**340.** *The Reaction of Pentafluorophenylmagnesium Bromide with Pentafluoronitrobenzene in Tetrahydrofuran*

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Treatment of pentafluoronitrobenzene with pentafluorophenylmagnesium bromide in tetrahydrofuran at -10 to $4°$ gave nonafluoro-2-nitrobiphenyl (II), nonafluoro-4-nitrobiphenyl (III), and 2,4-bispentafluorophenyl-3,5,6-trifluoronitrobenzene by simple nucleophilic replacement of fluorine. The nitrogen of the nitro-group was not attacked. The ratio of *ortho-* to *para-* replacement (relative to NO_2) (II) : (III) was about 1 : 10.

IN a recent publication [1] the preparation of a Grignard reagent from chloropentafluoro-benzene in diethyl ether using magnesium activated by 1,2-dibromoethane was described. With tetrahydrofuran as solvent, polymeric material similar to that which other workers have obtained when reacting bromopentafluorobenzene with magnesium in boiling tetra-hydrofuran,[2] was produced in high yield. Moreover, bromopentafluorobenzene readily forms a Grignard reagent in tetrahydrofuran at temperatures below $5°$ and when this was reacted with hexafluorobenzene, polymeric material of high molecular weight was again obtained; there was no evidence for the formation of significant amounts of fluorinated bi- or ter-phenyls. Presumably these polymers were formed by nucleophilic displacement of halogen in the fluoro-aromatic ring by the Grignard reagent.
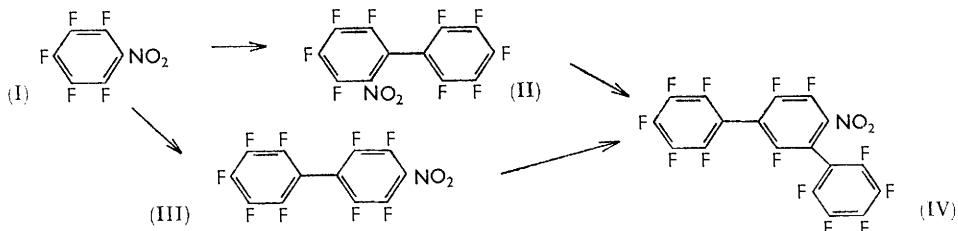
When hydrocarbon Grignard reagents react with highly fluorinated aromatic compounds, only simple reaction products result; Pummer and Wall [3] reported a low yield of 2,3,4,5,6-pentafluorotoluene from hexafluorobenzene and methylmagnesium iodide in ether solution,

[1] G. M. Brooke, R. D. Chambers, J. Heyes, and W. K. R. Musgrave, *J.*, 1964, 729.
[2] E. J. P. Fear, J. Thrower, and M. A. White, XIXth International Congress of Pure and Applied Chemistry, London, July 1963.
[3] W. J. Pummer and L. A. Wall, *J. Res. Nat. Bur. Stand.*, 1959, 63*A*, 167.

and Harper and Tamborski [4] obtained 1,4-dibenzyltetrafluorobenzene in 54% yield from hexafluorobenzene and a benzyl Grignard reagent in tetrahydrofuran solution. Until now however, there has not been a reaction reported in which a highly fluorinated aromatic Grignard reagent has reacted with a highly fluorinated aromatic compound to give simple, low-molecular-weight products. We now report the reaction of pentafluorophenyl-magnesium bromide in tetrahydrofuran with pentafluoronitrobenzene, to give bi- and ter-phenyl derivatives.

Treatment of pentafluoronitrobenzene with pentafluorophenylmagnesium bromide (1·34 Equiv.) in tetrahydrofuran, at −10 to 4° gave a complex mixture of products which was shown by analytical gas-phase chromatography to consist of seven components, in order of their retention times: (i) pentafluoronitrobenzene (16%); (ii) decafluorobiphenyl (1%); (iii) nonafluoro-2-nitrobiphenyl (6%); (iv) nonafluoro-4-nitrobiphenyl (61%); (v) and (vi) (2%) and (0·5%), respectively, were not identified; and (vii) 2,4-bispenta-fluorophenyl-3,5,6-trifluoronitrobenzene (13%). The figures represent the percentage area under each peak. A partial separation of the products was effected by distillation *in vacuo*. Further fractional distillation of the lower-boiling fractions enabled the known decafluorobiphenyl [5] to be isolated and identified. Compound (II) was obtained in an enriched fraction and was obtained as a pure solid by preparative scale gas-phase chromato-graphy followed by crystallisation. Compound (III) was prepared in the pure state by preliminary enrichment by fractional distillation *in vacuo*, followed by hydrogenation over Raney nickel to give the amine. Purification of the amine by fractional crystallisation, and oxidation with peroxytrifluoroacetic acid gave pure compound (III), which was a liquid. The highest-boiling fraction from the preliminary distillation solidified slowly, and compound (IV) was obtained pure from the mixture by fractional crystallisation.

Compounds (II) and (III) were shown to be nonafluoro-2- and -4-nitrobiphenyl, re-spectively, first from a study of their nuclear magnetic resonance spectra. Chemical evidence for the structure of the 4-nitroanalogue was obtained by hydrogenation over Raney nickel to give the amine, which on treatment with aqueous ammonia, gave the known, 4,4'-diamino-octafluorobiphenyl.[6] The 4,4'-structure was confirmed by the presence of only two magnetically different types of fluorine in its nuclear magnetic resonance spectrum. The 4-aminononafluorobiphenyl was converted into 4-bromononafluorobiphenyl in high yield by diazotisation in 80% hydrofluoric acid [7] followed by treatment with cuprous bromide in hydrobromic acid.

Compound (IV) was shown to be a nitroterphenyl from its elemental analysis, its molecular weight, and the uptake of hydrogen on reduction over Raney nickel to the amine. The structure was shown to be 2,4-bispentafluorophenyl-3,5,6-trifluoronitro-benzene by separately treating nonafluoro-2-nitrobiphenyl and nonafluoro-4-nitrobi-phenyl with pentafluorophenylmagnesium bromide in tetrahydrofuran. The same tri-decafluoronitroterphenyl was obtained from each experiment, along with smaller amounts of unidentified material. It was identified by its retention times on analytical chromato-graphy columns of different polarity, and by its isolation, in each case from the mixture of products, by preparative-scale vapour phase chromatography. The nuclear magnetic resonance spectrum of its fluorine atoms was entirely consistent with the structure allo-cated.[8] Hydrogenation over Raney nickel gave 2,4-bispentafluorophenyl-3,5,6-trifluoro-aniline. Attempts to cyclise this compound to 3-pentafluorophenylheptafluorocarbazole with sodamide in liquid ammonia, and with sodium hydride in dioxan at elevated temper-atures, were unsuccessful. Only one other example of a reaction between pentafluoro-nitrobenzene and a nucleophile has been reported [9] and that is the reaction with ammonia

[4] R. J. Harper and C. Tamborski, *Chem. and Ind.*, 1962, 1824.
[5] E. Nield, R. Stephens, and J. C. Tatlow, *J.*, 1959, 166.
[6] Research Department, Imperial Smelting Corporation, Avonmouth.
[7] G. M. Brooke, E. J. Forbes, R. D. Richardson, M. Stacey, and J. C. Tatlow, *J.*, 1965, 2088.
[8] J. W. Emsley, unpublished results.
[9] G. M. Brooke, J. Burdon, and J. C. Tatlow, *J.*, 1961, 802.

in ether solution. The ratio of *ortho-* to *para*-replacement of fluorine in this reaction was about 7 : 3, whereas in the reaction now reported the ratio is about 1 : 10. One obvious explanation of this change from predominantly *ortho*-replacement of fluorine by ammonia to *para*-replacement by pentafluorophenylmagnesium bromide is in terms of steric hindrance; it is sterically easier for the pentafluorophenyl group to enter the position *para-* to the nitro-group than to enter into the *ortho*-position since the former site is flanked by two relatively small fluorine atoms, whilst the latter is flanked by a fluorine atom and a relatively large nitro-group. However, it is now believed that preferential *ortho*-replacement of fluorine in pentafluoronitrobenzene by ammonia is partly due to the ability of the nucleophile to form a hydrogen bond with an oxygen atom of the nitro-group when attacking at the *ortho*-position.[10] Bunnett has drawn attention to this rather specific effect of amines in their reaction with *ortho-* and *para*-halogenonitrobenzenes.[11] There is no such possibility of hydrogen bonding between the incoming pentafluorophenyl group and the nitro-group.

More recently,[12] the reaction of pentafluorophenyl-lithium with bromopentafluorobenzene in ether to give 2-bromononafluorobiphenyl in 30% yield has been described. This, however, was not interpreted as nucleophilic attack by the lithium compound on the bromopentafluorobenzene but was thought to be a reaction between bromopentafluorobenzene and the intermediate tetrafluorobenzyne, since reaction between simple nucleophiles and bromopentafluorobenzene caused the replacement of the *para*-fluorine atom.[13]

The production of fluorinated nitro-biphenyls and -terphenyl by the reaction between pentafluoronitrobenzene and pentafluoromagnesium bromide is also of interest because Grignard reagents normally react with nitro-compounds by initial attack at the nitrogen atom of the nitro-group to give complex mixtures of products.[14] Thus, phenylmagnesium bromide with nitrobenzene gives diphenylamine, biphenyl, and phenol.

In the reaction between pentafluorophenylmagnesium bromide and pentafluoronitrobenzene, we isolated a small amount of decafluorobiphenyl, but we have shown that some of this is formed during the formation of the Grignard reagent by replacement of bromine in bromopentafluorobenzene by the newly formed reagent. It is still not certain whether any direct replacement of the nitro-group in pentafluoronitrobenzene by the Grignard reagent occurred, but this did not occur in the only other reported reaction between pentafluoronitrobenzene and a nucleophile.[9]

We could find no evidence for the formation of pentafluorophenol [15] or decafluorodiphenylamine [16] which could arise if the Grignard reagent attacked the nitro-group. Model experiments showed that these two compounds can be resolved from the other products actually obtained, by analytical gas chromatography using Apiezon L grease–kieselguhr. About 90% of pentafluoronitrobenzene was accounted for in the production of bi- and terphenyl compounds. Thus, the reaction almost certainly proceeded by simple replacement of fluorine by a nucleophilic mechanism.

EXPERIMENTAL

Reaction of Pentafluoronitrobenzene with Pentafluorophenylmagnesium Bromide in Tetrahydrofuran.—Pentafluorobromobenzene (16·51 g.) was added to magnesium turnings (3·03 g.) in dry tetrahydrofuran (75 ml.) at −20° and washed in with more solvent (5 ml.). An exothermic

[10] J. Burdon, private communication.
[11] J. F. Bunnett, *Quart. Rev.*, 1958, **12**, 1.
[12] D. E. Fenton, A. J. Park, D. Shaw, and A. G. Massey, *Tetrahedron Letters*, 1964, 949.
[13] L. A. Wall, W. J. Pummer, J. E. Fearn, and J. M. Antonucci, *J. Res. Nat. Bur. Stand.*, 1963, **67**A, 481.
[14] M. S. Kharasch and O. Reinmuth, " Grignard Reactions of Nonmetallic Substances," Constable and Co., London, 1954, p. 1239.
[15] J. M. Birchall and R. N. Haszeldine, *J.*, 1959, 13; E. J. Forbes, R. D. Richardson, M. Stacey, and J. C. Tatlow, *J.*, 1959, 2019.
[16] G. M. Brooke, J. Burdon, M. Stacey, and J. C. Tatlow, *J.*, 1960, 1768.

reaction occurred after a short induction period and the temperature was not allowed to rise above 0° for 1 hr. The mixture was then allowed to warm up to 28·5° during 1 hr., and 2 hr. later the solution was decanted from the excess of magnesium and added dropwise during 1·5 hr. to pentafluoronitrobenzene [9] (10·65 g.) in dry tetrahydrofuan (75 ml.), the temperature being maintained between −10 and 4°. After 18 hr. at room temperature, water was added followed by dilute sulphuric acid, and the product was extracted with ether. The ether layer was separated, washed with water, and dried (MgSO₄). The solvent was removed by distillation and the residue, analysed by gas chromatography on silicone grease–kieselguhr at 183°, gave seven peaks, as mentioned previously. Distillation gave three fractions which were treated as follows.

Fraction 1. A liquid (0·31 g.), b. p. 50—83·5°/0·05—0·10 mm. Analytical gas-phase chromatography showed that it was mainly pentafluoronitrobenzene [components (i)], identified by its retention time.

Fraction 2. A liquid (12·1 g.), b. p. 85·5—100°/0·05—0·10 mm. Analytical gas-phase chromatography showed that it was mainly nonafluoro-2- and -4-nitrobiphenyls [components (iii) and (iv)] with a small amount of decafluorobiphenyl [components (ii)].

This mixture was partly separated into its components by fractional distillation *in vacuo* of material accumulated from similar experiments, followed by preparative-scale gas chromatography using silicone elastomer–kieselguhr at 220—240°. Decafluorobiphenyl [5] (0·06 g.) was identified by its m. p. 67·5—69°, mixed m. p., and infrared spectrum.

Nonafluoro-2-nitrobiphenyl crystallised from an enriched fraction as a pale yellow solid (1·06 g.) and was recrystallised from light petroleum (b. p. 40—60°) to give the pure compound (0·75 g.), m. p. 77—77·5 (Found: C, 39·7; F, 47·1%; *M*, 361. $C_{12}F_9NO_2$ requires C, 39·9; F, 47·4%; *M*, 361).

The fraction of the distillate enriched in nonafluoro-4-nitrobiphenyl (9·45 g.) was hydrogenated in ethanol over Raney nickel for 18 hr. at atmospheric pressure and room temperature (uptake about 1·6 l.). After filtration and evaporation, the residue was sublimed at 130° *in vacuo* and then recrystallised twice from benzene–light petroleum (b. p. 60—80°) to give 4-*aminononafluorobiphenyl* (5·53 g.), m. p. 144·5—146° (Found: C, 43·2; H, 0·8; F, 51·2. $C_{12}H_2F_9N$ requires C, 43·5; H, 0·6; F, 51·6%). It gave a *trifluoroacetyl derivative*, m. p. 189—190° (Found: C, 39·0; F, 53·1. $C_{14}HF_{12}NO$ requires C, 39·35; F, 53·35%).

Oxidation of 4-aminofluorobiphenyl. The 4-amino-compound (5·53 g.) in methylene chloride (10 ml.) was added over 10 min. to a mixture of methylene chloride (100 ml.), trifluoroacetic anhydride (25 ml.), and hydrogen peroxide (10 ml.; *ca.* 85%) which was being refluxed and stirred. After 16 hr. in all, the mixture was cooled and water (100 ml.) was added slowly. The methylene chloride layer was separated, washed with water, and dried (MgSO₄). Removal of solvent by distillation, followed by distillation *in vacuo*, gave chromatographically pure *nonafluoro-4-nitrobiphenyl* (5·31 g.), b. p. 72·5—73·5°/0·01 mm. (Found: C, 39·8; F, 47·4%; *M*, 362).

Fraction 3. A viscous liquid (4·74 g.), b. p. 100—143°/0·05—0·01 mm., which solidified on standing. It contained mainly peak (vii) accompanied by smaller amounts of peak (iv) and the unidentified (v) and (vi). Recrystallisation of accumulated material from light petroleum (b. p. 40—60°) gave 2,4-*bispentafluorophenyl-3,5,6-trifluoronitrobenzene*, a pale yellow solid, m. p. 110—110·5° (Found: C, 42·5; F, 48·15%; *M*, 507. $C_{18}F_{13}NO_2$ requires C, 42·5; F, 48·5%; *M*, 509).

Treatment of Nonafluoro-2-nitrobiphenyl with Pentafluorophenylmagnesium Bromide in Tetrahydrofuran.—The *o*-nitrobiphenyl (0·271 g.) in dry tetrahydrofuran (1·5 ml.) was treated at room temperature with pentafluorophenylmagnesium bromide in tetrahydrofuran (2·6 ml.; 0·37N). After 17·5 hr., at room temperature, the mixture was worked up as before. Analytical gas chromatography on both silicone grease–kieselguhr at 183° and Apiezon L grease–kieselguhr at 189° showed the presence of 2,4-bispentafluorophenyl-3,5,6-trifluoronitrobenzene accompanied by unchanged 2-nitrobiphenyl and two unidentified peaks present in very small amount. The ratio of the areas under the peaks were 68 : 23 : 2 : 7, respectively. The nitroterphenyl (0·11 g.) was separated from the mixture by preparative-scale chromatography on silicone grease at 250°, and identified by its infrared spectrum.

Treatment of Nonafluoro-4-nitrobiphenyl with Pentafluorophenylmagnesium Bromide in Tetrahydrofuran.—The 4-nitrobiphenyl (0·255 g.) in dry tetrahydrofuran (1·5 ml.) was treated at room temperature with pentafluorophenylmagnesium bromide in tetrahydrofuran (2·5 ml.;

0·37N). After 17·5 hr. at room temperature, the mixture was worked up as before. Analytical gas chromatography of the product on the same columns as in the previous experiment showed the presence of a compound having the same retention time as the nitroterphenyl, accompanied by unchanged starting material and an unidentified compound. The ratios of the areas under the peaks were 37 : 45 : 18, respectively. A sample of the nitroterphenyl was separated from the mixture as in the previous experiment, and was identified as 2,4-bispentafluorophenyl-3,5,6-nitrobenzene by its infrared spectrum.

The Production of Decafluorobiphenyl during the Preparation of Pentafluoromagnesium Bromide.—Bromopentafluorobenzene (4·98 g.) was added to magnesium turnings (1·23 g.) in dry tetrahydrofuran (50 ml.) which had been cooled to −12°, and was washed in with more solvent (5 ml.). The temperature was maintained below 5° for 1 hr., and 3 hr. later the solution was decanted from the excess of magnesium. The solution was allowed to reach room temperature and after 18 hr. it was acidified with dilute sulphuric acid and extracted with ether. The extracts were dried ($MgSO_4$) and most of the solvent and pentafluorobenzene removed by simple distillation. Gas-chromatographic analysis of the residue on di-n-decylphathalate–kieselguhr at 177° and on Apiezon L grease–kieselguhr at 189° showed the presence of a very small amount of decafluorobiphenyl [5] (0·05 g. overall yield), identified by its retention times.

Hydrogenation of 2,4-Bispentafluorophenyl-3,5,6-trifluoronitrobenzene.—The compound (4·06 g.), m. p. 109—110·5°, was hydrogenated in ethanol over Raney nickel for 18 hr. at atmospheric pressure and room temperature (uptake about 0·56 l.). After filtration and evaporation, the residue was distilled at 125°/0·01—0·05 mm. The viscous distillate solidified when scratched to give a white solid (3·73 g.), m. p. 82·5—84·5°. Recrystallisation from light petroleum (b. p. 40—60°) gave 2,4-*bispentafluorophenyl-3,5,6-trifluoroaniline* (1·24 g.), m. p. 85·5—86·0° (Found: C, 45·1; H, 0·5; F, 51·4. $C_{18}H_2F_{13}N$ requires C, 45·1; H, 0·4; F, 51·5%).

Reaction of 4-Aminononafluorobiphenyl with Aqueous Ammonia.—The amine (0·905 g.) and aqueous ammonia (5 ml.; *d* 0·88) were heated together in a sealed tube at 157° for 16 hr. The mixture was diluted with water and extracted with ether. Evaporation of the dried ($MgSO_4$) extracts gave 4,4′-diamino-octafluorobiphenyl (0·93 g.), m. p. 175·5—177·5° which was sublimed at 130° *in vacuo* and recrystallised from benzene to give the pure diamine (0·66 g.), m. p. and mixed [6] m. p. 181—181·5°. It had the correct infrared spectrum.

4-Bromononafluorobiphenyl.—Sodium nitrite (3·99 g.) was added at 0° during 20 min. to 4-aminononafluorobiphenyl (5·4 g.) in hydrofluoric acid (75 ml.; 80% w/w). The mixture was stirred in a polythene beaker and the temperature was kept at 0° for 1 hr. A solution of cuprous bromide [from hydrated copper sulphate (30 g.) and potassium bromide (20 g.) dissolved in boiling water (150 ml.) to which was added hydrated sodium sulphite (*ca.* 10 g.) and the white precipitate of cuprous bromide filtered off and washed with water] dissolved in hydrobromic acid (50 ml.; 48% w/w) was then added dropwise over 20 min. to the diazotised amine, the temperature again being kept at 0°. After a further 2½ hr., during which the temperature was allowed to rise to that of the room, the mixture was diluted with water, extracted with ether, and the extracts washed with water until neutral. Evaporation of the dried ($MgSO_4$) extracts gave a residue which was sublimed at 120° *in vacuo*. Recrystallisation of the sublimate (5·95 g.) from light petroleum (b. p. 40—80°) gave 4-*bromononafluorobiphenyl* (4·8 g.), m. p. 101—102·5° (Found: Br, 20·2; F, 43·1. $C_{12}BrF_9$ requires Br, 20·2; F, 43·3%).

[19]*F Nuclear Magnetic Resonance Spectra.—Nonafluoro-2-nitrobiphenyl.* The spectrum was recorded at 60 Mc./sec. on an A.E.I. R.S.2 spectrometer, with C_6F_6 as an internal reference. The spectrum contained seven groups of chemically shifted peaks with the shifts and relative intensities shown in Table 1.

TABLE 1

Chemical shifts (from C_6F_6) for nonafluoro-2-nitrobiphenyl

Peak..............	1	2	3	4	5	6	7
c./sec.[−1]	1779·0	1475·6	1194·6	900·1	870·4	783·9	127·3
P.p.m.	29·650	24·593	19·910	15·002	14·507	13·065	2·122
Rel. intensity ...	1	2	1	1	1	1	2

The number and relative intensities of the peaks show that the nine fluorines give rise to seven chemically equivalent groups of nuclei, and for a monosubstituted nonafluorobiphenyl this can arise only for an *ortho-* or *meta*-substituted compound, relative to the inter-ring linkage. By

comparing the chemical shifts with those in decafluorobiphenyl and pentafluoronitrobenzene it is possible to choose between the two possible structures.

Peaks 2 and 7 can be assigned immediately, because of their intensity, to the fluorines at positions 2′ and 6′ in the case of peak 2, and 3′ and 5′ for peak 7. Comparison of the chemical shifts of these peaks with those in decafluorobiphenyl (24·03 and 1·52 p.p.m., respectively) shows that substitution in one ring has only a small effect on the shifts in the other ring. Consequently, the shift of the 4′-fluorine would be expected at about 12·01 p.p.m. (the value in decafluorobiphenyl). Peak 6 has a shift of 13·06 p.p.m. and the fine structure of a triplet of triplets confirms that this arises from the 4′-fluorine. This leaves peaks 1, 3, 4, and 5 to be assigned to the fluorines in the substituted ring, which is done by utilising the fact that the effect on ^{19}F shifts of a substituent in a fluoro-aromatic system is approximately additive, so that the shifts of the fluorines at positions, 2,3,4,5 and 6 in a nonofluoronitrobiphenyl can be predicted from the known substituent effects of a nitro-group and a C_6F_5-group, and these are shown in Table 2.

TABLE 2

Substituent parameters for NO_2 and C_6F_5 groups in fluoro-aromatic systems
(p.p.m. rel. to C_6F_6)

Position rel. to substituent	NO_2	C_6F_5
ortho	17·04	24·03
meta	4·13	1·52
para	16·22	12·01

Using these values, for nonafluoro-2-nitrobiphenyl and nonafluoro-3-nitrobiphenyl the approximate chemical shifts should be:

Ring position	2	3	4	5	6
Nonafluoro-2-nitrobiphenyl	—	18·56	16·14	17·74	28·16
Nonafluoro-3-nitrobiphenyl	41·07	—	29·05	5·65	40·25

The predicted shifts for the 2-nitro-compound do correspond to the observed pattern of shifts, that is, one peak at *ca.* 29 p.p.m. and the other three between 14 and 20 p.p.m., whereas the predicted shifts for the 3-nitro-compound are very different and include shifts of *ca.* 40 and *ca.* 6 p.p.m. which do not appear at all, even to within 5 p.p.m., in the observed spectrum.

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