# Aromatic Detritiation. Part VI.[1] Pentafluorobiphenyl: The Novel Effect of the Pentafluorophenyl Substituent

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Rates of protiodetritiation of 2',3',4',5',6'-pentafluoro[2-, 3-, and 4-$^3$H]biphenyl, together with those of [2-,3-, and 4-$^3$H]biphenyl, some labelled monofluorobiphenyls, and [$^3$H]benzene have been measured in trifluoroacetic acid containing aqueous perchloric acid at temperatures between 25 and 110°. Partial rate factors for protiodetritiation of pentafluorobiphenyl are: 0·0095 (2-), 0·0053 (3-), and 0·0158 (4-position), which yield $\sigma^+$-values of 0·285 (*meta*) and 0·225 (*para*). The greater electron withdrawal by this substituent from the *meta*- than from the *para*-position contrasts with its effect in reactions which yield σ-values where the withdrawal is greater from the *para*-position. The pentafluoro-phenyl substituent therefore shares (with the ethynyl substituent) the novelty of being capable of producing greater electron withdrawal at either position depending upon the demand for resonance stabilisation of the transition state.

The effects of the five fluoro-substituents are less than predicted from the additivity principle (this same deviation having previously been found in electrophilic substitution of pentafluorobenzene), but it is unlikely that this arises from through-space interaction of the lone pairs of the *ortho*-fluorines with the deficient π-cloud of the ring undergoing substitution, since the effect of a single *ortho*-fluorine substituent appears to be normal.

The contradiction between the prediction from hydrogen exchange of substantial *meta*-substitution in other electrophilic reactions and the published data, is traced to the difficulty of resolving the *meta*- and *para*-derivatives. Re-examination of these reactions shows that up to 18% of *meta*-substitution occurs, and under suitable conditions this can be increased to 25%, the amount predicted. The nitration of pentafluorobiphenyl by nitric acid–sulphuric acid in acetic acid gives an *ortho*:*para*-ratio of *ca.* 0·45 and this is unaffected by the presence of nitrous acid. With nitric acid in acetic anhydride, acetoxylation is the main (though very slow) reaction.

A new route to the preparation of biphenylene is briefly described, as are the properties of some new bromofluorobiphenyls, and an unusual preparation of 2-butyl-2'-bromobiphenyl.

HYDROGEN exchange has the advantage over all other electrophilic aromatic substitutions of being the least susceptible to steric effects (only one possible example of steric hindrance in the reaction having been detected [1]), provides a kinetic method capable of giving accurate reactivities, even for positions which undergo very minor substitution, and has been used to predict the presence of previously undetected isomers in other electrophilic substitutions.[2] In addition more quantitative substituents effect data are now available for this reaction that for any other.[3] This paper describes the extension of the method to provide the first quantitative measurement of the electrophilic reactivity of pentafluorobiphenyl.

The only previous measurements of the reactivity of pentafluorobiphenyl have been made by Stephens and his co-workers [4] who found that aluminium bromide-catalysed bromination in cyclohexane gave 90% *para*-substitution (and probably 10% *ortho*), and nitration by fuming nitric acid–sulphuric acid in acetic acid gave *ortho*- and *para*-products in 1 : 3 mole ratio. In neither reaction were any *meta* products isolated, though because of the difficulty of resolving *meta*- and *para*-compounds, even using v.p.c. and especially of pentafluoro-compounds which have a reduced retention time compared to their hydrogen-containing analogues, the possibility of significant *meta*-substitution in these reactions was not excluded and we have therefore re-examined these reactions.

Knowledge of the quantitative reactivity of the molecule is also desirable because of the failure of the additivity principle to predict the reactivity of pentafluorobenzene in protodesilylation,[5] and protodestannylation [5] and the pyrolysis of 1-arylethyl acetates;[6] the small bathochromic shift produced by the pentafluorophenyl substituent in pentafluoromalachite green also indicates that the electron withdrawal is less than expected.[7] For pentafluorobiphenyl, Sheppard [8] has proposed that interaction of the lone pairs of the *ortho*-fluorines with π-cloud of the other ring may account for the apparent electron *release* by the pentafluoro-substituent in measurements of $pK_a$ values of substituted benzoic acids (Table 1). However, two points are relevant here.

TABLE 1

Methods yielding σ-values for the $C_6F_5$ substituent

| Reaction | $\sigma_m$ | $\sigma_p$ | Ref. |
|---|---|---|---|
| $pK_a$, Dimethylanilines | 0·34 | 0·41 | 8 |
| Substituted pentafluorobenzenes with sodium pentafluorophenolate [a] | | 0·42 | 9 |
| $^{19}$F N.m.r. of pentafluorophenylphosphines, $C_6F_5PXY$ [b] | 0·22 | | 10 |
| $^{19}$F N.m.r. of hexafluorobiphenyls | 0·26 | 0·27 | 8 |
| $pK_a$, Carboxylic acids | −0·12 | −0·03 | 8 |

[a] The rate for decafluorobiphenyl leads to the required σ-value. [b] X and Y Represent a range of substituents including $C_6F_5$.

[1] H. V. Ansell, R. B. Clegg, and R. Taylor, *J.C.S. Perkin II*, 1972, 766.
[2] R. Taylor, *Chimia*, 1968, **22**, 1.
[3] R. Taylor, 'Comprehensive Chemical Kinetics,' vol. 13, Elsevier, Amsterdam, 1972.
[4] P. J. N. Brown, M. T. Chaudhry, and R. Stephens, *J. Chem. Soc.* (*C*), 1969, 2747.
[5] C. Eaborn, J. A. Treverton, and D. R. M. Walton, *J. Organometallic Chem.*, 1967, **9**, 259.
[6] R. Taylor, *J. Chem. Soc.* (*B*), 1971, 255.
[7] G. Hallas, D. E. Grocock, J. D. Hepworth, and A. M. Jones, *Tetrahedron*, 1972, **28**, 893.
[8] W. A. Sheppard, *J. Amer. Chem. Soc.*, 1970, **92**, 5419.
[9] R. J. de Pasquale and C. Tamborski, *J. Org. Chem.*, 1967, **32**, 3163.
[10] M. G. Barlow, M. Green, R. N. Haszeldine, and H. G. Higson, *J. Chem. Soc.* (*B*), 1966, 1025.

First some of the other fluorine-containing substituents gave σ-values from this system (measurements in 75% methanol–25% water) which differed substantially from the literature values (being up to 0·13 units more negative than the latter), and only two non-fluorine-containing substituents were measured under these conditions. Secondly if this electron release operates in pentafluorobiphenyl it should also operate in *ortho*-fluorobiphenyl since the angles between the aromatic rings will be fairly similar in both molecules. Consequently we have measured rates of exchange of a number of labelled monofluorobiphenyls including some with *ortho*-fluoro-substituents.

TABLE 2

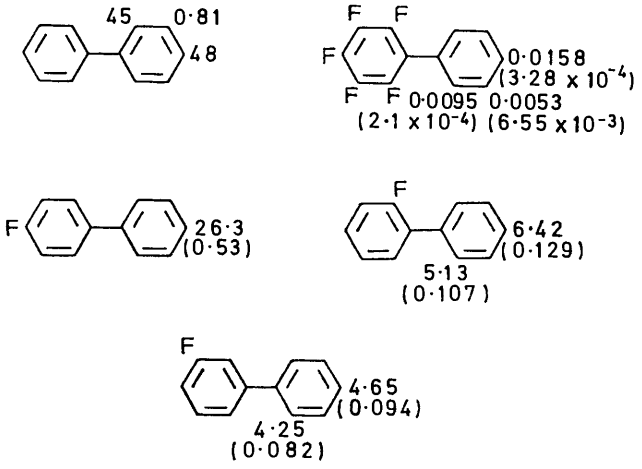
Rate coefficients, $10^7k/s^{-1}$, for protiodetritiation of [$^3$H]-Ar in aq.-perchloric acid–trifluoroacetic acid

| | $t$/°C | | | | | | | $E$ |
|---|---|---|---|---|---|---|---|---|
| Ar | 25 | 35 | 45 | 70 | 80 | 100 | 110 | kcal mol$^{-1}$ |
| $C_6H_5$ | 12·35 [a] | | 151 [b] | 2200 | | | | 23·4 |
| 2-$C_6H_5$·$C_6H_4$ | 645 [a] | | 7200 | 100,000 [b] | | | | |
| 3-$C_6H_5$·$C_6H_4$ | | | 104 | 1790 | | | | 24·0 |
| 4-$C_6H_5$·$C_6H_4$ | 645 | 2305 | 7500 | 107,000 [b] | | | | 22·9 |
| 2-$C_6F_5$·$C_6H_4$ | | | | 21·0 | 55·1 | 363 | 798 | 23·2 |
| 3-$C_6F_5$·$C_6H_4$ | | | | 9·4 | | | 440 | 24·9 |
| 4-$C_6F_5$·$C_6H_4$ | | | | 35·1 | | 610 | 1308 | 23·2 |
| 4-(4′-$FC_6H_4$)$C_6H_4$ | | | 3970 | | | | | |
| 4-(2′-$FC_6H_4$)$C_6H_4$ | | | 970 | | | | | |
| 2-(2′-$FC_6H_4$)$C_6H_4$ | | | 775 | | | | | |
| 2-(3′-$FC_6H_4$)$C_6H_4$ | | | 640 | | | | | |
| 4-(3′-$FC_6H_4$)$C_6H_4$ | | | 702 | | | | | |

[a] Interpolated from rates obtained previously [11] in a closely similar medium, and the measured rate for [4-$^3$H]biphenyl. [b] Rates extrapolated or interpolated from those at other temperatures.

## RESULTS AND DISCUSSION

Rate coefficients at the temperatures indicated and the activation energies are given in Table 2. The derived partial rate factors are given in Scheme 1 together with values of $k_{rel}$ (relative to the parent biphenyl) shown in parentheses. The values of $k_{rel}$ for the monofluorobiphenyls are obtained at a lower temperature (45°) than those for pentafluorobiphenyl (70°), but this will not introduce an error sufficiently significant to affect our conclusions. This is indicated by the partial rate factors for biphenyl which may be compared with those *viz.* 51 (*ortho*), 0·68 (*meta*), and 51 (*para*) obtained [11] at 25° in a closely similar medium (that gave $10^7k/s^{-1}$ for benzene = 14·3). The differences are very small and are in the direction required by the reactivity–selectivity relationship.




SCHEME 1 Partial rate factors and (in parentheses) rates relative to the corresponding non-fluorinated biphenyl for protiodetritiation

The main features of the results are as follows. (i) The pentafluoro-substituent is *ortho* : *para*-directing and deactivating, and using a value of ρ of −8·0 for detritiation in this medium, we obtain σ$^+$-values of +0·225 (*para*), +0·285 (*meta*) [and +0·255 (*ortho*)]. While the use of σ$^+$-values for *ortho*-substitution is not generally valid it is very probably justifiable in the case of hydrogen exchange because of the lack of steric hindrance; * the use of these numerical values is helpful in the subsequent analysis. Comparison of these values with σ-values (Table 1) is interesting. Though there is considerable disagreement in the latter (and the values derived from p$K_a$ measurements of the acids are difficult to evaluate for reasons given above), one feature which clearly emerges is that the greatest concentration of electrons is at the *meta*-position in these reactions (due to the operation of the $-M$ effect), whereas in hydrogen exchange the greatest concentration is at the *para* (and *ortho*)-positions. This may be rationalised in terms of the greater demand for resonance stabilisation of the transition state in electrophilic substitution, the electron release being specifically relayed to the *ortho*- and *para*-positions of the non-fluorinated ring in pentafluorobiphenyl (as in biphenyl). Thus the electronic effect of the pentafluorophenyl substituent can vary from $-M$ to $+M$ as the electron demand is increased. This latter shows that pentafluorobiphenyl can attain a near planar configuration in the transition state,

* This supposition is now reinforced by our discovery that the ratio $\log f_o : \log f_p$ for a wide range of substituents in hydrogen exchange is 0·86 ± 0·05, the value predicted from the charge distribution in the Wheland intermediate; the present data give a value of 0·88 (H. V. Ansell, J. Le Guen, and R. Taylor, *Tetrahedron Letters*, in the press).

[11] C. Eaborn and R. Taylor, *J. Chem. Soc.*, 1961, 1012.

consequently steric hindrance to coplanarity from the two *ortho* fluorines is not of overriding significance.

This reversal of substituent effect is almost unique, only the ethynyl substituent has thus been shown to be capable of it, having $\sigma_m = 0{\cdot}205$, $\sigma_p = 0{\cdot}233$,[12] $\sigma_m^+ = 0{\cdot}33$, $\sigma_p^+ = 0{\cdot}179$.[13] However, this is a less clear cut example because $\sigma_m^+$ is more positive than $\sigma_m$ which is difficult to interpret [13] and suggests that one of the values might be in error. Both substituents are formally similar in being composed of electronegative elements (fluorine or *sp*-hybridised carbon) and possessing polarisable π-electrons.

(ii) The partial rate factors for biphenyl yield $\sigma^+$-values of −0·20 (*para*) and +0·012 (*meta*) for hydrogen exchange in this medium. The difference in $\sigma^+$-values for the hydrogen- and fluorine-containing compounds is therefore 0·425 (*para*) and 0·275 (*meta*). This shows that the lower reactivity of the pentafluoro-compound arises from a reduced π-electron density in the ring undergoing substitutions, which may be attributed to either the electronegativity of the substituent fluorines in the other ring, or (and this we believe to be less likely for reasons given below) a markedly increased twisting of the aromatic rings away from coplanarity in the pentafluoro-compound. The difference in the σ values for the *ortho*-positions is 0·455, slightly more than for the *para*-position, and consistent with the greater inductive and field effect of the pentafluoro-substituent compared to the phenyl substituent.

(iii) Comparison of the observed partial rate factors for pentafluorobiphenyl calculated on the basis of the additivity principle is interesting. For the *para*-position the calculated deactivation is $0{\cdot}53 \times (0{\cdot}094)^2 \times (0{\cdot}129)^2 = 7{\cdot}8 \times 10^{-5}$ which may be compared with the observed value of $3{\cdot}28 \times 10^{-4}$. The discrepancy of only *ca.* 4-fold is in the same direction previously noted for pentafluorobenzene,[5,6] and no doubt derives from the same cause. The deviation is slightly less than for pentafluorobenzene and this is of course consistent with the smaller ρ-factor for hydrogen exchange in biphenyls (*ca.* −2·1).[14] The consistency provides very strong grounds for supposing that the angle between the aromatic rings in pentafluorobiphenyl in the reaction transition state is not significantly different from that in *ortho*-fluorobiphenyl and unless special electronic relay effects (as proposed by Sheppard) [8] operate in the latter molecule, they do not operate in pentafluorobiphenyl either.

(iv) Evidence that special electronic effects are not operative in *ortho*-fluorobiphenyl may be adduced by comparing the quantitative substituent effects of *ortho*-, *meta*-, and *para*-fluorine for hydrogen exchange in benzene [15] with those produced in biphenyl (tritium in the *para* position of the *non*-fluorinated ring) (Table 3). The large difference in the *meta*-values reflects the difference in ρ-factors in the two reactions, and the values in parentheses give the relative rates calculated using the literature value [16] of $\sigma^+$ for the *m*-fluoro-substituent of

TABLE 3

Substituent effect of fluorine in protiodetritiation of F-substituted aromatics

| Position of fluorine | [$^3$H]Benzene | [4′-$^3$H]Biphenyl |
|---|---|---|
| *ortho* | 0·132 | 0·129 |
| *meta* | *ca.* 0·002 | 0·094 |
| | (0·0015) [a] | (0·18) [a] |
| *para* | 1·79 | 0·53 |
| ρ-factor | −8·0 | −2·1 |

[a] See text.

0·352, and the given ρ-values; the agreement between calculated and observed factors is good. The deactivating factor for *meta*-fluoro in biphenyl is also in good agreement with the literature [14] value for *meta*-chloro of 0·12 and the slightly greater deactivation by the fluoro-substituent, contrary to the prediction of $\sigma^+$-values [16] almost certainly reflects the reduced effectiveness of conjugation factors in biphenyl. Evidence for the reduced conjugation in biphenyl compared to benzene is clearly demonstrated by the effect of the *para*-fluoro-substituent which activates in benzene and deactivates in biphenyl (as it does in some electrophilic substitutions of benzene in which there is a reduced demand for resonance [17]). On this basis one might expect the *ortho*-fluoro-substituent to deactivate rather more in biphenyl than in benzene. However, in biphenyl this substituent is removed considerably from the reaction site compared to benzene, and this should produce less deactivation in biphenyl because of the reduced inductive/field effects. Consequently, on balance the observed similarities of the substituent effects in both molecules are not unexpected and provide no grounds for proposing extra mechanisms of supplying electrons from fluorine to the reaction site.

(v) Whereas changing the position of a fluoro-substituent from *para* to *ortho* in one ring decreases the reactivity of the *para*-position in the other ring by a factor of *ca.* 4, keeping the position of the fluorine constant and changing the position of substitution from *ortho* to *para* in the other ring produces a rate change of only 20% (when the fluorine is *ortho*) and a mere 6% (when the fluorine is *meta*). Three points follow from this. First, significant direct field effects are ruled out, because the change in relative deactivation from 20 to 6% when fluorine is *ortho* and *meta* respectively is commensurate with a normal inductive effect. Secondly the fluorophenyl substituent produces its effect almost entirely by altering the electron density at the carbon by which it is attached to the phenyl ring undergoing reaction. Thirdly the very small

[12] J. A. Landgrebe and R. M. Rynbrandt, *J. Org. Chem.*, 1966, **31**, 2585.
[13] C. Eaborn, A. R. Thompson, and D. R. M. Walton, *J. Chem. Soc.* (*B*), 1969, 859.
[14] R. Baker, R. W. Bott, C. Eaborn, and P. M. Greasley, *J. Chem. Soc.* (*B*), 1964, 627.
[15] C. Eaborn and R. Taylor, *J. Chem. Soc.*, 1961, 2388.
[16] L. M. Stock and H. C. Brown, *Adv. Phys. Org. Chem.*, 1963, **1**, 35.
[17] R. O. C. Norman and R. Taylor, 'Electrophilic Substitution in Benzenoid Compounds,' Elsevier, Amsterdam, 1965.

differences in deactivation at the *ortho*- and *para*-positions in one ring by the *ortho*- and *meta*-fluorines in the other show clearly that the correspondingly large effects produced by phenyl substituents [1] (which are of much lower polarity than fluorine) cannot be reasonably ascribed to other than steric effects.

(vi) The hydrogen exchange data leads one to expect considerable *meta*-substitution in other electrophilic substitutions of pentafluorobiphenyl. The 90% of *para*-substitution reported [4] for aluminium bromide-catalysed bromination is based on v.p.c. analysis which could possibly have failed to resolve a *meta* and *para*-mixture. In this work a pure sample of sharply melting (82—83°) *p*-bromopentafluorobiphenyl was isolated, but this constituted less than 1% of the crude reaction product.

We have therefore re-examined these reactions. For bromination under the above conditions we obtained (on analysis with a silicon oil-based column operated at 180°) two main peaks of approximate area ratio of 1 : 10 as reported in the literature, the peak of longest retention time being the largest and attributed [4] to the *para*-bromo-derivative. However, separate preparation of the pure *meta*-bromopentafluorobiphenyl (m.p. 64—65°) showed it to have the same retention time as the '*para*-compound' on this column and the i.r. spectra of each indicated the latter to contain *ca.* 5% of the *meta*-isomer. Reanalysis of the reaction product with a free fatty acid phase column (F.F.A.P.) (5% on 100—120 Chromosorb G operated at 170°) produced total resolution of the *meta*- and *para*-isomers and confirmed that they constituted 4—5% and 84% of the reaction product respectively; the other main peak was confirmed *via* isolation with preparative gas chromatography and mass spectral analysis of the product to be the *ortho*-bromo isomer, m.p. 39°. Isolation of the *meta*-/*para*-mixture *via* preparative gas chromatography showed it to melt fairly sharply at 82—84°, similar to that (82—83°) reported [4] for the *para*-compound isolated by recrystallisation of the crude reaction mixture.

Thus although *meta*-product was in fact formed in this bromination, the *para* : *meta*-ratio of *ca.* 19 is far from that (*ca.* 2·5) predicted from the $\sigma^+$-values and a $\rho$-factor of *ca.* −12. Likewise the *para* : *ortho*-ratio of *ca.* 7 is well removed from the value of *ca.* 1·0 expected and it is possible that the *meta* as well as the *ortho*-position is affected by steric hindrance to substitution by the bulky bromine–aluminium bromide complex that is the electrophile. We therefore carried out a further bromination with bromine in acetic acid, catalysed by iodine, which being a 'linear' catalyst could be expected to give less hindrance. This was indeed so, the approximate percentages of substitution being: *ortho* (12), *meta* (23), and *para* (65%). Significantly here the *para* : *meta* ratio is 2·8, almost exactly that predicted and the *para* : *ortho* ratio is closer to expectation.

For nitration by fuming nitric acid–sulphuric acid in acetic acid we confirmed that there appeared, on analysis with a silicon oil-based column, operated at 180°, to be only two products with peak areas of *ca.* 1 : 4, the latter having the longest retention time. However, use of the F.F.A.P. column operated at 210° showed that the 'main product' was in fact a *meta*/*para*-mixture and the approximate percentages of products in this reaction were: *ortho* (25), *meta* (18), and *para* (57%). (In contrast to the nitration of biphenyl,[18] these product ratios were unaffected by the presence of nitrous acid which is consistent with nitration *via* nitrosation occurring only with more reactive aromatics). Of all electrophilic substitutions other than hydrogen exchange, nitration appears to be one of the least hindered and so it is not surprising to find that here the *para* : *ortho*-ratio is smaller than for bromination above (the *para* : *meta*-ratio being similar in both cases).

Attempted nitration of pentafluorobiphenyl with nitric acid–acetic anhydride produced four reaction products in a very slow reaction. Two of these seemed from the v.p.c. analysis to be the *ortho*- and *para*-nitro-derivatives, the other two components having longer retention times. Mass spectral analysis of the crude reaction product showed, however, only the presence of pentafluorobiphenyl ($m/e = 244$) and acetoxypentafluorobiphenyl ($m/e = 302$) and no trace of the nitro-derivatives ($m/e = 289$) so that we may only safely conclude that acetoxylation occurs under these conditions.

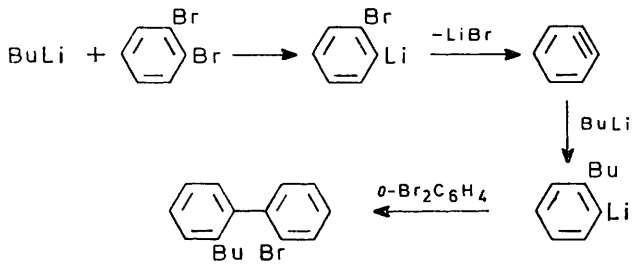
In summary, the detection of the reaction products previously unobserved, yet predicted by the hydrogen-exchange reaction, further demonstrates that this reaction is the outstanding model for electrophilic aromatic substitution.

*Formation of Biphenylene.*—The attempted preparation of 2′-fluoro[2-$^3$H]biphenyl from 2-bromo-2′-fluorobiphenyl *via* reaction with n-butyl-lithium in ether followed by hydrolysis with tritiated water, produced the desired product, together with biphenyl (a trace) and a substantial amount of biphenylene (both these latter being radioactive), as well as two further compounds which appear to be isomers of n-butylbiphenyl. We hope to report upon this reaction further, but note for the present that the corresponding reaction with 2,2′-dibromobiphenyl produced no biphenylene at all. One possible route to biphenylene involves replacing the bromine by lithium and subsequent elimination of lithium fluoride in a reaction analogous to the formation of benzyne, in this case to give biphenylene; the acquisition of the tritium label could occur in a subsequent reaction of the biphenylene with n-butyl-lithium followed by hydrolysis.[19]

*Formation of 2-Butyl-2′-bromobiphenyl.*—In an attempt to prepare 2-bromo-2′,3′,4′,5′,6′-pentafluorobiphenyl for resolution of the above reaction data, n-butyl-lithium was refluxed with *o*-dibromobenzene, hexafluorobenzene being then added followed by

[18] R. Taylor, *Tetrahedron Letters*, 1972, 1755.
[19] J. M. Blatchly and R. Taylor, *J. Chem. Soc.*, 1964, 4641.

further reflux; this method gives the desired 3-bromo- and 4-bromo-products with other dibromobenzenes. However, none of the required product was obtained, the main product, a yellow oil, being shown after isolation by v.p.c. and mass spectral analysis to be 2-butyl-2′-bromobiphenyl, the formation of which probably proceeds *via* Scheme 2.




SCHEME 2

EXPERIMENTAL

The general kinetic technique has been described in previous papers in this series,[19] and the acid for kinetic studies was made up to be similar to that described in ref. 11.

All separations involving preparative gas chromatography employed a 9 ft column packed with SE 52 (20%) on 100—120 mesh Chromosorb G, operated at 180° and with 150 ml $min^{-1}$ nitrogen flow rate.

2′,3′,4′,5′,6′-*Pentafluoro*[2-, 3-, *and* 4-$^3$H]*biphenyl*.—*ortho*-, *meta*-, and *para*-Dibromobenzene were purified by fractional distillation and converted into bromo[2-, 3-, and 4-$^3$H]benzene by the standard Grignard method.[15] These gave, *via* reaction of the tritiated phenyl-lithium intermediates with hexafluorobenzene [20] and after sublimation and recrystallisation from petroleum, 2′,3′,4′,5′,6′-*pentafluoro*[2-, 3-, *and* 4-$^3$H]*biphenyl*, m.p. 110—111° (lit., 110—112 [20] and 111—112° [21]).

4-*Fluoro*[4-$^3$H]*biphenyl*.—4-Bromo-4′-fluorobiphenyl (2·5 g, 0·01 mol) supplied by Koch–Light Ltd., was treated with magnesium (1·2 g, excess) with entrainment with 1,2-dibromoethane (1·9 g, 0·01 mol) and the resultant Grignard was hydrolysed with tritiated water (excess) to give after normal work-up, sublimation, and recrystallisation from ethanol 4′-*fluoro*[4-$^3$H]*biphenyl* (0·7 g, 41%), m.p. 75° (lit.,[22] 74·2°).

2′-*Fluoro*[4-$^3$H]*biphenyl*.—2-Fluorobiphenyl (3·0 g, 0·017 mmol) (supplied by Koch–Light Ltd.) was brominated with bromine (10·5 g, 0·058 mol) in trifluoroacetic acid (30 ml). (This reagent has very high selectivity and tends to substitute mainly in the *para*-position.[23,24]) Analysis of the crude reaction product on a gas chromatograph–mass spectrometer showed the presence of two monobromofluorobiphenyls as expected and these can confidently be stated to be 2-bromo-2′-fluorobiphenyl and 4-bromo-2′-fluorobiphenyl, the latter being present in by far the larger quantity. Recrystallisation from ethanol yielded pure 4-*bromo*-2′-*fluorobiphenyl* (1·5 g, 35%), m.p. 45—46°, *m/e* 250 and 252); this (0·5 g) was treated with an excess of 1·5M-n-butyl-lithium in hexane, followed by hydrolysis with tritiated water (excess). V.p.c. analysis of the crude reaction product showed it to consist almost entirely of 2-fluorobiphenyl and addition of further 2-fluorobiphenyl to assist work-up gave 2′-*fluoro*[4-$^3$H]*biphenyl*, m.p. 72° (lit.,[22] 73·5°) after sublimation and recrystallisation from ethanol.

3′-*Fluoro*[2-$^3$H]*biphenyl*.—The Gomberg reaction between *m*-fluoroaniline (22 g, 0·2 mol) and bromobenzene (150 ml, excess) gave the three expected bromofluorobiphenyls, the predominant isomer being, as expected, the *o*-bromo-isomer, and consistent with this, it possessed the lowest v.p.c. retention time. Column chromatography of a portion of this mixture gave the *ortho*-isomer as a pale lemon oil with a purity of >97%. Reaction of this compound (0·5 g) with n-butyl-lithium (excess) followed by hydrolysis with tritiated water (excess) gave, after work-up, 3′-*fluoro*[2-$^3$H]*biphenyl* (0·20 g, 58%), m.p. 27° (lit.,[22] 26—27°) which was shown to be >98% pure by v.p.c. analysis.

3′-*Fluoro*[2-$^3$H]*biphenyl*.—The Gomberg reaction between *o*-fluoroaniline (33 g, 0·3 mol) and bromobenzene (200 ml, excess) gave a product showing two major peaks in the gas chromatogram; as above, the major component (the expected *ortho*-bromo-isomer) had the shortest retention time. Separation of a portion of the mixture by preparative v.p.c. gave pure 2-*bromo*-2′-*fluorobiphenyl*, a white solid, m.p. 41—42°, *m/e*, 250 and 252. Reaction of this compound with n-butyl-lithium (excess) followed by hydrolysis with tritiated water yielded a crude reaction product shown by v.p.c. to contain at least three products. Separation of these by preparative v.p.c. yielded biphenylene (the major product), biphenyl (the minor product), and the expected 2′-fluoro[2-$^3$H]biphenyl. The other two components were both active but this activity may have arisen from lithiation of the inactive reaction products and biphenylene at least is known to undergo ready lithiation.[19]

3′-*Fluoro*[4-$^3$H]*biphenyl*.—3-Nitrobiphenyl, m.p. 55—60° was prepared in 14% yield from 3-nitroaniline by the method of Elks, Haworth, and Hey.[25] Bromination by the method of Blakey and Scarborough [26] gave 4-bromo-3′-nitrobiphenyl in 72% yield, m.p. 92°, after recrystallisation from ethanol. Reduction of this nitro-compound by the literature method [26] gave 3-amino-4′-bromobiphenyl in 51% yield, m.p. 106°. A Balz–Schiemann reaction on this amine yielded pure 4-*bromo*-3′-*fluorobiphenyl* (4 g, 26%), $n_D^{20}$ 1·6245; *m/e*, 250 and 252. Reaction of a small portion of this with butyl-lithium (excess) followed by tritiated water (excess) and work-up *via* preparative v.p.c. yielded pure 3′-*fluoro*[4-$^3$H]*biphenyl*, m.p. 29° (lit.,[22] 26—27°).

An attempt to prepare 4-bromo-3′-fluorobiphenyl *via* bromination of 3-fluorobiphenyl by bromine in trifluoroacetic acid was unsuccessful probably due to the presence of an excess of bromine. However, from the crude product was isolated, *via* recrystallisation from ethanol, 4,4′-*dibromo*-3′-*fluorobiphenyl*, m.p. 96·5°, *m/e*, 328, 330, and 332 (Found: C, 43·75; H, 2·45. Calc. for $C_{12}H_7Br_2F$: C, 43·8; H, 2·15%). The identification as this isomer follows

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by implication from the method of bromination (which goes extremely selectively in the *para*-positions of biphenyl) and also by its v.p.c. retention time which was almost identical with that of 4,4′-dibromobiphenyl; a single fluoro-substituent is known to produce a trivial modification of v.p.c. retention times and we also have found this to be so.

[2-, 3-, *and* 4-$^3H$]*Biphenyl.*—These compounds were available from a previous study.[11]

3-*Bromo*-2′,3′,4′,5′,6′-*Pentafluorobiphenyl.*— *meta*-Dibromobenzene (1 g, 0·004 mol) in ether (20 ml) was treated with butyl-lithium (0·004 mol) in hexane, and then added to hexafluorobenzene (0·74 g, 0·004 mol); the mixture was refluxed during 1 h. Hydrolysis, work-up, and analysis of the product by a gas chromatograph–mass spectrometer showed the presence of two main peaks. The predominant component had the shorter retention time and gave *m/e* = 458, 460, 462, and fragments at 380, 300, and 224, as well as *m/2e* at 229, 230, and 231. The other component gave *m/e* = 322 and 324. Recrystallisation from ethanol produced fine white needles of the former compound which was clearly 3,3″-*dibromo*-2′,3′,5′,6′-*tetrafluoro*-p-*terphenyl*, m.p. 212° (*cf.* 237—238° for the 4,4″-dibromo-isomer obtained by an analogous route [4]). From the residue, white plates of 3-*bromo*-2′,3′,4′,5′,6′-*pentafluorobiphenyl*, m.p. 64—65° were isolated by preparative gas chromatography. The i.r. spectrum of this compound showed maxima at 1651, 1597, 1567, 1523, 1499, 1482, 1401, 1325, 1096, 1080, 1067, 993, and 882 cm$^{-1}$. The retention time of this compound on a v.p.c. column consisting of SE 30 (5%) on 100—120 mesh Chromosorb G operated at 180° (similar conditions to those used in ref. 4) showed that it was not resolvable from the main component of bromination of pentafluorobiphenyl. The latter, isolated by preparative chromatography had m.p. 82—84° and gave i.r. maxima at 1655, 1590, 1568, 1525, 1494, 1396, 1325, 1199, 1063, 1015, 992, 857, and 834 cm$^{-1}$. Both compounds were resolved by using a 5 ft column packed with free fatty-acid phase (5%) on 100—120 mesh Chromosorb G operated at 170°.

*Preparation of* 2-*Bromo*-2′-*butylbiphenyl.*—In an attempt to prepare 2-bromo-2′,3′,4′,5′,6′-pentafluorobiphenyl, an analogous preparation to the above was performed using *ortho*-dibromobenzene (with longer reflux times). V.p.c. analysis of the crude reaction product showed total absence of the desired product (an authentic sample being available from bromination of pentafluorobiphenyl), and isolation of the main product (a yellow oil) by preparative v.p.c. followed by mass spectral analysis [*m/e* 290, 288, 261, 259, 247, 245, 233, 231, and 152 (loss of fragments of butyl followed by bromine) and 209, 180, 166, and 152 (loss of bromine followed by fragments of butyl)] showed conclusively that this compound must be substituted by butyl and bromine and must be 2-*bromo*-2′-*butylbiphenyl*.

*Bromination by Bromine Catalysed by Aluminium Tribromide in Cyclohexane.*—This reaction was carried out as described in the literature.[4]

*Bromination by Bromine Catalysed by Iodine in Acetic Acid.*—Pentafluorobiphenyl (0·5 g, 0·002 mol) in acetic acid (20 ml) was refluxed with bromine (0·96 g, 0·006 mol) and iodine (0·1 g) during 24 h. Very little reaction occurred during this time though it was sufficient for a satisfactory v.p.c. analysis of the reaction products (after work-up) to be made.

*Nitration by Fuming Nitric Acid–Sulphuric Acid in Acetic Acid.*—This reaction was carried out as described in the literature,[4] and also in the presence of 0·2 g of urea. Analyses were performed with the SE 30 column described above (which failed to resolve the *meta*- and *para*-nitro-derivatives) and with the free fatty-acid phase column operated at 210° (which resolved them completely).

*Reaction with Nitric Acid in Acetic Anhydride.*—This was carried out using the conditions described in the literature for nitration of biphenyl,[27] but with a longer reaction time (*ca.* 4 days) and a temperature of *ca.* 25°.

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