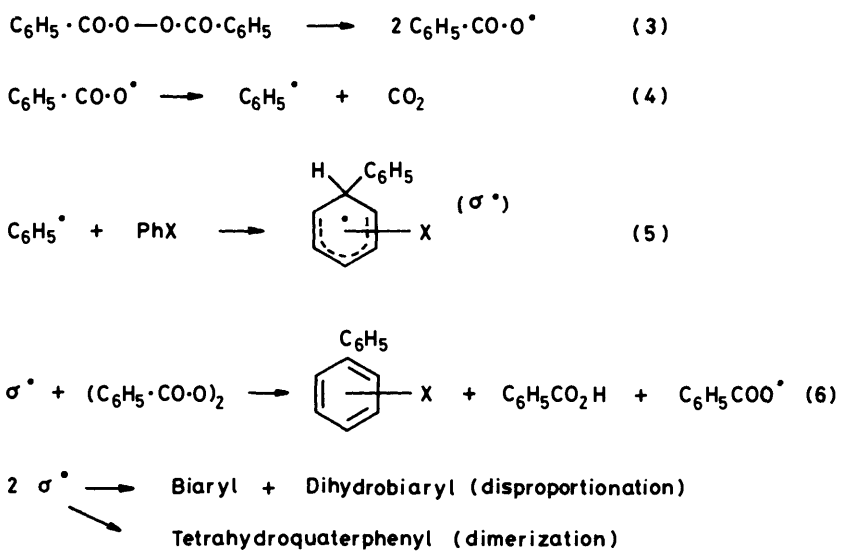
Scheme 1

showed three possible contributions. The 'spontaneous' decomposition of the peroxide is a first-order process; fission of the O–O bond may also be induced by attack upon the peroxide by the intermediate sigma radical (1) and this may show first-order kinetics or a three-halves order contribution depending upon the nature of the termination step. The incursion of these induced processes may be shown by observing the kinetics in the presence of radical inhibitors such as 'galvinoxyl' or of 2,2-diphenyl-1-(2,4,6-trinitrophenyl)hydrazyl (DPPH; 2) when only the contribu-



(2)

tion from the spontaneous process is observed. The incidence of induced decomposition of the peroxide by (1) is paralleled by unusually high yields of benzoic acid and of the biaryls at the expense of the high-boiling tars. The proposed mechanisms are shown in Scheme 2.



Scheme 2

The homolysis of the peroxy link initially gives rise to benzoyloxy radicals (Ph·CO·O•, BzO•) and these may lose carbon dioxide to give the less stable phenyl radical. The benzoyloxy radical may itself attack some arenes; the formation of perceptible amounts of *o*- and *p*-aryl benzoates only from attack of toluene and anisole suggests that BzO• has some electrophilic character[21] and this is confirmed by earlier observations of the rates and orientation of aroyloxylation by benzoyl peroxide–$CuCl_2$ mixtures of PhX substrates in MeCN;[22] in addition, benzoyloxy radicals may trap intermediates in the arylation process as noted above. The intermediacy of the phenyl radical in the formation of biaryls from the products of thermolysis of benzoyl peroxide in arenes was deduced principally from the orientations and rates of formation of these biaryls. Biaryl formation is part of the slow step of such reactions, for some biaryl is formed from the σ-radical-induced homolysis of the peroxide; the rate constants found for these processes should not be compared, because biaryl formation also occurs by other routes (Scheme 2) and the relative contributions of each process towards the total yield of biaryl is unknown.

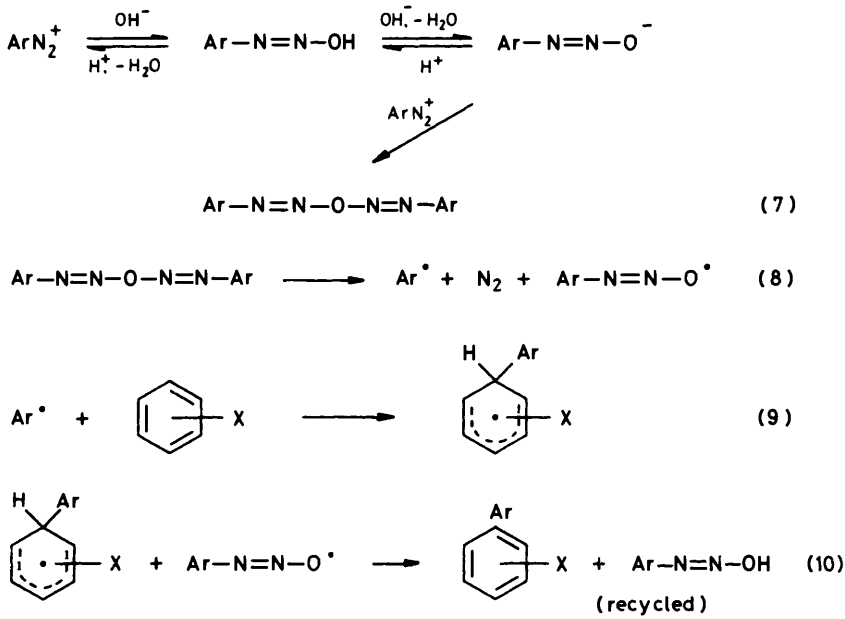
A number of compounds are known to improve the yield of biaryl in this reaction; they include nitro-arenes and their various reduction products and salts of transition metals, especially copper(II) and iron(III) benzoates.[23–26] The

[21] R. Bolton, B. N. Dailly, K. Hirakubo, K. H. Lee, and G. H. Williams, *J. Chem. Soc., Perkin Trans. 2*, 1981, 1109.
[22] M. Kurz and M. E. Pellegrini, *J. Org. Chem.*, 1970, **35**, 995.
[23] D. R. Augood and G. H. Williams, *Chem. Rev.* 1957, **57**, 123.
[24] D. H. Hey, M. J. Perkins, and G. H. Williams, *Chem. Ind.*, 1963, 83.
[25] G. B. Gill and G. H. Williams, *J. Chem. Soc.* (*B*) 1966, 880.
[26] G. R. Chalfont, D. H. Hey, K. S. Y. Liang, and M. J. Perkins, *J. Chem. Soc.* (*B*), 1971, 233.

improvement in yield does not always occur; sometimes the additive is positively deleterious[24] and at others the effect itself seems non-reproducible. This occurred particularly when molecular oxygen, previously[27,28] advocated as a source of great improvement in biaryl yields in such reactions, was found to be quite inactive[21] and emphasized the complexity of the system and the importance of minor variations in the reaction conditions. However, the anticipated discrepancies between relative reactivities of PhX derivatives towards phenyl radicals generated from benzoyl peroxide thermolysis were not seen; the values obtained by direct competition were similar whether additives were present to promote the formation of biaryl[21] or not.[29] Evidence for such anomalies is found in the polyfluoroaromatic systems, and is reviewed later.

4 Aryl Radicals from Diazo Sources

Aryldiazonium salts ($ArN_2^+X^-$) exist in equilibrium with their covalently bonded isomers (Ar–N=N–X), a problem to which Hantzsch devoted much time. These covalent isomers are soluble in organic solvents, so that arenes give biaryls if they are stirred with aqueous solutions of diazonium salts while the pH of the mixture is raised steadily. Scheme 3 shows a sequence commonly proposed.[30]



Scheme 3

[27] M. Eberhardt and E. L. Eliel, *J. Org. Chem.*, 1962, **27**, 2289.
[28] R. T. Morrison, J. Case, N. Samkoff, and C. A. Howe, *J. Am. Chem. Soc.*, 1962, **84**, 4152.
[29] B. Summers, D. I. Davies, and D. H. Hey, *J. Chem. Soc.* (*C*), 1971, 2681.
[30] O. Ruchardt and E. Merz, *Tetrahedron Lett.*, 1964, 2431; E. L. Eliel, P. P. Saha, and E. S. Meyerson, *J. Org. Chem.*, 1965, **30**, 2386.

In its original form, the process was experimentally tedious and difficult, although the use of phase-transfer catalysts helped.[31] The improvement of using a solution of the amine ($ArNH_2$) in the arene (Ar'H) and treating this with a nitrite ester with[32] or without[33] the simultaneous addition of acetic acid makes this process much more preparatively attractive. Studies[34] of the process confirm the essentially homolytic nature of the arylation step. t-Butyl thionitrate[35] may replace the more commonly used 'amyl' nitrite.

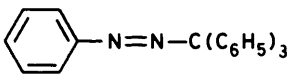
Aryldiazonium salts themselves may serve as arylating agents, and the nature of the true reactant formed under the various necessary reaction conditions has been a rich source of controversy. Phenyldiazonium borofluoride in DMSO at 80 °C gives Ph$^{\bullet}$ when sodium nitrite or pyridine is added[36,37] and the PhN_2^+–NO_2^- system, along with phenylazotriphenylmethane and *N*-nitrosoacetanilide (*q.v.*), showed little primary kinetic isotope effect excepting at the 2-position of *m*-dinitrobenzene, when $k_H/k_D = 11$.[38] These observations may be explained if the two fates of the intermediate radical (*i.e.* oxidation or dedeuteration, and dimerization) are considered. Dimerization is less likely to be affected by deuterium exchange than is oxidation, which involves fission of the C–D bond. Deuteration might therefore be expected empirically to be associated with a lower relative yield of biaryl. The steric congestion at C-2 in *m*-dinitrobenzene may also be important.

The Meerwein reaction, in which aryldiazonium tetrafluoroborates decompose under the influence of Cu^{II} chloride[39] may provide aryl radicals; thus, both phenyl and *p*-nitrophenyl radicals have been trapped by Me_3CNO or $PhCH{=}N(O)CMe_3$ under these conditions.[40] In contrast, M. G. Bartle, R. K. Mackie, and J. M. Tedder report[41] that 2,4-dinitrophenyldiazonium ions in acetic–sulphuric acid mixtures arylate thiophene, 2- and 3-methylthiophene, and thionaphthene but form azo-dyes with 2-and 3-methylthionaphthene, as they do with anisole; benzene is inert. Phenylation involving Ph^+ can be seen with phenyldiazonium trifluoroacetate, with phenylazotriphenylmethane, or with phenyldiazotosylate in the presence of trifluoroacetic acid[42] and with phenyldiazonium tetrafluoroborate.[42,43] The latter group found that *p*-nitrophenyldiazonium tetrafluoroborate gives derivatives of 4-nitrobiphenyl by a homolytic process, as judged by the effects of oxygen, iodine,

[31] J. R. Beadle, S. H. Korzeniowski, D. E. Rosenberg, B. J. Garcia-Slanga, and G. W. Gokel, *J. Org. Chem.*, 1984, **49**, 1594.
[32] Huang Shuh, *Acta Chim. Sinica*, 1959, **23**, 171.
[33] J. I. G. Cadogan, *J. Chem. Soc.*, 1962, 4257.
[34] L. Friedman and J. F. Chlebowski, *J. Org. Chem.*, 1968, **33**, 1633, 1636.
[35] S. Oae, K. Shinhama, and Y. K. Kim, *Chem. Lett.*, 1979, 939.
[36] H. Eustathopoulos, J. Rinaudo, and J. M. Bonnier, *Bull. Soc. Chim. Fr.*, 1974, (12, Pt. 2), 2911.
[37] R. A. Abramovitch and F. F. Gadallah, *J. Chem. Soc.* (*B*), 1968, 497.
[38] N. Kamigata, H. Minato, and M. Kobayashi, *Bull. Chem. Soc. Jpn.*, 1972, **45**, 2042.
[39] C. S. Rondestvedt, *Org. React.*, 1960, **11**, 189.
[40] R. G. Gasanov, B. V. Kopylova, L. V. Yashkina, and R. Kh. Freidlina, *Izv. Akad. Nauk SSSR. Ser. Khim.*, 1982, 1915.
[41] M. G. Bartle, R. K. Mackie, and J. M. Tedder *J. Chem. Soc., Chem. Commun.*, 1974, 271.
[42] N. Kamigata, R. Hisada, H. Minato, and M. Kobayashi, *Bull. Chem. Soc. Jpn.*, 1973, **46**, 1016.
[43] B. Gloor, B. L. Kaul, and H. Zollinger, *Helv. Chim. Acta*, 1972, **55**, 1598.

iodobenzene, and diphenylhydroxylamine on the yields of biaryls formed by attack upon benzene and nitrobenzene. Phenyldiazonium tetrafluoroborate under these conditions gave Ph^+, as shown by the change in the isomer distribution in the biaryls formed; when Ph^+ is regarded as the reagent, the electron density of the arene under attack is now critically important in determining not only the relative rate of phenylation but also the orientation. Remarkably, when Ph^+ is held to be the true reagent, the selectivity of the reagent between molecules is generally less than that shown by $Ph^\bullet$, despite the heterolytic nature of the attacking species; for example, partial rate factors for attack at the 1-position of naphthalene are 13.5 ($Ph^\bullet$) and 2.12 (Ph^+).[36] The internal selectivity between sites is also less when Ph^+ attacks naphthalene (Ph^+, 69% 1-attack; $Ph^\bullet$, 81% 1-attack).

Aryltriazens in acid conditions also provide phenyl radicals, and an improved process has been recently described.[44] The decomposition of ArN=NNHPh in the presence of 72% aqueous perchloric acid and PPh_3 was reported[45] to provide $Ph^\bullet$ as shown by the formation of biaryls from added arenes. Similarly, Ph·NH·N=S=O undergoes slow thermolysis in aromatic solvents at 135 °C to give biaryls whose isomer distribution, together with the simultaneous formation of benzene, indicate a homolytic phenylation process.[46]



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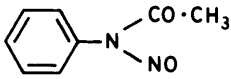

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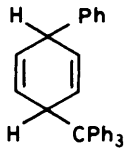


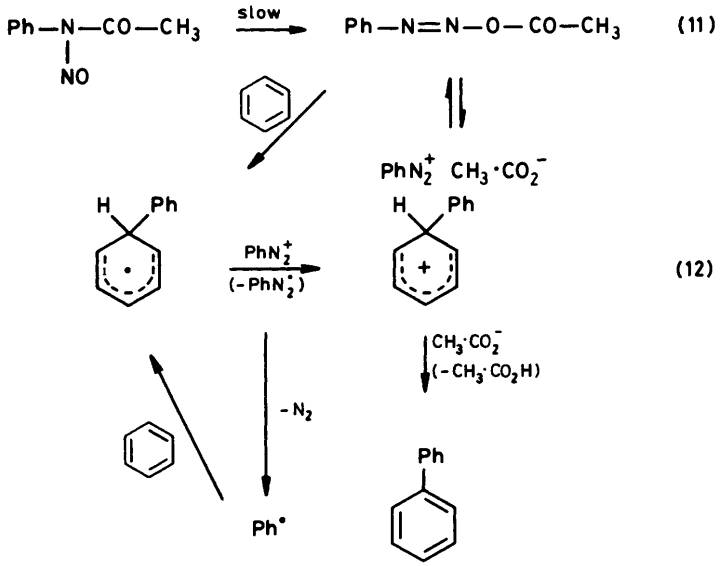
(5)

Among the phenylazo-derivatives most studied are phenylazotriphenylmethane [PAT, (3)] and *N*-nitrosoacetanilide [NNA, (4)]. PAT loses nitrogen readily at 60 °C, a consequence of the stability of the $Ph_3C^\bullet$ system, since azobenzene may be distilled with little decomposition. Recent ESR and CIDNP studies show the intermediacy of a radical pair ($Ph^\bullet$ $^\bullet CPh_3$)[47] which readily explains the formation of biphenyl, triphenylmethane, and the *cis*- and *trans*-isomers of 1,4-dihydro-4-triphenylmethylbiphenyl (5).[18] These adducts also give triphenylmethane and biphenyl, but at somewhat higher temperatures; it seems that radical–radical bonding and hydrogen abstraction proceed concurrently between $^\bullet CPh_3$ and the sigma intermediate. In some cases the dihydrobiphenyl derivatives are unusually stable; for example, 2-chloro-(5) is much more stable than its isomers so that the

[44] T. B. Patrick, R. P. Willaredt, and D. J. deGonia, *J. Org. Chem.*, 1985, **50**, 2232.
[45] G. de Luca, C. Panattoni, G. Renzi, and L. Toniolo, *Tetrahedron Lett.*, 1972, 2463.
[46] G. de Luca, G. Renzi, R. Cipollini, and A. Pizzabiocca, *J. Chem. Soc., Perkin Trans. 1*, 1980, 1901.
[47] T. Suehiro, R. Nakausa, S. Masuda, and M. Kobayashi, *Chem. Lett.*, 1982, 1191.

isomer distribution in the biaryls isolated from the decomposition of PAT in chlorobenzene is remarkably low in *ortho*-isomer unless precautions are taken to decompose this adduct as well, when the 'normal' distribution expected of Ph• attack is found.[48]

N-Nitrosoacetanilide (4) undergoes rearrangement at room temperature; the process shows first-order kinetics, and in the presence of arenes biaryls are formed. The orientation of attack of these arenes suggests the intermediacy of Ph•, but homolysis of the rearrangement product, Ph–N=N–OAc, is expected to give acetyloxy radical. This is unstable with respect to decarboxylation so that the isolation of large amounts of acetic acid and the lack of formation of methane, ethane, and other products from Me• are incompatible with this homolysis. Acetate ions are held to remove hydrogen from the phenylation intermediate; this must therefore be a carbocation rather than a resonance stabilized radical. This in turn suggests a one-electron transfer to explain the attack by Ph• (the presence of which may be shown by conventional trapping), the reduction of the intermediate to the carbocation, and the loss of a proton. The aryldiazonium ion is the logical acceptor of this single electron and the mechanism of the process becomes necessarily complicated to meet the instability of the acetyloxy radical (Scheme 4).[49]



Scheme 4

[48] M. J. Perkins, D. J. Atkinson, and P. Ward, *J. Chem. Soc.* (*C*), 1971, 3240.
[49] J. I. G. Cadogan, in 'Essays on Free Radical Chemistry', Special Publication No. 24, The Chemical Society, London, 1970, p. 71.

5 Arylation of Polybenzenoid Systems

Thermolysis of aroyl peroxides is not a useful source of phenyl radicals in polybenzenoid systems, for the benzoyloxy radical reacts with these more reactive arenes, and decarboxylation to form Ph$^{\bullet}$ is a minor process. Thus, naphthalene gives the two isomeric naphthyl benzoates and binaphthyls, but very little phenylnaphthalene product.[50] Phenyldiazo precursors have been used in successful studies of the phenylation of polybenzenoid arenes. The reaction of $PhN_2^+BF_4^-$ with either $NaNO_2$ or pyridine provides Ph$^{\bullet}$ whose relative orientation and rates of attack of naphthalene and anthracene agree with those found in the more extensive study of phenylation of naphthalene, anthracene, phenanthrene, pyrene, and biphenylene by Ph$^{\bullet}$ from the Meerwein reaction (PhN_2^+–$CuCl_2$) and from NNA.[51] Attack of naphthalene or anthracene by Ph$^+$, formed from the diazonium tetrafluoroborate, showed less selectivity both between sites in the molecule and intermolecularly.[44] Phenylation of 9-methylanthracene using diazonium ion sources showed that Ph$^{\bullet}$ did not abstract hydrogen from the side-chain, but instead attacked C-10, even when this site was substituted by chlorine or bromine; in the 9-halogenoanthracenes, bromine displacement did not occur as readily as chlorine displacement, as judged by the relative extents of attack at C-9 and C-10; this, however, need not reflect anomalous C–halogen bond strengths, for the relative rates of the two processes cannot be compared directly on the evidence available.[52] Partial rate factors and products of phenylation of 1,4-, 1,5-, 2,3-, 2,6-, and 2,7-dimethylnaphthalene have also been reported.[53]

6 Arylation of Heterocyclic Systems

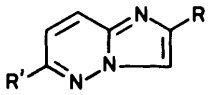
Many heterocyclic compounds have been reported to undergo phenylation. The present selection is based upon novelty or mechanistic significance, without attempting comprehensive coverage.

Isoquinoline reacts with $PhNH_2$–AmONO or with $PhTl(OCOCF_3)_2$ on irradiation to give the isomeric phenylisoquinolines in relative amounts ($1 > 5 > 8 > 4 > 3, 6, 7$) at variance with eight separate theoretical predictions.[54] In thiophene, 3-substituents are reported to make the two alpha-positions non-equivalent and to activate the 2-position relative to the 5-position. This unremarkable conclusion could be anticipated from comparison with the behaviour of mono-substituted benzenes.[55] The phenylation of benzo[*b*]furan and benzo[*b*]thiophene by NNA proceeds at 8.3 and 7.3 times the rate of attack of benzene respectively, but while the benzothiophene is attacked equally at all sites of both rings, benzo[*b*]furan undergoes preferential attack at the heterocyclic ring.[56]

[50] D. I. Davies, D. H. Hey, and G. H. Williams, *J. Chem. Soc.*, 1958, 1878.
[51] S. C. Dickerman, W. M. Feigenbaum, M. Fryd, N. Milstein, G. B. Vermont, I. Zimmermann, and J. F. W. McOmie, *J. Am. Chem. Soc.*, 1973, **95**, 4624.
[52] F. M. Cromarty, R. Hendriquez, and D. C. Nonhebel, *J. Chem. Res.*, (S), 1977, 309.
[53] H. Eustathopoulos, J. Rinaudo, and J. M. Bonnier, *Bull. Chem. Soc. Fr.*, 1973, (7–8) (Pt. 2), 2384.
[54] L. K. Dyall and C. J. Pullen, *Aust. J. Chem.*, 1979, **32**, 345.
[55] C. M. Camaggi, G. de Luca, and A. Tundo, *J. Chem. Soc., Perkin Trans. 2*, 1972, 1594.
[56] P. Spagnolo, M. Tiecco, A. Tundo, and G. Martelli, *J. Chem. Soc., Perkin Trans. 1*, 1972, 556.

Thieno[3,2-*b*]thiophene is attacked faster than thiophene and mainly at the 2-position; the [2,3-*b*] isomer reacts slower than thiophene to give the 2- (40%) and 3-phenyl (60%) products; both $PhNH_2$–AmONO and NNA give similar phenylation results in these systems.[57]

The phenylation products of (6), (7), and (8) have also been reported.[58]



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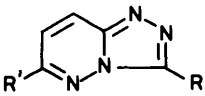

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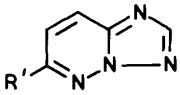
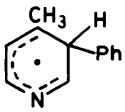
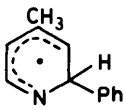


(8)

Attack upon 4-methylpyridine provides some points which, if general, have considerable mechanistic significance. The ratio of 2- and 3-phenyl-4-methylpyridine formed during the thermolysis of benzoyl peroxide in mixtures of benzene and 4-methylpyridine depends upon the initial peroxide concentration only if nitrobenzene is absent. The improvement of biaryl yield which this additive often causes suggests that the competition between dimerization and oxidation of the intermediate radicals occurs to different extents in the two isomeric species (9) and (10). This is consistent with the deuterium isotope effect seen only in attack at the 3-position ($k_H/k_D = 3.7$)[59] and not at C-2, and the isolation of the two isomers, 2(4-biphenylyl)-4-methyl-3- and -5-phenylpyridine, as secondary products presumably arising from the capture of one intermediate radical by another different species coming from the phenylation of benzene.[60] After considering the effects of nitrobenzene and copper(II) acetate, both materials which should improve the yields of biaryls at the expense of secondary products, the authors advise caution in interpreting their results in terms of the reversibility of addition of Ph$^{\bullet}$ to arenes.



(9)



(10)

Interestingly, the response of phenyl radicals towards pyridinium ion systems is somewhat different from that shown towards the pyridines.[61] The isomer distribution of arylation of 4-methylpyridine by a number of *p*-substituted phenyl

[57] P. Spagnolo. L. Testaferri, M. Tiecco, and G. Martelli, *J. Chem. Soc., Perkin Trans. 1*, 1971, 93.
[58] A. Furlan, M. Furlan, B. Stanovnik, and M. Tisler, *Monatsh. Chem.*, 1974, **105**, 834 (*Chem. Abstr.*, 1974, **81**, 136081).
[59] S. Vidal, J. Court, and J. M. Bonnier, *J. Chem. Soc., Perkin Trans. 2*, 1976, 497.
[60] S. Vidal, J. Court, and J. M. Bonnier, *Tetrahedron Lett.*, 1976, 2023.
[61] J. M. Bonnier and J. Court, *Bull. Chim. Soc. Fr.*, 1972, 1834.

radicals is unaffected by the nature of the substituent; in contrast both rates of attack and orientation of substitution of the corresponding pyridinium ions are so affected.[62] Evidence for the nucleophilic character of Ph$^{\bullet}$ is provided[63] by the sensitivity of the rate of attack at C-2 of some 4-substituted pyridines upon the nature of the substituent in the radical. The different reaction conditions favoured by different research groups may explain some of the apparent discrepancies, we suggest; the consequence of generating phenylating species from precursors which may co-ordinate with heterocyclic nitrogen to provide substrates with pyridinium-like properties may be more fundamental than cursory consideration might indicate.

Photolytic homolysis of benzoyl peroxide in furan or in thiophene has been followed by ESR studies, which indicated the formation of radicals derived from the attack, at C-2, of both phenyl and benzoyloxy radicals.[64] The thermolysis of PAT (3) gives 2-phenyl-5-triphenylmethylthiazole from thiazole, a product which presumably arises from the oxidation of the trapping product, by analogy with observations in the pyridine and benzene system.[65] 2,5-Dimethylfuran appears to compete very effectively with arenes towards most radical sources. In a 1:6-mixture with benzene, it trapped 97% of the radicals from thermolysing benzoyl peroxide in the form of benzoic acid and 5-methyl-2-(benzoyloxymethyl)furan.[66] An electron-transfer mechanism may also explain the high reactivity of 2,5-dimethylfuran towards aroyloxylation. NNA under the same conditions provided 2-benzyl-5-methylfuran, apparently by the acetate ion deprotonation of the dimethylfuran–PhN_2^+ complex.[67] Derivatives of NNA were studied in this competition; the parent compound gave 2-benzyl-5-methylfuran (27%) and 3-acetyl-5-methyl-1-phenyl-4-(phenylazo)pyrazole (20%).[68] Such results give information on the behaviour of NNA under thermolysis but because of the concurrence of heterolytic and homolytic reactions may not be generally applicable to the arylation process.

7 Other Sources of Aryl Radicals

Aryl radicals may be made by a number of processes; photolysis of p-Me·C_6H_4·SO_2-N=N·C_6H_4·X (X = Cl or H) provides them[69] and Ph$^{\bullet}$ and p-MeO·$C_6H_4^{\bullet}$ have been trapped.[70] Photolysis of chlorobenzene similarly provides chlorobiphenyls whose isomer distribution parallel those found using other sources of Ph$^{\bullet}$, but only at low concentrations. In more concentrated solutions, the p-isomer is formed in greatest amount; this is attributed to a triplet excimer of PhCl.[71] Gamma-radiolysis

[62] R. Arnaud, J. Court, J. M. Bonnier, and J. Fossey, *Nouv. J. Chem.*, 1980, **4**, 299 (*Chem. Abstr.*, 1980, **93**, 180306k).
[63] A. Clerici, F. Minisci, and O. Porta, *Gazz. Chim. Ital.*, 1973, **103**, 171.
[64] L. Lunazzi, G. Placucci, and L. Grossi, *J. Chem. Soc., Perkin Trans. 2*, 1982, 875.
[65] G. Fenech, A. Chimirri, and R. Ficarra, *J. Pharm. Sci.*, 1978, **67**, 1432.
[66] J. I. G. Cadogan, J. R. Mitchell, and J. T. Sharp, *Chem. Comm.*, 1971, 1433.
[67] J. I. G. Cadogan, J. R. Mitchell, M. J. P. Harger, and J. T. Sharp, *Chem. Comm.*, 1971, 1432.
[68] J. I. G. Cadogan, J. R. Mitchell, and J. T. Sharp, *J. Chem. Soc., Perkin Trans. 1*, 1972, 1304.
[69] M. Kobayashi, S. Fujii, and H. Minato, *Bull. Chem. Soc. Jpn.*, 1972, **45**, 2039.
[70] M. Kobayashi, E. Akiyama, H. Minato, and N. Kito, *Bull. Chem. Soc. Jpn.*, 1974, **47**, 1504.
[71] M. Kojima, H. Sakuragi, and K. Tokumaru, *Chem. Lett.*, 1981, 1539 (*Chem. Abstr.* 1982, **96**, 43745w)

of nitrobenzene gives nitrobiphenyls in which contributions came from a free-radical component [40% of the reaction, and quenched by DPPH (2)] and an ionic component (33% of the reaction, quenched by SF_6, and associated with $C_6H_5NO_2^-$). Galvinoxyl specifically improved the yield of 2-nitrobiphenyl, and was therefore thought[72] to provide a new and more selective phenylating species. Flash photolysis of p-$C_6H_4Br_2$ in benzene showed the intermediacy of cyclohexadienyl radicals in the formation of 4-bromobiphenyl and p-terphenyl. Deuterium was less easily displaced than hydrogen by a factor of 1.8 (p-$C_6H_4Br_2$) or 1.5 (p-Br·C_6H_4·Ph).[73] Radiolysis of benzene in aqueous media gave phenol, biphenyl, dicyclohexadienes, and phenyl-2,4- and -2,5-cyclohexadiene.[74] Aryl radicals are also formed in the vapour-phase pyrolysis of nitrobenzene[75a] and of a number of benzene derivatives;[75b] in each case, biaryls can be obtained.

8 Details of Mechanism

The intermediacy of phenyl radicals, and of phenylcyclohexadienyl radicals (sigma-radicals) seems undoubted. The details of the chemistry of these radicals, which determines so critically the observed products of reaction and their relative amounts, are mainly known by inference. Increasingly, however, direct measurements are becoming available of the properties of these species.

While earlier assessments suggested that Ph$^\bullet$ was a most reactive species unlikely to survive many collisions, an opinion justified by the relatively small differences in reactivity observed by competition reactions, calculations suggest a somewhat greater stability.[75,76] Competition reactions using PAT and iodine in simple arenes and generating Ph$^\bullet$ photolytically suggested rate constants for the attack by Ph$^\bullet$ upon ArH of the order of 10^6 M^{-1} s^{-1}, a value[77] rather less than that (k_2, *ca.* 3×10^9 M^{-1} s^{-1}) expected of diffusion control. Direct measurement of the rates of reaction of Ph$^\bullet$ (generated by the photolysis of iodobenzene or of benzoyl peroxide in Freon 113 at 25 °C) upon benzene, toluene, or chlorobenzene show rate constants (0.45, 1.7, and 1.2×10^7 M^{-1} s^{-1} respectively) which again are rather less than those expected of a nearly diffusion-controlled process. However, the relative rates of attack deduced from these rate constants are rather greater than those commonly proposed from competition studies in the classical homolytic phenylation studies (*e.g.* k_{PhMe}/k_{PhH}, 1.23; k_{PhCl}/k_{PhH}, 1.15).

This discrepancy might be explained by postulating the reversibility of attack by Ph$^\bullet$ upon the arene; this then allows a range of apparent relative rates of reaction

[72] J. A. Knight, *Radiat. Res.*, 1973, **54**, 207 (*Chem. Abstr.*, 1973, **79**, 11943s).
[73] C. L. Pederson and C. Lohse, *Acta Chem. Scand.. Ser. B*, 1979, **B33**, 649.
[74] M. K. Eberhardt, *J. Phys. Chem.*, 1974, **78**, 1795.
[75] (*a*) E. K. Fields and S. Meyerson, *J. Org. Chem.*, 1967, **32**, 3114; (*b*) R. Louw and H. J. Lucas, *Recl. Trav. Chim. Pays-Bas*, 1973, **92**, 55.
[76] J. M. McBride, *J. Am. Chem. Soc.*, 1977, **99**, 6760; V. Palm and R. Hiob, *Org. React.* (*Tartu*) 1981, **18**, 152.
[77] R. G. Kryger, J. P. Lorand, N. R. Stevens, and N. R. Herron, *J. Am. Chem. Soc.*, 1977, **99**, 7589.

depending upon whether the processes studied were truly kinetically controlled, or thermodynamically controlled. However, the reaction between two sigma intermediate radicals proceeds at an apparent rate (k_2, 7—9 × 10^8 M^{-1} s^{-1})[78] not much less than that expected of a diffusion-controlled process. The above explanation would therefore not be tenable if the biaryl products are formed only by disproportionation of these radicals. In general, this is not the case; other oxidizing agents such as BzO$^\bullet$ (whose reaction with the intermediate radical might also be expected to be very fast, since Griller *et al.* argue that BzO$^\bullet$ must have only a very short lifetime) or Bz_2O_2 are usually thought to be major contributors to biaryl formation in reactions with benzoyl peroxide.

Theoretical studies of phenylation processes seem to confirm the classical mechanism. A MNDO study of the addition of Ph$^\bullet$ to PhH suggests the process to be strongly exothermic and therefore to have a transition state occurring early along the reaction path;[79] reversibility becomes unlikely under such conditions. A study of the attack of Me$^\bullet$, HO$^\bullet$, or Ph$^\bullet$ upon PhMe, PhCl, and $PhNO_2$ suggests that the high incidence of *o*-substitution during homolytic phenylation arises from the rearrangement of *ipso*-intermediates.[80] The theoretical studies show this process to be kinetically preferred to substitution in the case of *ipso*-attack, and that, under kinetic control, the probability of this rearrangement depends upon the polarity of the attacking aryl radical. The suggestion of rearrangement of an *ipso*-intermediate is not a novel explanation of the high incidence of *ortho*-attack, nor does it explain why over 50% of substitution appears to take place at these sites in the majority of PhX substrates.[1–3] Displacement of substituents (*i.e. ipso*-attack) can involve the loss of halogen, especially iodine,[81,82] and even fragments like $-CO_2Me$,[83] and fluorine (see below). Frontier orbital theory has been applied to understanding the phenylation process,[84] with only moderate success but has led to the explanation of some unusual aspects of the substitution process.

Critical bond-length calculations[85] assess the formation of Ph$^\bullet$ from PhX or, alternatively, the ease of abstraction of X by Ph$^\bullet$. The calculations used two methods; the disagreement between results was worse for PhX than for MeX. Such calculations are relevant, of course, in the formation of phenyl radicals from iodobenzene. The transfer of iodine from one aryl fragment to another

$$\mathrm{ArI} + \mathrm{Ar'}^\bullet = \mathrm{Ar'I} + \mathrm{Ar}^\bullet \qquad (13)$$

is held to proceed *via* a '9-I-2 intermediate'[86] also formed by the reduction of

[78] D. Griller, P. R. Marriott, D. C. Nonhebel, M. J. Perkins, and P. C. Wong, *J. Am. Chem. Soc.*, 1981, **103**, 7761.
[79] R. Arnoud, J. Douady, and R. Subra, *Nouv. J. Chim.*, 1981, **5**, 181, *Chem. Abstr.*, 1981, **95**, 42111d.
[80] S. V. Volovik, G. G. Dyadyusha, and V. I. Staninets, *Zh. Org. Khim.*, 1982, **18**, 1142
[81] J. F. Bunnett and C. C. Wamser, *J. Am. Chem. Soc.*, 1966, **88**, 5534.
[82] D. L. Brydon and J. I. G. Cadogan, *J. Chem. Soc. (C)*, 1968, 819.
[83] G. H. Jones, *J. Chem. Res. (S)*, 1982, 288.
[84] I. Fleming, Frontier Orbitals and Organic Chemical Reactions, J. Wiley and Sons, N.Y., 1976.
[85] A. D. Shuklov, Yu. D. Orlov, Yu. A. Pankrushev, *Kinet. Katal.*, 1983, **24**, 991.
[86] D. D. Tanner, D. W. Reed, and B. P. Setiloane, *J. Am. Chem. Soc.*, 1982, **104**, 3917.

unsymmetrically substituted diaryliodonium ions ($[Ar–I–Ar']^+$). This reduction may be brought about by 2,6-di-t-butylphenoxide ion; the diaryl ether products may then arise either from capture of $Ar^\bullet$ by $Ar'O^\bullet$, or by nucleophilic attack upon the diaryliodonium ion, a process assisted by *p*-CN or *p*-NO_2 groups and referring back to the earlier work of Beringer.[87]

Probably the greatest impediment to understanding the details of the arylation reactions will be removed with direct studies of the fate of the aryl radical, for here there is less ambiguity of interpretation. The arguments based upon the nature and efficiency of the oxidation process remain, but perhaps the greatest difficulty has been the rapidity of the elementary processes. Where rates of reaction approach the diffusion-controlled limit it is improper to apply conventional solution kinetic analysis, for the homogeneity of the reacting system is not assured, and discrimination between possible reaction sites may not be completely free, either because of preliminary aggregation of potential sites and reactants or because the short life of the radical precludes complete selection between sites. In this context, the recent study of phenyl radical reaction in SDS micelles[88] may show unexpected parallels between the behaviour of $Ph^\bullet$ in this 'constrained' situation and in solution where formally it is free.

9 Reactions with Polyfluoroaromatic Radicals and Polyfluoroarenes

Replacement of a number of hydrogen atoms by fluorine drastically alters the chemical properties of aromatic systems, partly because of the much greater electronegativity of fluorine than of hydrogen, and partly because of the greater dissociation energy of C–F then of C–H bonds. Hence arylation reactions in which such replacements have been made in the substrate, the radical, or both are of interest and have been studied. The simplest examples (equations 14—16) of the three above situations are those in which all of the appropriate hydrogens have been replaced by fluorine.

$$C_6H_5^\bullet + C_6F_6 \longrightarrow C_6H_5{\cdot}C_6F_5 \qquad (14)$$

$$C_6F_5^\bullet + C_6H_6 \longrightarrow C_6F_5{\cdot}C_6H_5 \qquad (15)$$

$$C_6F_5^\bullet + C_6F_6 \longrightarrow C_6F_5{\cdot}C_6F_5 \qquad (16)$$

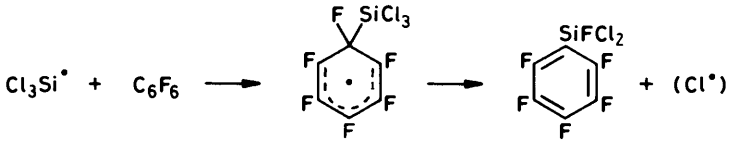
Reactions 14 and 16 are aryldefluorinations and reaction 15 is an aryldehydrogenation, like the reactions discussed in the previous sections.

10 Arylation of Polyfluorobenzenes

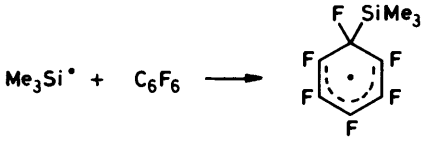
Aryldefluorination is different from aryldehydrogenation since it is the stronger C–F bond which has to be broken in the analogue of equation 2, and defluorination can in no sense be regarded as oxidation. Its mechanism must therefore be different from those of dehydrogenation. Additionally, the electron-withdrawal from the nuclei of polyfluoroarenes by the electronegative fluorine atoms would be expected

[87] F. M. Beringer and E. M. Gindler, *J. Am. Chem. Soc.*, 1955, **77**, 3200, 3203.
[88] E. G. Janzen and G. A. Coulter, *J. Am. Chem. Soc.*, 1984, **106**, 1962.

to render them susceptible to attack by nucleophilic rather than by electrophilic radicals. Thus silicon-centred radicals were the first to be shown to effect substitution in hexafluorobenzene. Homolytic attack on the nucleus of hexafluorobenzene by trichlorosilyl radicals has been demonstrated by Birchall, Daniewski, Haszeldine, and Holden[89] although the reaction is complicated by halogen exchange and the products of direct substitution are not formed (equation 17). Trimethylsilylation of hexafluorobenzene (equations 18 and 19) does however occur when a mixture of trimethylsilane and hexafluorobenzene is irradiated with ultraviolet light. The reaction presumably involves attack upon the nucleus of hexafluorobenzene by trimethylsilyl radicals.



(17)



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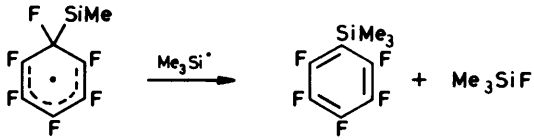


(19)

Phenyl radicals have no very pronounced polar character[2] and hence their attack on polyfluorophenyl nuclei should not be greatly inhibited for polar reasons. Likewise, while polar character can be observed in simple derivatives of phenyl radicals, its magnitude should not be a serious barrier to this process. Various sources of aryl radicals have been used[2] but most studies have been based upon the use of aroyl peroxides, whose thermolysis in simple arenes was discussed in Section 3 and summarized in Scheme 2. In hexafluorobenzene, the decomposition of benzoyl peroxide and of some simple derivatives proceeds readily and gives remarkably good yields of the biaryls (ArC_6F_5) arising from attack of the solvent[90] (Table 1).

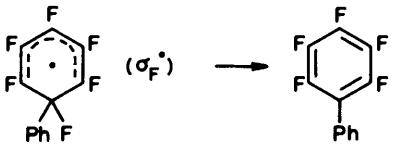
The two points of interest here were (i) that the generated radicals attacked hexafluorobenzene, and (ii) that the resulting intermediate radicals were able to lose fluorine. The contribution of an induced three-halves-order process to the decomposition of the peroxide has been demonstrated.[91]

[89] J. M. Birchall, W. H. Daniewski, R. N. Haszeldine, and L. S. Holden, *J. Chem. Soc.*, 1965, 6702.
[90] P. A. Claret, G. H. Williams, and J. Coulson, *J. Chem. Soc.* (*C*), 1968, 341.
[91] R. Bolton, M. W. Coleman, and G. H. Williams, *J. Fluorine Chem.*, 1974, **4**, 36.

Table 1 *Formation of derivatives of* 2,3,4,5,6-*pentafluorobiphenyl by decomposition of aroyl peroxides in hexafluorobenzene* (80 °C).

Substituent in peroxide	*Yield of biaryl (moles per mole peroxide)*
—	1.43
m-Me	1.10
m-Cl	0.64
m-Br	0.56

Although the parallel behaviour of benzene and of hexafluorobenzene suggests analogous mechanisms, problems arise when the defluorination of the intermediate complex ($\sigma_F^{\bullet}$) is considered (equation 20).

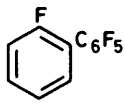


(20)

It is evident that a strong C–F bond cannot undergo homolysis to form either free fluorine atoms or fluorine molecules, since both of these processes must be strongly endothermic. The kinetics suggest a reaction with benzoyl peroxide (equation 21) by analogy with the hydrogen system (Scheme 2). This suggestion explains the formation of hydrogen fluoride and of benzoic acid (which are among the products) as resulting from the hydrolysis of fluorine benzoate, presumably with intermediate loss of oxygen from the originally formed perbenzoic acid.

$$\sigma_F^{\bullet} + Bz_2O_2 \longrightarrow Ph{\cdot}C_6F_5 + BzO^{\bullet} + BzOF \qquad (21)$$

Such a postulate must be rejected, however, since the reaction mixtures have no oxidizing properties other than those of the unreacted benzoyl peroxide, and reaction 21 is endothermic by *ca.* 200 kJ mol^{-1}. Such a process might explain the induced decomposition, but the yields of hydrogen fluoride and of benzoic acid do not reflect more than a minor contribution by this induced process, and certainly are insufficient to explain the much larger yields of biaryl.

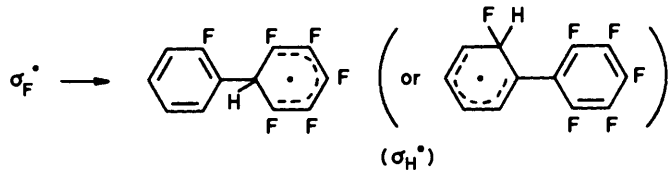


(11)

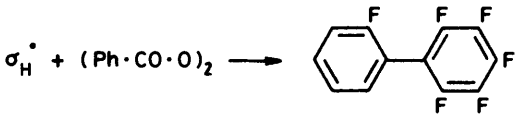
A little (5—10%) 2,2′,3,4,5,6-hexafluorobiphenyl (11) is formed[91,92] in this reaction, and rearrangement of $\sigma_F^{\bullet}$ to $\sigma_H^{\bullet}$ (equation 22) with subsequent dehydrogenation of the latter, probably by a reaction such as shown in equation 23, has been suggested to account for this. This sequence is a minor contributor to the

[92] E. K. Fields and S. Meyerson, *J. Org. Chem.*, 1967, **32**, 3114.

induced decomposition but provides an important source of benzoic acid whose significance in biaryl formation has now been realized (*q.v.*). More 2,3,4,5,6-pentafluorobiphenyl is formed by thermal decomposition of the reaction products during distillation at elevated temperatures.[93] However, even after due allowance has been made for these processes, a considerable proportion of the yield of the pentafluorobiphenyl formed by defluorination of $\sigma_F^{\bullet}$ during the reaction itself remains to be explained.



(22)



(23)

(11)

Table 2 *Products formed in the thermolysis of benzoyl peroxide* (0.10 M) *with* p-*fluorobenzoic acid in hexafluorobenzene*

[p-F·C_6H_4·CO_2H] (M)	0.0	0.1	0.45
Wt. of PhC_6F_5 (mg)	20	20	29
Wt. of 2,2′,3,4,5,6-hexafluorobiphenyl (mg)	1	0.0	0.0
Wt. of 2,3,4,4′,5,6-hexafluorobiphenyl (mg)	0.0	2	9

Added aroic acid assists the fluorination of $\sigma_F^{\bullet}$.[94,95] In the presence of p-fluorobenzoic acid the yield of 2,3,4,5,6-pentafluorobiphenyl from benzoyl peroxide and hexafluorobenzene was increased to the detriment of both the radical–radical addition process and the yield of 2,2′,3,4,5,6-hexafluorobiphenyl formed by equation 22. The results are shown in Table 2. The 2,3,4,4′,5,6-hexafluorobiphenyl must have arisen from arylation of hexafluorobenzene by p-fluorophenyl radicals formed through the sequence shown in equations 24 and 25,

$$\sigma_F^{\bullet} + p\text{-F}\cdot C_6H_4\cdot COOH \longrightarrow Ph\cdot C_6F_5 + p\text{-F}\cdot C_6H_4COO^{\bullet} + HF \qquad (24)$$

$$p\text{-F}\cdot C_6H_4\cdot COO^{\bullet} \longrightarrow p\text{-F}\cdot C_6H_4^{\bullet} + CO_2 \qquad (25)$$

[93] P. H. Oldham, G. H. Williams, and B. A. Wilson, *J. Chem. Soc.* (*B*) 1970, 1346.
[94] R. Bolton and J. P. B. Sandall, *J. Chem. Soc., Chem. Commun.*, 1973, 286.
[95] R. Bolton, J. P. B. Sandall, and G. H. Williams, *J. Fluorine Chem.*, 1974, **4**, 347.

An analogous sequence is possible with the benzoic acid which is formed during the arylation of hexafluorobenzene by benzoyl peroxide; this benzoic acid could then be responsible for the defluorination of $\sigma_F^{\bullet}$ (equation 26).

$$Ph{\cdot}C_6F_6^{\bullet} + BzOH \longrightarrow Ph{\cdot}C_6F_5 + HF + BzO^{\bullet} \qquad (26)$$

This hypothesis is supported by a study of the decomposition of PAT (3) in hexafluorobenzene. This gives very little 2,3,4,5,6-pentafluorobiphenyl, since no mechanism exists for the defluorination of the intermediate radical formed by the addition of phenyl radicals from PAT to hexafluorobenzene. The yield of biaryl was raised by added benzoic acid even though this must compete with hexafluorobenzene for the available phenyl radicals.

This hypothesis suffers from the difficulty that when it is applied to the reaction between benzoyl peroxide and hexafluorobenzene in the absence of added aroic acid neither the hydrogen fluoride nor the benzoic acid formed during the decomposition are commensurate with the requirements of the proposed mechanism. However, a cyclic process is available in which benzoic acid is supplied continuously during the reaction. Reactions of benzoyloxy radicals analogous to those of phenyl radicals must take place and must lead to the formation of the intermediate $\sigma'_F{}^{\bullet}$ (27) which may dimerize or react with other radicals, including $\sigma_F^{\bullet}$.

$$BzO^{\bullet} + C_6F_6 \longrightarrow [BzO{-}C_6F_6]^{\bullet}\ (\sigma'_F{}^{\bullet}) \qquad (27)$$

The products are inevitably benzoate esters of tertiary alcohols, and as such must be cleaved by hydrogen fluoride, thus regenerating benzoic acid (equation 8).

$$R{-}C_6F_6{-}OBz + HF \longrightarrow R{-}C_6F_7 + BzOH \qquad (28)$$

The same benzoyloxy radical may account for two products, for it may first terminate a radical reaction or attack the solvent to give $\sigma'_F{}^{\bullet}$ and may then produce benzoic acid. When this forms pentafluorobiphenyl in defluorinating $\sigma_F^{\bullet}$ it regenerates a benzoyloxy radical which may undergo any one of a number of fates (equations 29—30).

$$BzO^{\bullet} \longrightarrow Ph^{\bullet} + CO_2 \qquad (29)$$

$$BzO^{\bullet} + X^{\bullet} \longrightarrow X{-}OBz\ (X = \text{any radical}) \qquad (30)$$

Disproportionation (equation 32) is not a significant source of pentafluorobiphenyl, for when $\sigma_F^{\bullet}$ is formed during the thermolysis of PAT in hexafluorobenzene neither this radical nor triphenylmethyl radical abstract fluorine from $\sigma_F^{\bullet}$, and both preferentially undergo simple radical–radical combination reactions (equation 31).

$$2\sigma_F^{\bullet} \longrightarrow \sigma_F\text{–}\sigma_F \text{ (Dimer)} \tag{31}$$

$$2\sigma_F^{\bullet} \not\longrightarrow \text{Ph}\cdot C_6F_5 + \text{Ph}\cdot C_6F_7 \tag{32}$$

This proposed mechanism[91,95] for the decomposition of benzoyl peroxide in hexafluorobenzene is set out below (Scheme 5) for completeness. The processes described explain (i) the ease of defluorination of the radical intermediate, (ii) the formation of relatively small amounts of hydrogen fluoride and of benzoic acid, and (iii) the observed kinetics of the reaction.

$$Bz_2O_2 \longrightarrow 2BzO^{\bullet} \quad \text{(initiation)} \tag{33}$$

$$BzO^{\bullet} \longrightarrow Ph^{\bullet} + CO_2 \tag{34}$$

$$Ph^{\bullet} + C_6F_6 \longrightarrow \sigma_F^{\bullet} \tag{35}$$

$$2\sigma_F^{\bullet} \longrightarrow \sigma_F\text{–}\sigma_F \quad \text{(termination)} \tag{36}$$

$$BzO^{\bullet} + C_6F_6 \longrightarrow \sigma_F'^{\bullet} \tag{37}$$

$$2\sigma_F'^{\bullet} \longrightarrow \sigma_F'\text{–}\sigma_F' \quad \text{(termination)} \tag{38}$$

$$\sigma_F^{\bullet} \longrightarrow \sigma_H^{\bullet} \quad \text{(rearrangement)} \tag{39}$$

$$\sigma_H^{\bullet} + BzO^{\bullet}(Bz_2O_2) \longrightarrow 2'\text{-F}\cdot C_6H_4\cdot C_6F_5 + BzOH(+BzO^{\bullet}) \tag{40}$$

$$\sigma_F^{\bullet} + BzO^{\bullet}(Bz_2O_2) \longrightarrow \sigma_F - OBz(+BzO^{\bullet}) \tag{41}$$

$$\sigma_F^{\bullet} + BzOH \longrightarrow \text{Ph}\cdot C_6F_5 + HF + BzO^{\bullet} \tag{42}$$

$$\sigma_F^{\bullet}\text{–}OBz + HF \longrightarrow \text{Ph}\cdot C_6F_7 + BzOH \tag{43}$$

Scheme 5

Transesterification processes similar to equation 43 can also occur with other products (*e.g.* σ_F'–Ph, σ_F'–OBz). Derivatives of dihydrobiphenyl, such as $\text{Ph}\cdot C_6F_7$, have been shown to occur among the products[96] and are a necessary consequence of the transesterification process (equation 43) although they may be explained by a disproportionation reaction (see, however, above).

The kinetics of the decomposition of benzoyl peroxide now depend upon equation 33 as the origin of the spontaneous decomposition contribution, and upon equations 40 and 41 as the source of the induced decomposition, the kinetic order of which would (*cf.* benzene) depend upon whether the termination stage was brought about by like, or by unlike radicals.

Scheme 5 also explains the order of radical displacement ($F > NO_2 > Cl, Br$)[93] which is also the order of displacement by nucleophiles and is a consequence of hydrogen bonding between the emergent leaving group and either a hydroxylic solvent in heterolytic nucleophilic displacements[97,98] or a carboxylic acid in the radical displacements under discussion.

[96] R. Bolton, W. K. A. Moss, J. P. B. Sandall, and G. H. Williams, *J. Fluorine Chem.*, 1976, **7**, 597.
[97] A. J. Parker, *Quart. Rev.*, 1962, **16**, 163.
[98] J. Burdon, *Tetrahedron*, 1965, **21**, 3373.

Derivatives of terphenyl which are formed in this reaction have been shown by mass spectrometry[99] to be of the form $Ph{\cdot}C_6H_4{\cdot}Ph$ (12). Products of the type $Ph{\cdot}C_6F_4{\cdot}Ph$ (13) do not occur. These products must therefore arise by arylation of the peroxide (equation 44) or of benzoic acid (which also is formed when concentrated solutions of benzoyl peroxide decompose in benzene) (equation 45),[20,23] followed by the formation of biphenylyl radicals ($Ph{\cdot}C_6H_4^{\bullet}$) which arylate the hexafluorobenzene to give (12) only, rather than by further arylation of the initial product 2,3,4,5,6-pentafluorobiphenyl, which must give (13) as well as (12).

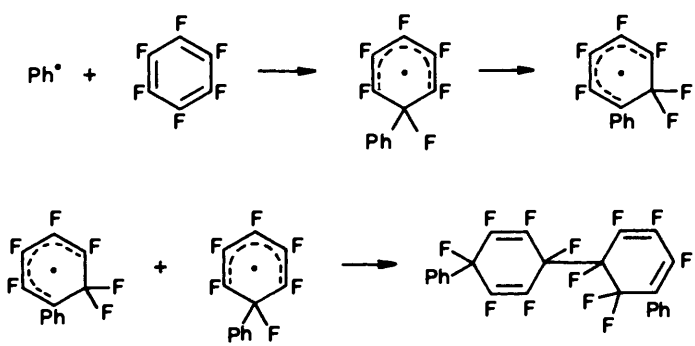
$$Ph^{\bullet} + Ph{\cdot}CO{\cdot}O{-}O{\cdot}CO{\cdot}Ph \longrightarrow Ph{\cdot}C_6H_4{\cdot}CO{\cdot}O{-}O{\cdot}CO{\cdot}Ph \qquad (44)$$

$$Ph^{\bullet} + PhCO_2H \longrightarrow Ph{\cdot}C_6H_4{\cdot}CO_2H \qquad (45)$$

These processes also provide an additional route to benzoic acid by the dehydrogenation (Scheme 2) of the radicals which they necessarily involve.

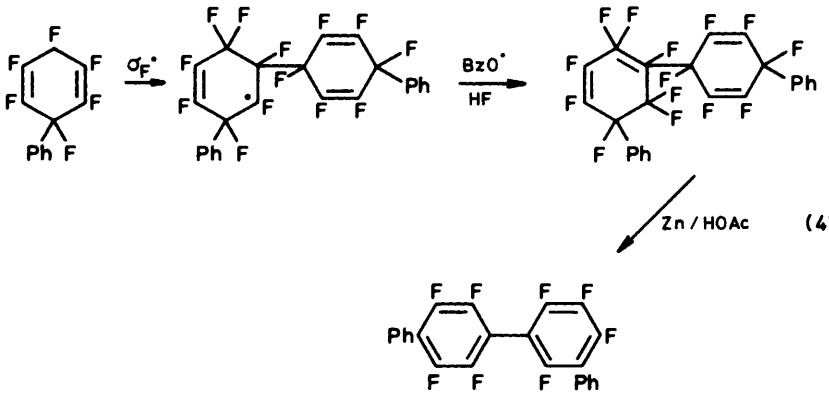
In the absence of any additives, the formed aroic acid is the defluorinating agent; other hydrogen donors, notably containing O–H bonds, can also fulfil this function; in some cases leading to improved yields of the biaryl.[96] The most effective such additive seems to be trichloroacetic acid.

These results and conclusions are consistent with products found to be formed in the thermolysis of benzoyl peroxide in hexafluorobenzene by Vlasova, Kobrina, and Yakobson,[100] who reported that the dehalogenation of the less volatile products gave derivatives of both 3,4′-and 4,4′-quaterphenyl ($Ph{\cdot}C_6H_4{\cdot}C_6H_4{\cdot}Ph$). The first structure is not expected from combination reactions of the radical intermediate, and 1,2-migration of a fluorine atom in this intermediate was suggested to explain the unexpected orientation of the derived polyfluoroquaterphenyls (equation 46).



(46)

[99] R. Bolton, W. A. Moss, J. P. B. Sandall, and G. H. Williams, *J. Fluorine Chem.*, 1975, **5**, 61.
[100] L. V. Vlasova, L. S. Kobrina, and G. G. Yakobson, *Izv. Sib. Otd. Akad. Nauk SSSR*, 1974, **3**, 97.



(47)

Polyfluoropolyhydroquaterphenyls may also be formed in addition reactions between the conventional radical intermediate $\sigma_F^{\bullet}$ and 1,4-dihydro-1,2,3,4,4,5,6-heptafluorobiphenyl (47), a product which has been identified[96] in the reaction mixture.

The yield of pentafluorobiphenyl formed in this thermolysis at 80 °C increases considerably from 0.67 moles (after 30 h) to 1.25 moles per mole of peroxide after 100 h. As the half-life of benzoyl peroxide is of the order of 10 h[91] the increased amounts of biaryl cannot principally arise from this reagent. It was similarly noted that both the amount of the identified tetranuclear products and the relative amount of the polyfluoropolyhydro-4,4′-quaterphenyl in this mixture fell in the course of further heating at 80 °C. While the reversible formation of this less volatile product was first noticed some years ago,[93] so that pyrolysis of the residue gave further amounts of biaryl, this work suggests that dimerization of the reaction intermediate, $\sigma_F^{\bullet}$, which is the origin of some of the quaterphenyl derivatives, is reversible even at 80 °C. This explains both the steady formation of biaryl after the obvious precursor (peroxide) was effectively all consumed, and the simultaneous diminution in the amount of the dimer of the reaction intermediate. As the formation of dimer is a kinetically controlled process, it may be the main termination step of the kinetic process (as shown above) and yet allow the formation of biaryl by thermodynamic control.[101]

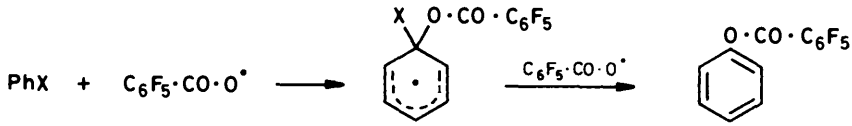
The reaction of alkyl and perfluoroalkyl peroxides with hexafluorobenzene also leads to the formation of σ-complexes by addition, but the fate of these appears[102] to be dimerization without fluorine loss.

Although several measurements of isomer ratios and relative rates of arylation of polyfluorobenzenes have been reported, the interpretation is complicated by other factors and they are therefore discussed in Section 12.

[101] L. S. Kobrina, V. P. Sass, S. V. Sokolov, and G. G. Yakobson, *Zh. Org. Khim.*, 1977, **13**, 1246.
[102] L. S. Kobrina and G. G. Yakobson, *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk*, 1967, 76.

11 Polyfluorophenylation of Arenes

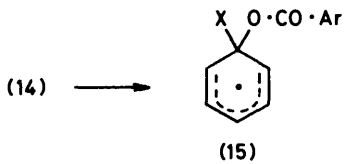
Reaction 15 has been shown to occur, since the thermolysis of pentafluorobenzoyl peroxide in benzene gives 2,3,4,5,6-pentafluorobiphenyl together with 2,3,4,5,6-pentafluorobenzoic acid and small amounts of phenyl pentafluorobenzoate.[103–105] A little high-boiling residue is formed, probably by dimerization of σ-complexes, and so the decomposition appears to follow Scheme 2. In chlorobenzene and in bromobenzene, however, the decomposition of pentafluorobenzoyl peroxide gives very little biaryl, the major product being phenyl (rather than halogenophenyl) pentafluorobenzoate formed by the *ipso*-replacement of the halogen by pentafluorobenzoyloxy radicals.[104] Fluorobenzene gives appreciable quantities of hexafluorobiphenyls and (fluorophenyl) pentafluorobenzoates,[105] but in all three halogenobenzenes the major processes involve halogen displacement. A mechanism (equation 48) has been suggested and discussed in some detail;[6] while not satisfactory in all respects it is consistent with the experimental findings.



$$+ \quad C_6F_5{\cdot}CO{\cdot}OX \qquad (48)$$

Ipso-attack by pentafluorobenzoyloxy-radicals is rationalized in terms of complexes formed initially by electron transfer between aroyloxy radicals and the halogen substituent. This suggestion allows an explanation of the remarkable vulnerability of the carbon–halogen bond (equation 49), although it needs

$$\mathrm{Ar{\cdot}CO{\cdot}O^{\bullet}} + \mathrm{X-Ph} \longrightarrow \underset{(14)}{\mathrm{Ar{\cdot}CO{\cdot}O^{-}}} \quad \overset{+\bullet}{\mathrm{X}}\mathrm{-Ph} \qquad (49)$$



(50)

electron transfer from halogen to oxygen, sometimes an implausible postulate. The resulting ion-pair may be stabilized by delocalization of the positive charge into the aromatic nucleus, thus rendering the electron transference more favourable. This process is also assisted by the electron attraction of the fluorine substituents which greatly enhances the electronegativity of the pentafluorobenzoyloxy radical.

[103] J. Burdon, J. G. Campbell, and J. C. Tatlow, *J. Chem. Soc.* (*C*), 1969, 882.
[104] P. H. Oldham and G. H. Williams, *J. Chem. Soc.* (*C*), 1970, 1260.
[105] M. W. Coleman, Ph.D. Thesis, London, 1972.

Collapse of (14) to form a σ-intermediate (15) (equation 50) must proceed by attack upon C-1, the removal of the halogen atom occurring through further reaction of (15) with the pentafluorobenzoyloxy radical (equation 48). The first-order kinetics shown in the decomposition of bis(pentafluorobenzoyl) peroxide in halogenobenzenes[105] are also consistent with such a termination stage. Such complexes have been suggested previously in the decomposition of benzoyl peroxide in bromobenzene (*cf.* Section 3) to explain the greater stability of benzoyloxy radicals in this solvent, although no *ipso*-substitution was observed there.

The decomposition of bis(pentafluorobenzoyl) peroxide in nitrobenzene gives mainly the isomeric nitro-2,3,4,5,6-pentafluorobiphenyls although some *ipso*-arylation provides pentafluorobiphenyl.[6] An analogous complex with pentafluorobenzoyloxy radicals, such as $PhX^{+\bullet}\ Ar^{-}$, may be involved here.

Thus bis(pentafluorobenzoyl) peroxide, because of the incidence of *ipso*-substitution, is not a good source of pentafluorophenyl radicals for the arylation of arenes other than benzene.

Aromatic amines, however, yield diazonium ions which, in the Gomberg reaction or with pentyl nitrite (Section 4) are sources of aryl radicals and ultimately of biaryls. Pentafluoroaniline cannot be successfully diazotized in predominantly aqueous media.[106] The diazonium ion first formed then undergoes nucleophilic attack to give a hydroxytetrafluorophenyl diazonium ion through the solubilizing and activating effects of the $-N_2^{+}$ substituent, and indeed tetrafluorohydroquinone is one of the isolated products. Diazotization by pentyl nitrite, however, takes place in initially anhydrous media. If the azo-ether (ArN=NOR) is formed through the condensation shown in equation 51, loss of fluorine caused by the nucleophilic attack of water is minimized because of the absence of the diazonium ion precursor. This procedure with pentafluoroaniline gives pentafluorobiphenyl with benzene, and an isomeric mixture of the corresponding derivatives with mono-substituted benzene.[107]

Phenols and azo-compounds are also formed, as is pentanol. The alcohol might arise from the dehydrogenation of the intermediate radical ($\sigma_H\cdot$) (equation 54) and the equations 51—54 offer a rationalization.

$$C_6F_5{\cdot}NH_2 + O{=}N{\cdot}OR \longrightarrow C_6F_5{\cdot}N{=}N{\cdot}OR + H_2O \qquad (51)$$

$$C_6F_5{\cdot}N{=}N{\cdot}OR \longrightarrow C_6F_5^{\bullet} + N_2 + {}^{\bullet}OR \qquad (52)$$

$$C_6F_5^{\bullet} + ArH \longrightarrow |C_6F_5{-}Ar{-}H|^{\bullet}(\sigma_H^{\bullet}) \qquad (53)$$

$$|C_6F_5{-}Ar{-}H|^{\bullet} + {}^{\bullet}OR \longrightarrow C_6F_5Ar + HOR \qquad (54)$$

The corresponding reaction between aniline and hexafluorobenzene in the presence of pentyl nitrite gives some pentafluorobiphenyl and this must occur through the defluorination of $\sigma_F^{\bullet}$ which may occur through equations 55 and/or 56, since some fluorobenzene and some hydrogen fluoride are formed.[6]

[106] J. M. Birchall, R. N. Haszeldine, and A. R. Parkinson, *J. Chem. Soc.*, 1962, 4966.
[107] P. H. Oldham, G. H. Williams, and B. A. Wilson, *J. Chem. Soc.* (*C*), 1971, 1094.

$$\sigma_F^{\bullet} + Ph^{\bullet} \longrightarrow PhF + PhC_6F_5 \quad (55)$$

$$\sigma_F^{\bullet} + ROH \longrightarrow PhC_6F_5 + HF + RO^{\bullet} \quad (56)$$

Isomer ratios and relative rates for pentafluorophenylation of arenes by this method have been measured and are discussed in Section 12.

The oxidation of 2,3,4,5,6-pentafluorophenylhydrazine in benzene by either silver oxide or bleaching powder gives good yields of pentafluorobiphenyl. The reaction is general, and appears to involve the formation of pentafluorophenyl radicals. With hexafluorobenzene as substrate, very little biaryl is formed. Pentafluorobenzene is the main reaction product, suggesting the reaction sequence 57—59. The initial product, pentafluorophenyl di-imine (equation 57) may either lose nitrogen to form pentafluorobenzene or suffer further oxidation to give the pentafluorophenyl radical (equation 58). The factors which determine which process prevails are not fully known, and the sequence shown in equations 57—59 does not describe the process in detail. A complex between pentafluorophenyldi-imine and the aromatic substrate might stabilize this species sufficiently to permit its further oxidation; such a complex would be unlikely with hexafluorobenzene as substrate, and so explain the collapse of the di-imine to lose nitrogen before oxidation occurs in this case.

$$C_6F_5{\cdot}NH{\cdot}NH_2 \longrightarrow [C_6F_5{\cdot}N{=}NH] \quad (57)$$

$$[C_6F_5{\cdot}N{=}NH] \xrightarrow{-H^{\bullet}} C_6F_5^{\bullet} + N_2 \quad (58)$$

$$[C_6F_5{\cdot}N{=}NH] \longrightarrow C_6F_5H + N_2 \quad (59)$$

Pentafluorophenylazotriphenylmethane has been prepared by conventional methods from pentafluorophenylhydrazine.[108,109] Its thermal decomposition in benzene gives nitrogen, triphenylmethane, and pentafluorobiphenyl; similarly predictable products arise from the corresponding decomposition in chloro-, bromo-, and nitro-benzene.

12 Complex Formation and its Influence on Isomer Ratios and Relative Rates

The formation of stable complexes between arenes and polyfluoroarenes is well known to occur, because of the strong electrical interactions between the respectively electron-rich and electron-poor nuclei.[110,111] Similar interactions would be expected to occur between the species in processes 14 and 15, and such interactions are likely to exert a profound effect upon the apparent relative rates of arylation of different aromatic compounds when these rates are deduced by competition methods. A similar effect might be found in the isomer distribution

[108] G. Wedzicha, Ph.D. Thesis, London, 1975.
[109] R. Bolton, J. P. B. Sandall, and G. H. Williams, *8th International Symposium on Fluorine Chemistry. Abstracts*, Kyoto, 1976, 0—34.
[110] E. M. Dantzler and C. M. Knobler, *J. Phys. Chem.*, 1969, **73**, 1602.
[111] M. E. Baur, C. M. Knobler, D. A. Horsma, and P. Perez, *J. Phys. Chem.*, 1970, **74**, 4694.

ratio of products formed in such processes. The measurement of partial rate factors relies upon such competition processes, and so the extent of any complicating effect arising from complex formation must be determined and, if necessary, allowance should be made for it.

The earlier reports[2] of results of competitive phenylation of mixtures of polyfluoroarenes with benzene cannot be regarded as reliable because of the non-ideal behaviour of such mixtures.[112,113] The problems may be minimized by using the hexafluorobenzene as the standard, and not benzene; the probability of complex formation between the aryl radical or a precursor and the individual substrates still remains. A suitable test for the existence of interactions which disturb free competition among substrates for a reagent is the 'additivity principle' concerning substituent effects. If free competition prevails, the effects of several substituents upon the observed relative rates of substitution at individual sites of polysubstituted arenes are expected to be additive. Such additivity has been shown to prevail in the simple phenylation of mono- and di-substituted benzenes, although some perturbation is observed with tri-substituted benzenes.[21,29] In contrast, little evidence is found for additivity of effect when pentafluorobenzene, bromopentafluorobenzene, and octafluorotoluene are allowed to compete with hexafluorobenzene for phenyl radicals generated by the thermolysis of benzoyl peroxide.[114] Partial rate factors derived from such experiments did not form a consistent set. However, the isomer distribution did not change in the presence of a competing substrate, and the orientation of attack upon all the derivatives of pentafluorobenzene was consistent and susceptible to logical explanation. It was therefore suggested that interactions between radical (or radical precursor) and substrate affected intermolecular, but not intramolecular, selection. This is understandable if two substrates form complexes of different stabilities with the radical or with a precursor, for the observed competition between substrates must reflect not only the intrinsic reactivities of the substrates towards the radical but also the extent of formation of the complexes, the collapse of which allows virtually no opportunity for the second substrate to compete. Competition among different sites within a substrate would not be expected to be similarly influenced unless the complex has a specific and well-defined structure which enhances the chance of some sites being attacked. In general, these complexes do not have rigidly defined structures and the radical can discriminate between possible substrate sites according to their intrinsic reactivity.

The isomer ratios obtained in such work are shown in Figure 1. Clearly in pentafluorobenzene hydrogen is more readily replaced than fluorine, reflecting the different mechanisms of dehydrogenation and defluorination (*cf.* Section 10; this competition is further discussed in Section 13). Apart from the hydrogen-bearing C-1, C-3 is the most reactive site. These two positions were considered to be the most susceptible because the σ-complex arising from their attack is stabilized by resonance contributions from three fluorine atoms *ortho* and *para* to them and may

[112] C. R. Patrick and G. S. Prosser, *Nature*, 1960, **187**, 1021.
[113] J. M. Birchall, R. Hazard, R. N. Haszeldine, and A. W. Wakalski, *J. Chem. Soc.* (*C*), 1967, 47.
[114] R. Bolton, J. P. B. Sandall, and G. H. Williams, *J. Fluorine Chem.*, 1974, **4**, 355.

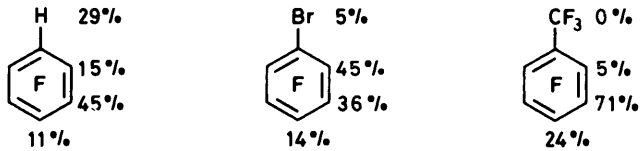


Figure 1 *Yields of isomeric phenylation products from thermolysis of benzoyl peroxide in* C_6F_5X

therefore be more readily formed than those arising from attack at C-2 and C-4 where only two fluorine substituents may participate in the stabilization.

Although in benzene derivatives (PhX) *ortho*:*para* ratios of above 2 are common, a directly opposite effect is evident in pentafluorobenzene, regarding hydrogen as the substituent. The explanation is common to both systems; σ-intermediates are stabilized by *ortho* substituents more than by *para* substituents, and the C-4 site is flanked by two fluorine atoms whereas C-2 has only one such group.

The same effect is seen in the arylation of octafluorotoluene, with a steric effect further lowering the reactivity at C-2. As in pentafluorobenzene, C-3 is the most susceptible site, probably for similar reasons. The relative reactivities of C-3 and C-4 in both systems arises from the presence of three, and not two, fluorine substituents contributing to the stability of the C-3 intermediates.

The above conclusions regarding complex formation between phenyl radicals or their precursors and polyfluorobenzenes were substantiated by a detailed study of the phenylation of a series of ten polyfluorobenzenes $C_6H_xF_{6-x}$ (x = 2—6), both singly and in as many pairs as was analytically possible.[115] The results showed (i) that the isomer ratios measured (intramolecular competition) for reactions involving both dehydrogenation and defluorination were mutually consistent and could be predicted by application of the additivity principle (see also Section 13), (ii) that such a consistent set of factors could not be obtained from results of reactions involving intermolecular competition, (iii) that these disturbances were much more serious when penta- or hexa-fluorobenzene was a competing substrate, which was consistent with complex formation, (iv) that the specific presence of hexafluorobenzene leads to increased selectivity in the phenylation of less fully fluorinated substrates, even in intramolecular competition, which implied that the phenyl radical was stabilized by complex formation between itself and hexafluorobenzene.

As expected, similar complexes can be formed, with similar effects, in the pentafluorophenylation of non-fluorinated arenes (equation 15) and again it is inter- rather than intra-molecular competition which is affected. These conclusions were established by a study of the pentafluorophenylation ($C_6F_5NH_2/C_5H_{11}ONO$) of a series of mono- and di-substituted benzene derivatives (fluorobenzene, toluene, anisole, *p*-fluoroanisole, *p*-fluorotoluene, and *p*-difluorobenzene) both singly and in competition with each other and with benzene.[116] As well as using the additivity

[115] K. J. Allen, R. Bolton, and G. H. Williams, *J. Chem. Soc., Perkin Trans. 2*, 1983, 691.
[116] R. Bolton, J. P. B. Sandall, and G. H. Williams, *J. Chem. Res.* (*S*), 1977, 24; (*M*), 0323.

principle a second test was applied to the results of competition experiments. Equation 60 (where, for example, ${}^{A}K_{C}$ is the rate of arylation of substrate A relative to that of substrate C and ${}^{A}K_{B}$ and ${}^{B}K_{C}$ are defined analogously) should be obeyed if the substrates compete freely for the radicals, but discrepancies can be expected if radical–substrate complexes are formed.

$$ {}^{A}K_{C} = {}^{A}K_{B} \cdot {}^{B}K_{C} \qquad (60) $$

Both tests revealed discrepancies, those in the latter test showing differences of between 11% and 43% between observed and calculated values. Such discrepancies were well outside the experimental error.

It follows that conclusions relating to effects of substituents in these reactions, as in the aryldefluorinations discussed earlier, should be based only on isomer ratios and not on relative rates because the latter are dependent upon other selection processes. Isomer ratios for the pentafluorophenylation of arenes confirm unequivocally the highly electrophilic nature of the pentafluorophenyl radical, postulated earlier on the basis of less extensive information.[2] These results given in Table 3

Table 3 *Orientation of phenylation and pentafluorophenylation of arenes*

		Isomer distribution (%)				
Substrate	*Radical*	*ortho*	*meta*	*para*	*(o + p)/m*	*Ref.*
PhF	$C_6H_5\cdot$	55.2	29.8	15.0	2.4	13
PhF	$C_6F_5\cdot$	39	19	42	4.3	45
PhCl	$C_6H_5\cdot$	57.6	26.1	17.3	2.9	42
PhCl	$C_6F_5\cdot$	64.7	20.6	14.7	3.9	2
PhBr	$C_6H_5\cdot$	54.5	29.5	16.0	2.4	42
PhBr	$C_6F_5\cdot$	61.6	26.3	12.1	2.8	2
$PhNO_2$	$C_6H_5\cdot$	62.5	9.8	27.7	9.2	2
$PhNO_2$	$C_6F_5\cdot$	20.8	53.4	25.8	0.87	2
$PhCH_3$	$C_6H_5\cdot$	60.9	21.6	17.5	3.6	42
$PhCH_3$	$C_6F_5\cdot$	54	23	23	3.3	45
$PhOCH_3$	$C_6H_5\cdot$	68.8	20.1	11.1	4.0	42
$PhOCH_3$	$C_6F_5\cdot$	50	10	40	9.0	45

show clearly that the (*ortho* + *para*)/(*meta*) ratios for pentafluorophenylation are higher than those for phenylation when X in the substrate PhX is *ortho–para* directing towards electrophiles and lower when X is *meta* directing. Particularly striking differences are seen with anisole and nitrobenzene; the results for toluene show a slight anomaly, the small observed change being in the 'wrong' direction. This might be an experimental artefact arising from the increased difficulty of accurate measurement of isomer ratios in a substrate which is also susceptible to attack upon the side-chain to yield other binuclear products.

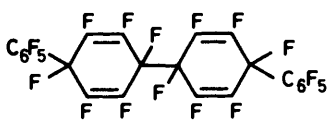
13 The Relative Replaceability of Hydrogen and Fluorine

Although replacement of aromatic fluorine by aryl radicals is a relatively easy process (Section 12), the direct measurement of the relative reactivities of hydrogen- and fluorine-bearing sites towards aryl radicals (*e.g.* competition with mixtures of

benzene and hexafluorobenzene) cannot give reliable results because of complex formation between potential reactants. The comparison may be made indirectly from the measurements of the relative yields of all the possible products of both phenyldefluorination and phenyldehydrogenation of nine polyfluorobenzenes ($C_6H_xF_{6-x}$ where $x = 2$—5).[115-117] By using the known partial rate factors for the phenylation of fluorobenzene (f_{o^-F}, 2.0; f_{m-F}, 1.1; f_{p-F}, 1.1) and applying the additivity principle the observed yields of the products of both aryldehydrogenation and aryldefluorination could be predicted, provided that an additional parameter was included to reflect the relative eases of displacement of fluorine and of hydrogen. The parameter had the empirically obtained single value of 0.3; the match between calculated and observed orientations was very good for all di- and tri-fluorobenzenes and for 1,2,3,4-tetrafluorobenzene, but was somewhat poorer for 1,2,3,5- and 1,2,4,5-tetrafluorobenzenes, and for pentafluorobenzene.

Of the three possible processes [equations 13, 14, and 15] mentioned in Section 9, only equation 15, aryldefluorination with polyfluorophenyl radicals, remains to be discussed. There are two possible reasons which suggest themselves to explain the difficulty of this process. Firstly, attack by the highly electrophilic pentafluorophenyl radical upon a highly fluorinated arene, necessarily highly deactivated towards electrophiles, is not expected to be favoured. Secondly, even if an intermediate radical, $\sigma_F\cdot$, can be formed in such a system, no defluorination mechanisms exists if both radical and substrate are fully fluorinated because there is no hydrogen to furnish the aroic acid which is the defluorinating agent (Section 10).

Reactions of bis(pentafluorobenzoyl) peroxide with hexafluorobenzene, octafluorotoluene, and decafluorobiphenyl have been reported and give mainly products of dimerization of $\sigma_F^{\bullet}$ radicals forming species such as (16).[118,119] Some



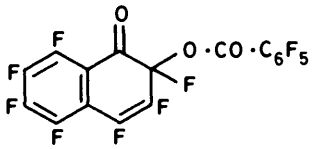
(16)

rearrangement of σ-complexes by 1,2-fluorine migration can also occur. The lack of a defluorination mechanism, rather than any difficulty of formation of $\sigma_F^{\bullet}$, evidently precludes the formation of biaryls in these systems. Added aroic acid in this case has no effect upon the yield of biaryl, suggesting that dimerization of the radical intermediate $\sigma_F^{\bullet}$ is a fast process.

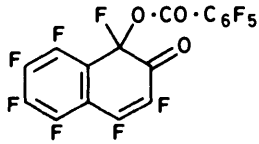
Pentafluorobenzoyloxylation occurs when bis(pentafluorobenzoyl) peroxide decomposes in the presence of heptafluoro-1- or -2-naphthol which give (17) and

[117] R. Bolton, J. P. B. Sandall, and G. H. Williams, *J. Fluorine Chem.*, 1978, **11**, 591.
[118] L. V. Vlasova, L. S. Kobrina, and G. G. Yakobson, *Zh. Org. Khim.*, 1974, **10**, 787.
[119] L. S. Kobrina, V. L. Salenko, and G. G. Yakobson, *J. Fluorine Chem.*, 1976, **8**, 193; 1977, **13**, 1693.

(18) among other products.[120] The reaction of bis(pentafluorobenzoyl) peroxide



(17)



(18)

with methoxybenzene derivatives[121] seems also to involve electron-transfer processes, earlier postulated in the aroyloxylation of arenes.[122]

[120] L. S. Kobrina, N. V. Popkova, and G. G. Yakobson, *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk*, 1976, 140.
[121] C. Zhao, X. Jiang, and J. Zhang, *J. Fluorine Chem.*, 1985, **24**, 401.
[122] C. Walling and C. Zhao, *Tetrahedron*, 1982, **38**, 1105.