FLUORINE AS A LABEL FOR DETECTING REACTION MECHANISM

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Abstract—By means of nucleophilically activated fluorine transient ion pair formation is demonstrated during thermal decomposition of the following aryl radical generators in a non-polar solvent: *p*-fluorophenylazotriphenylmethane, *p*-fluorophenyldiazopiperidide, *p*-fluorophenyldiazoaminobenzene, and *p*-fluorophenylhydrazine. Negative results were obtained with *p*-fluorobenzoyl peroxide.

IT HAS been previously shown¹ by use of nucleophilically activated fluorine as a "label" that the occurrence of ionic processes during the free radical breakdown of acylarylnitrosamines can be detected. We have now applied this technique to other conventional aryl radical sources in order to detect the participation of fleeting ionic processes.

EXPERIMENTAL RESULTS

(A) Decomposition of p-fluorophenylazotriphenylmethane in benzene

(a) The azo-compound (1.6 g) was dissolved in dry benzene (100 ml) and the solution refluxed for 6 hr. An aqueous extract contained no fluoride ions. Evaporation of the benzene yielded a yellow, waxy substance which on trituration with ether gave bis(triphenylmethyl)peroxide (0.14 g) as a white solid, m.p. 181° (dec) (Found: C, 87.5; H, 5.7. Calc. for $C_{38}H_{30}O_2$: C, 87.9; H, 5.8%). Lit.² m.p. 185° (dec). The ether extract contained 0.32 g 4-fluorobiphenyl (cf. Table 1).

(b) In presence of N-nitrosoacetanilide. To a boiling solution of the azo-compound (1.5 g) in dry benzene (100 ml) freshly prepared N-nitrosoacetanilide (4.5 g) was added. The dark-red solution was set aside for 3 days. Fluoride ions were present in the mixture which was extracted with sodium hydrogen carbonate and then with water. The solvent was evaporated and the residual oil (2.44 g) steam distilled yielding a mixture the composition of which is given in Table 1.

(B) Decomposition of p-fluorophenyldiazopiperidide in benzene

(a) With acetic acid. The above piperidide (1.5 g) was decomposed by refluxing the dry benzene solution (100 ml) containing acetic acid (10 ml) for 2 days. Acetic acid was removed with sodium hydrogen carbonate solution and the solvent evaporated (red. press.). The residual oil (1.25 g) on steam distillation afforded a pale-yellow wax (0.7 g) the composition of which is given in Table 1.

(b) With hydrogen chloride. The piperidide (1.5 g) was refluxed in benzene (100 ml) for 2 hr while a constant stream of dry hydrogen chloride was passed into the reaction mixture. The flow of gas was stopped and the solution allowed to reflux for 5 days and then worked up as under (a). For analysis see Table 1.

^{1a} I. K. Barben and H. Suschitzky, J. Chem. Soc. 2735 (1960);

¹⁹ P. Miles and H. Suschitzky, Tetrahedron 18, 1369 (1962).

¹ V. E. Oliveri-Mandalà et al., Gazz. Chim. Ital. 70, 579 (1940).

Composition of reaction mixture (g)	Products $R \cdot C_6 H_4 \cdot C_6 H_5$			
	R	Yield (g)⁰	Yield (%)	Retention Volume ^c
$p-F \cdot C_{e}H_{4} \cdot N_{2} \cdot CPh_{3}$ (1.6)	4-F-	0.32	100	1
p-F·C ₈ H ₄ N ₂ ·CPh ₂ (1.5)	74-F	1.0	12.6	1-1
$C_{6}H_{\delta} \cdot N(NO) \cdot COMe (4.5)$	{4-H	}1·0	82·8	1.1
	4-AcOd	0.12	4.6	3.5
p-FC ₆ H ₄ ·N ₂ ·NC ₅ H ₁₀ (1·5)	 4-F	0.41	80.7	1
AcOH (10 ml)	4-AcOd	0.13	19-3	3.5
$p - F \cdot C_6 H_4 \cdot N_8 C_6 H_{10} (1.5)$	(4-F	lac	95.0	1
HCl gas	4-C1	10.0	5.0	1.60
p-F·C,H, NH·NH, (2.0)	(4-F	1.1	39-4	1
Ag _a O (4·0)	{4-н		44.7	1.1
$C_{6}H_{\delta}N(NO) \cdot COMe (3.0)$	4-AcOd	0.16	15-9	3.20

TABLE 1. PRODUCT ANALYSIS OF DECOMPOSITIONS IN BENZENE

^a Obtained by column chromatography as described previously^{1b}

^b Relative composition of biphenyls obtained by G.L.C. analysis as described previously^{1b}

^o Relative retention volume based upon 4-fluorobiphenyl being taken as unity.

^d Estimated as 4-hydroxybiphenyl^{1b}

(C) Decomposition of p,p'-difluorodiazoaminobenzene

The diazoaminocompound (2.5 g) was refluxed in chlorobenzene (50 ml) for 3 days. A sublimate in the reflux condenser proved to be *p*-fluoroaniline hydrofluoride and the reaction mixture contained fluoride ions. Removal of the solvent left an intractable oil.

(D) Oxidation of p-fluorophenylhydrazine with silver oxide in benzene

(a) To a stirred, ice-cooled solution of p-fluorophenylhydrazine $(1\cdot 2 \text{ g})$ in dry benzene (100 ml) freshly prepared silver oxide powder $(2\cdot 4 \text{ g})$ was added piecemeal and agitation continued (2 hr). From the benzene solution 4-fluorobiphenyl (0.32 g) was obtained by steam distillation. No fluoride ions were present.

(b) In presence of N-nitrosoacetanilide. To the reaction mixture prepared as above from p-fluorophenylhydrazine (2 g) freshly prepared N-nitrosoacetanilide (3.0 g) was added and agitation continued for 2 hr. Fluoride ions were present in an aqueous extract of the precipitated silver compounds. The residues obtained after driving off the benzene (2.23 g) were steam distilled to give a pale-yellow solid (1.4 g), the analysis is quoted in Table 1.

(E) Decomposition of p-fluorobenzoyl peroxide in benzene

The peroxide (4.6 g) was refluxed in benzene (100 ml) for 30 hr. White crystals of p,p'-difluoro-p-quaterphenyl (0.12 g) m.p. 306° were collected (Found: C, 83.7; H, 4.8. $C_{24}H_{16}F_2$ requires: C, 84.2; H, 4.7%. Fluorine present) (λ_{max} 290; log ε 4.9). An alkaline extract of the benzene solution gave *p*-fluorobenzoic acid (1.24 g). The benzene solution was chromatographed on an alumina column (benzene as eluent) yielding a solid (1.7 g) which on sublimation gave 4-fluorobiphenyl (1.6 g) m.p. 73°.

DISCUSSION

Earlier attempts to induce and discover ionic tendencies in the free radical breakdown of the unsymmetrically substituted azo-compound (I; $R = NO_2$, R' = OMe) in various solvents failed. For the purpose of studying the same problem p-fluorophenylazotriphenylmethane (I; R = F, R' = H) was made to decompose in boiling benzene but gave only products (cf. section A and Table 1) indicative of a free radical process (I \rightarrow route a). We thought, however, that ionic dissociation (route b) of the azo-compound (I; R = F, R' = H) could have taken place simultaneously producing the weakly nucleophilic and bulky triphenylmethyl anion (III; R' = H). Since such an anion was unlikely to replace the labile fluorine atom on the diazonium cation (II; R = F), occurrence of a heterolytic pathway (route b) could remain unnoticed. Thus the reaction was repeated in presence of N-nitroso acetanilide (A-b) which is known to yield acetate ions (VI) derived from the ion pair (V + VI) under the reaction conditions.¹ The fact that the reaction mixture now contained fluoride ions and 4acetoxybiphenyl (VII) is diagnostic of the transient ion pair formation (II and III; R = F, R' = H) for this reason: formation of the biphenyl (VII) is rationally accounted for by the chemical interaction of the ions (II and VI; R = F) with the result shown in route c.



Thermolysis of triazens (e.g. VIII; R = H) in solutions containing acid is known to follow a free radical pattern⁴ producing nitrogen, biphenyl, and a dialkylamine salt (cf. VIII $\rightarrow X$ via route d). On decomposing the fluorotriazen (VIII; R = F) in a boiling mixture of benzene and acetic acid (cf. section B and Table 1) the reaction mixture contained, apart from the expected 4-fluorobiphenyl, fluoride ions and 4-acetoxybiphenyl. In an analogous way, when dry hydrogen chloride was used instead of acetic acid, fluorine was replaced and 4-chlorobiphenyl formed. The appearance of these two biphenyls is best accounted for by a dual mechanism of the breakdown: a covalent diazo-compound⁵ (IX; R = F, X = AcO or Cl) formed by agency of the acid (HCl or HAOc) breaks up into free radicals (IX \rightarrow route d) and into ion pairs (IX \rightarrow route e) producing the observed products (X; R = F and XI; X = OAc or Cl). The possibility that the triazen gives rise directly to an ion pair

⁸ M. D. Cohen, J. E. Leffler and L. M. Barbato, J. Amer. Chem. Soc. 76, 4169 (1954).

⁴ J. Elks and D. H. Hey, J. Chem. Soc. 441 (1943).

⁵ W. A. Waters, The Chemistry of Free Radicals p. 155. Clarendon Press, Oxford (1948).

(e.g. XII) was readily eliminated because piperidinobiphenyl is not one of the reaction products.

$$\begin{array}{c|c} p\text{-R}\cdot C_{6}H_{4}\cdot N:N\cdot N\cdot C_{6}H_{10} \xrightarrow{HX} C_{6}H_{10}NH + p\text{-R}\cdot C_{6}H_{4}\cdot N:N\cdot X \\ \hline \\ \text{VIII} \\ N_{2} \div HX + p\text{-R}\cdot C_{6}H_{4}\cdot Ph \xrightarrow{route d}_{homolytic} & \downarrow \\ P\text{-X}\cdot C_{6}H_{4}\cdot Ph + N_{2} + HR \xrightarrow{ln}_{C_{6}H_{6}} p\text{-X}\cdot C_{8}H_{4}\cdot N_{2}\cdot R \xleftarrow{} p\text{-X}\cdot C_{8}H_{8}\cdot N_{2}\cdot R \xleftarrow{} p\text{-X}\cdot C_{8}H_{8}\cdot N_{8}\cdot R \xleftarrow{} p\text{-X}\cdot C_{8}H_{8}\cdot N_{8}\cdot R \xleftarrow{} p\text{-X}\cdot C_{8}\cdot R \xleftarrow{}$$

The related diazoaminobenzenes (e.g. XIII; R = H) have recently been shown by Hardie and Thompson⁶ to decompose thermally to give aryl and anilino radicals (XIII \rightarrow XIV). Decomposition of the fluoro-analogue (XIII; R = F) in chlorobenzene gave *p*-fluoroaniline hydrofluoride (cf. C). This substance is undoubtedly formed by the combination of *p*-fluoroaniline (XIV; R = F) due to homolysis with hydrogen fluoride (XV; R = F) due to intermediate ion formation as shown below:

Oxidation of phenylhydrazines' with silver oxide in an aromatic solvent provides another source of free aryl radicals (XVI \rightarrow route f). They are probably formed by decomposition of the covalent diazo-compound (XVII; R = H) which is an oxidation product of the hydrazine. No fluorine replacement occurred when *p*-fluorophenylhydrazine was treated with silver oxide. 4-Fluorobiphenyl, the chief reaction product, is typical of a homolytic arylation of the solvent as shown below (XVI \rightarrow route f). Even if ionic dissociation of the covalent diazo-compound (XVII \rightarrow XVIII; R = F) had occurred, fluorine replacement by a hydride ion which is unlikely to exist for any length of time in the presence of an oxidizing agent, can hardly be expected. This is why in another experiment the reaction was carried out in presence of N-nitrosoacetanilide which provides a stable anion (cf. IV \rightarrow VI). Fluoride ions were now present in the silver residues and 4-hydroxybiphenyl instead of the anticipated 4-acetoxybiphenyl was one of the reaction products. Since the latter biphenyl was found to hydrolyse readily when in contact with silver oxide under the conditions of the reaction, 4-hydroxybiphenyl is deemed diagnostic of ion pair formation (XVIII; R = F). The

⁶ R. L. Hardie and R. H. Thomson, J. Chem. Soc. 1286 (1958).

⁷ R. L. Hardie and R. H. Thomson, J. Chem. Soc. 2512 (1957).

discussed changes are illustrated by the sequence below (XVI \longrightarrow XVII and route f; XVI \longrightarrow XVII and route g; R = F in both cases):

The thermal decomposition of diaroyl peroxides in solvents provides probably the most convenient source of aryl radicals and is well documented.⁸ Leffler⁹ has found that unsymmetrical peroxides in which the substituents reinforce each other in their electronic tendencies (e.g. XIX; R = OMe, R' = H, $R'' = NO_2$) will disintegrate in nitrobenzene by an ionic mechanism as evidenced by product analysis. Yet no heterolysis was observed in the peroxide (XIX; R = H, R' = I, $R'' = NO_2$). When we caused the fluorine substituted peroxide (XIX; R = R'' = F, R' = H) to decompose in benzene, alone or together with N-nitrosoacetanilide, no fluorine replacement occurred. Reaction products included *p*-fluorobenzoic acid, 4-fluorobiphenyl, and a small quantity of *p*,*p*'-difluoro-*p*-quaterphenyl (XX) which are all accountable by a free radical process.

$$\begin{array}{cccc} R' & & & \\ R & & & \\$$

EXPERIMENTAL

Detection of fluoride ions was carried out by the zirconium-alizarin method.¹⁰

p-Fluorophenylazotriphenylmethane. Triphenylmethyl bromide was prepared by addition of a 48% solution of hydrobromic acid to a 2% solution of triphenylmethanol in acetic anhydride and had m.p. 152°. To a solution of the bromide in ether (5.5 g in 100 ml) was added p-fluorophenylhydrazine (4.16 g) made by the method of Olah et al.¹¹ The reaction mixture was refluxed for 5 hr on a water-bath, the precipitate (p-fluorophenylhydrazotriphenyl methyl hydrobromide) filtered off and p-fluorophenylhydrazotriphenylmethane (6.22 g) m.p. 122–125° obtained by evaporation of the filtrate. Attempts to prepare an analytical sample failed owing to aerial oxidation. An ethereal solution of the hydrazocompound (5.8 g in 500 ml) was oxidized by addition of a 30% aqueous solution of hydrogen peroxide

- ⁸ G. H. Williams, Homolytic Aromatic Substitution p. 35. Pergamon Press, Oxford (1960);
 - P. Gelisson and P. H. Hermans, Ber. Dtsch. Chem. Ges. 58, 285 (1925);
- D. H. Hey, J. Chem. Soc. 1966 (1934).
- ⁹ J. E. Leffler, J. Amer. Chem. Soc. 72, 67 (1950).
- ¹⁰ Feigl, Spot Tests II, Organic Applications p. 67. Elsevier, New York (1954).
- ¹¹ G. Oláh, A. Pavlath, and I. Kuhn Acta Chim., Acad. Scient. Hung. 7, 65 (1955).

(10 ml) in presence of saturated sodium hydrogen carbonate solution (50 ml) with vigorous stirring (5 hr). Separation of the ether layer and removal of the solvent afforded a dark red oil which on trituration with ethanol (5 ml) yielded *p*-fluorophenylazotriphenylmethane as a yellow solid (3.3 g) m.p. 111-112° (dec.) (Found: C, 81.7; H, 5.5. $C_{15}H_{19}FN_2$ requires: C, 81.9; H, 5.2%. Fluorine present.

p-Fluorophenyldiazopiperidide. A solution of p-fluoroaniline hydrochloride (3.8 g) in aqueous hydrochloric acid (50 ml water and 1.42 g conc. HCl) was diazotized at 0° with a 20% aqueous solution of sodium nitrite. The diazo-solution was then added dropwise with stirring to an ice-cooled aqueous solution of piperidine (30%; 2.24 g) containing sodium carbonate (4.6 g). The reaction mixture yielded on extraction with pet. ether, b.p. 40–60° (3 × 25 ml) and after evaporation of the solvent p-fluorodiazopiperidide as yellow platelets (2 g) m.p. 26° (Found: C, 63.4; H, 7.1; N, 20.2. $C_{11}H_{14}FN_a$ requires: C, 63.7; H, 6.8; N, 20.3%. Fluorine present).

4-Piperidinobiphenyl. A solution of p-chloronitrobenzene (15.7 g) in 25 ml piperidine was warmed for 2 hr on the steam-bath and then cooled, thereby yielding 4-nitropiperidinobenzene as yellow needles, m.p. 107°. Reduction of the nitro-compound by Finger and Reed's method¹³ with reduced iron and ammonium chloride yielded the corresponding amine (95%). The base hydrochloride (8.5 g) was diazotized at 0° in a mixture of conc. HCl (6 ml) and water (25 ml) with a 20% aqueous solution of sodium nitrite (2.7 g). To the stirred diazonium solution benzene (150 ml) was added followed by dropwise addition of a 20% solution of sodium hydroxide (13 ml). Steam distillation of the washed benzene layer furnished a quickly darkening oil. Its dipicrate m.p. 154° separated from ethanol (Found: N, 14.0. C₂₉H₂₅N₇O₁₄ requires: N, 14.1%).

p,p'-Difluorodiazoaminobenzene. An ice-cooled solution of p-fluoroaniline hydrochloride (6.9 g) was diazotized in 50 ml water containing conc. HCl (2.5 ml) with a cold 20% solution of sodium nitrite (1.72 g). Addition of sodium acetate (4.1 g in 25 ml water) precipitated p,p'-difluorodiazo-aminobenzene (3.6 g) as yellow needles (ethanol) m.p. 118° (Found: C, 61.55; H, 4.3; N, 18.2. $C_{12}H_9F_2N_8$ requires: C, 61.75; H, 3.9; N, 18.0%. Fluorine present).

p-Fluorophenylhydrazine. This was prepared¹¹ in 65% yield and m.p. 34°.

p-Fluorobenzoyl peroxide. An aqueous solution of 18 ml sodium hydroxide (15%) and p-fluorobenzoyl chloride (8.0 g) were added in small portions alternately to a 10% solution of hydrogen peroxide (25 ml) at a rate to maintain an alkaline medium. The reaction mixture was cooled in ice and shaken after each addition. It was kept for 24 hr at 0° and a white solid (7.0 g) was collected which on crystallization from methanol-petroleum ether b.p. 60–80° gave p-fluorobenzoylperoxide as white needles, m.p. 94–95° (dec.) (Found: C, 60.0; H, 3.15. $C_{14}H_8F_2O_4$ requires: C, 60.4; H, 2.9%. Fluorine present).

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¹³ G. C. Finger and F. H. Reed, J. Amer. Chem. Soc. 66, 1972 (1944).