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HOMOLYTIC REACTIONS OF POLYFLUOROAROMATIC COMPOUNDS PART VII.* PRODUCTS AND RELATIVE RATES OF PHENYLATION OF PENTAFLUOROBENZENE, BROMOPENTAFLUOROBENZENE AND OCTAFLUOROTOLUENE WITH BENZOYL PEROXIDE

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Summary

Competitive rates of arylation of the title compounds were measured using hexafluorobenzene as reference. The results suggest that the species responsible for intermolecular discrimination and those responsible for intramolecular selection are not the same. The significance of this observation is discussed.

Introduction

Benzoyl peroxide decomposes in hexafluorobenzene to give 2,3,4,5,6-pentafluorobiphenyl [2,3]; pentafluorophenyl analogues react similarly. For example, bromopentafluorobenzene gives the three isomeric bromotetrafluorobiphenyls [4]. The mechanism of this reaction, which involves displacement of fluorine, has been the subject of recent reports [1,5]; it is substantially different from that proposed [6] for the phenylation of benzene through the thermolysis of benzoyl peroxide. The relative rates of arylation of polyfluoroaromatic compounds have been reported [7] using benzene as the reference [4]. As this requires the use of mixtures of benzene and polyfluorobenzenes, which show far from ideal behaviour [8], and as the displaced atom and the associated mechanism of substitution are different in each case, the requirements for the successful use of the competition method are not met [9].

Competition reactions in which hexafluorobenzene is the reference compound should, in the main, avoid these particular objections. The displaced atom is now fluorine in both substrates. Also putative complexes between the substrates will be far less stable. We report the results of such reactions involving pentafluorobenzene, bromopentafluorobenzene, and octafluorotoluene.

* For Part VI, see ref. 1.

Results and Discussion

Mechanism of arylation of polyfluorinated aromatic systems

The thermolysis of benzoyl peroxide in hexafluorobenzene at 80 °C gives considerable yields of pentafluorobiphenyl, despite the differences in energies involved in displacing fluorine, and not hydrogen, from an aromatic carbon atom [2,3]. The mechanism of production of phenyl radicals in this reaction is generally thought to be that found in decompositions of the peroxide in benzene, since the process does not involve participation by the solvent in any of the proposed elementary steps, *i. e.*

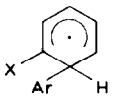
$Bz_2O_2 = 2BzO\cdot$

$BzO\cdot = Ph\cdot + CO_2$

although induced decomposition of the peroxide by radical intermediates may make different contributions in the two cases.

In hexafluorobenzene, the removal of fluorine is thought to involve the formation of hydrogen fluoride from species such as benzoic acid, formed in side-reactions; the oxidative aromatisation by benzoyloxy radicals or by benzoyl peroxide cannot now occur (*cf.* benzene).

The transition state in the arylation of simple substituted benzenes (*e. g.* C_6H_5X) is generally considered to have a structure between that of the ground state and that of the σ-intermediate (I):



$= \sigma_H\cdot$ (I)

Specifically, partial bonding occurs between the entrant radical and the carbon atom under attack, and delocalisation of electrons occurs throughout the ring and, where appropriate, the substituents. Such delocalisation by the substituent is considered responsible for the observed orientation of substitution in homolytic arylation. In the polyfluoroaromatic systems (C_6F_5X) the choice lies between structures using fluorine or X as substituents for delocalisation, and is not therefore as limited as in simple benzene systems where hydrogen cannot so participate. This may then cause different isomer distributions to be found in the arylation of C_6F_5X compared with those found for C_6H_5X. In the latter case, the *ortho* position is often the most vulnerable site to arylation, regardless of the electronic nature of X (*e. g.* anisole and nitrobenzene both give mixtures of biaryls containing more than 60% *ortho*-isomer); this activation is usually ascribed to a specific interaction between the substituent and the reagent. Such interactions can only selectively activate a site if the substituents in the substrate do not all undergo such a process; this certainly is so in C_6H_5X, but is not true in C_6F_5X.

These considerations prevail whether the product-determining stage in the arylation involves the attack on the substrate by phenyl radicals or by

some precursor of these radicals. While phenyl radicals are generally believed to be the true reagents in this product-determining step, the experimental observations do not demand this conclusion alone.

Isomer ratios in phenylation of C_6F_5X

The homolytic arylation of pentafluorobenzene, bromopentafluorobenzene and octafluorotoluene by thermal decomposition of benzoyl peroxide in these solvents gave yields of isomeric biaryls shown in Figure 1.

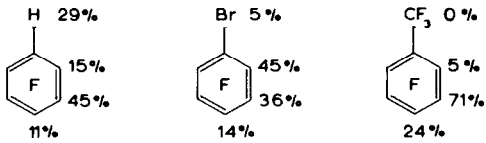


Fig. 1. Yields of isomeric phenylation products from thermolysis of benzoyl peroxide in C_6F_5X.

Hydrogen is more readily displaced than fluorine in *pentafluorobenzene*; this probably reflects the different mechanisms by which the relevant σ-intermediates regain aromatic character. Oxidation of $\sigma_H\cdot$ involves the presence of benzoyloxy radicals or of benzoyl peroxide, simultaneously providing the benzoic acid necessary for defluorination of $\sigma_F\cdot$ and hence a prerequisite for the latter reaction [5]. The σ-intermediate arising from attack at C-1 or C-3 is stabilised by resonance contributions from three fluorine atoms, and may therefore be more readily formed than those arising from attack at C-2 or C-4 where only two fluorine substituents may participate. Figure 1 shows that displacement occurs more readily at positions 1 and 3 of pentafluorobenzene.

Although in benzene derivatives (C_6H_5X) *ortho/para* ratios of above 2 are common, a directly opposite effect is apparent in pentafluorobenzene. This observation, like those in the simple benzene systems, may be explained by postulating that σ-intermediates are better stabilised by *ortho* substituents than by *para* substituents, for the C-4 position is flanked by two *ortho*-fluorine atoms whereas the C-2 site is flanked by only one.

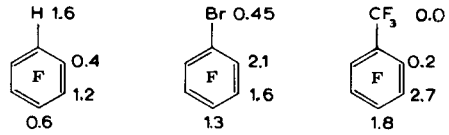
The same effect is evident in the arylation of *octafluorotoluene*, with the additional incursion of a steric effect further lowering the reactivity at C-2. As in pentafluorobenzene, the *meta* position (C-3) is the most susceptible site, probably for similar reasons. The relative reactivities of positions 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 resulting σ-intermediate.

Bromopentafluorobenzene differs from the other two substrates since all positions of attack result in a σ-intermediate which may be stabilised by three substituents. It seems that bromine is more effective than fluorine in the *ortho* position, so that the pattern of substitution resembles that of

bromobenzene. The relative reactivities of sites C-3 and C-4 are again consistent with the trend within the series, with little evidence of delocalisation from the *p*-bromine substituent in the intermediate.

Partial rate factors in phenylation of C_6F_5X

Competitive experiments, using equal volumes of hexafluorobenzene and C_6F_5X, gave relative rates of attack. These, in conjunction with the isomer ratios, allowed partial rate factors to be calculated in which the rate of attack of one site in C_6F_5X is compared with that of attack of a site in C_6F_6 (Fig. 2).



$k_{C_6F_5X}/k_{C_6F_6}$ = 0.9 1.5 1.2

Fig. 2. Partial rate factors and relative rates of phenylation of C_6F_5X.

The rate of attack of bromopentafluorobenzene relative to hexafluorobenzene (1.5) differs from that (1.0) in which both of these substrates competed separately with benzene [4,7]. Competition reactions in which bromopentafluorobenzene and hexafluorobenzene compete with octafluorotoluene for phenyl radical confirm our higher value ($k_{C_6F_5Br}/k_{C_7F_8}$ = 1.3). This disparity between the two sets of results presumably arises from the use of non-ideal solvent mixtures, and confirms our reservations of the significance of such competitions.

The partial rate factors also show some immediate anomalies. The relative rates of attack of C-3 in pentafluorobenzene, bromopentafluorobenzene and octafluorotoluene were explained by considering that there were three fluorine atoms available for stabilisation of the appropriate σ-intermediate compared with two fluorine atoms assisting attack at C-4. However, attack of hexafluorobenzene itself involves an intermediate assisted by three fluorine atoms at the *ortho* and *para* positions, yet the partial rate factors for attack at C-3 are almost certainly greater than unity for all three pentafluorophenyl derivatives. Similarly, the deactivation of C-4 in pentafluorobenzene may be explained by the arguments already advanced, but the activation of this site in both bromopentafluorobenzene and in octafluorotoluene cannot be so explained. It seems that, although the relative rates of attack within one molecule are readily explained, relative rates of attack *between* molecules are not. Indeed, to bring the observed partial rate factors at C-3 down to 1.0 requires a diminution of the relative rate of attack (Fig. 2) to 0.75 for pentafluorobenzene, 0.45 for octafluorotoluene and 0.95 for bromopentafluorobenzene. All of these values are well outside experimental error.

It seems therefore that the discrimination between sites of one substrate by the reagent is not carried through when sites in different molecules are

undergoing competition. This suggests that the factors involved in the two situations are different; that is, if phenyl radical is actively selecting between the sites in the one substrate molecule, it is not the only species which is selecting between substrate molecules. It seems probable that, between molecules, a precursor of the phenyl radical is also involved in the selection process.

The phenyl radical is a short-lived species, and its rate of reaction with aromatic substrates has been recently measured [10]. The second-order rate constant so obtained ($k_2 = 7 \times 10^7$ l mol^{-1} s^{-1}) is not very far removed from that expected from a diffusion-controlled process ($k_2 = 2 \times 10^9$ l mol^{-1} s^{-1}) and considerably greater than that previously advanced from an analysis of the kinetics of thermolysis of benzoyl peroxide in benzene ($k_2 = 2 \times 10^3$ l mol^{-1} s^{-1}) [11]. However, the competition method demands that the reagents involved in the product-determining stage are sufficiently long-lived and sufficiently free within the solution to have a completely random selection. There is little doubt that a phenyl radical in a polyfluoroaromatic solvent would experience considerable van der Waals' forces bonding it to specific molecules (or effectively making the medium seem more viscous) since quite strong complexes are known between simple benzene derivatives and hexafluorobenzene [12]. The existence of such attractive forces between the components of the interacting system lowers the collision frequency, and hence the derived diffusion-controlled rate constant, considerably.

These considerations suggest that the phenyl radical may spend all of its life in the vicinity of one polyfluoroaromatic molecule. Although the lifetime of the radical is sufficient to select successfully the more reactive sites for attack with this molecule, it is insufficient to enable distinction between sites in different molecules. In other words, the competition does not reflect the relative *molecular* reactivities towards phenyl radicals alone, although true competition conditions may exist for phenyl radicals between sites within a molecule. Between molecules, competition must involve some precursor of phenyl radicals, such as the benzoyloxy radical or even benzoyl peroxide itself, both of which have longer lives than the phenyl radical.

An apparent activation of a *meta* position may now be simply explained; it results from the formation of complexes of different stabilities between the precursor of the phenyl radical and the aromatic substrates, so that the phenyl radical subsequently generated attacks the aromatic portion of the original complex. On this premise, the relative reactivities of the substrate molecules, *i. e.* $C_6F_5Br > C_6F_5CF_3 > C_6F_6 > C_6F_5H$, arises from the different degrees of formation of the complexes.

Experimental

Reagents

Benzoyl peroxide, m.p. 105 - 106 °C, was commercial material which had been purified by crystallisation from chloroform/methanol mixtures.

Hexafluorobenzene, bromopentafluorobenzene, pentafluorobenzene and octafluorotoluene were all commercial samples (I.S.C. Avonmouth). Gas chromatography showed them to be 99% pure, the minor impurities being either less fully fluorinated aromatic compounds or polyfluorinated cyclohexane structures. These were shown [2,13] not to divert aryl radicals appreciably and so the solvents were used without further purification.

The products of decomposition of benzoyl peroxide in the various solvents were not fully investigated. In all cases, biaryls were found to be a major product of the reaction, and it was assumed [14] that the orientation of attack at each position of the substrate paralleled the yield of isomeric biaryls and that the ratio of yields of biaryls from each substrate was independent of the total yield in any competition experiment. When the same group was being removed to allow the σ-intermediate to achieve aromatic character, these approximations are more probably valid.

Approximately 10% solutions of benzoyl peroxide in the solvent(s) were maintained at 80 °C for 24 h. Benzoic and hydrofluoric acids were removed (Na_2CO_3), and the solvent(s) removed under reduced pressure. The resulting residue was analysed for its biaryl content by gas–liquid chromatography (Perkin–Elmer F21). The biaryl fraction was then removed by steam-distillation and its composition estimated by ^{19}F NMR spectrometry using a Varian HA-60 NMR spectrometer operating at 56.4 MHz and with 10% solutions in fluorotrichloromethane, the solvent being used as the internal standard.

The two analytical methods were used in both complementary and confirmatory senses. While substantially in agreement in most cases, the incomplete separation of peaks from either gas chromatography or NMR spectrometry introduced some source of error which could always be resolved by recourse to the other analytical method. Where possible, relative ratios of isomers in the ^{19}F NMR spectrum were measured by integrating closely adjacent absorptions to minimise inaccuracies due to changes of phase. In this way, relative yields of isomers could be measured to ± 2%.

TABLE 1

^{19}F NMR chemical shifts[a] used in analysis

2,3,4,5,6-Pentafluorobiphenyl	143.9	156.8	163.1		
2,3,4,5-Tetrafluorobiphenyl	140.4	144.3	156.0	158.0	
2,3,4,6-Tetrafluorobiphenyl	118.3	134.2	136.3	166.0	
2,3,5,6-Tetrafluorobiphenyl	139.9	144.3			
2-Bromo-3,4,5,6-tetrafluorobiphenyl	136.9	137.8	[b]	156.7	
3-Bromo-2,4,5,6-tetrafluorobiphenyl	112.8	127.1	128.7	162.4	
4-Bromo-2,3,5,6-tetrafluorobiphenyl	134.2	142.6			
α,α,α,2,3,4,5-Heptafluoro-6-methylbiphenyl					71.5[c]
α,α,α,2,3,4,6-Heptafluoro-5-methylbiphenyl	118.4	129.3	134.8	163.3	74.5[c]
α,α,α,2,3,5,6-Heptafluoro-4-methylbiphenyl	141.4	142.4			74.6[c]

[a] ppm upfield of $CFCl_3$.
[b] Obscured by bromofluorobenzene absorption at 155.1 ppm.
[c] Aliphatic fluorine of $-CF_3$.

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