184. *Migration Reactions in Polycyclic Systems. Part I. The Fries Rearrangement of 4-Benzoyloxydiphenyl.*

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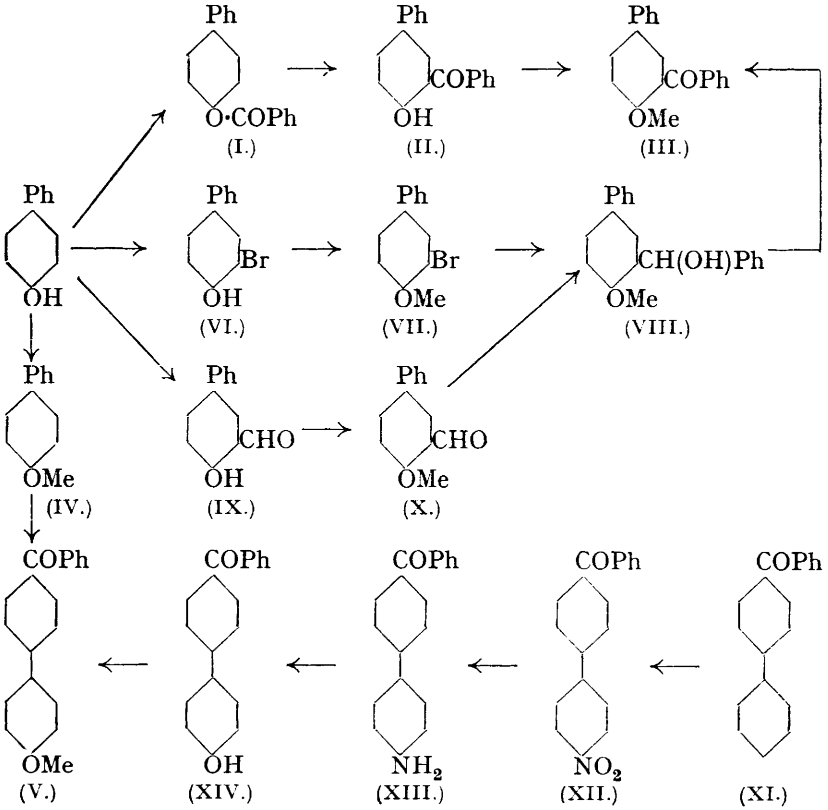
Comparatively few examples have been recorded of migration reactions, whether real or apparent, in polycyclic systems, particularly of reactions which involve a migration to one nucleus from a side chain attached to a second nucleus in the same molecule, since most migrations of this type proceed from an oxygen or a nitrogen atom attached to an aromatic nucleus which, being either potentially phenolic or basic, is particularly reactive. In the diphenyl series homonuclear migrations have been described by Bell, Kenyon, and Robinson (J., 1926, 1239) and by Scarborough and his co-workers (J., 1926, 557; 1927, 89, 3000) and the methylation of 4-aminodiphenyl hydrochloride in positions 3, 5, and 4′ by successive " migration " has been recorded by Hey and Jackson (J., 1934, 645).

Fries, von Auwers, and others have described many examples of homonuclear migration, mainly in the benzene and the naphthalene series, as the result of the action of aluminium or zinc chloride on phenolic esters whereby hydroxy-ketones are produced, but an example of heteronuclear migration of this type has been claimed by Blicke and Weinkauff (*J. Amer. Chem. Soc.*, 1932, **54**, 330) in the action of aluminium chloride on the benzoate of 4-hydroxydiphenyl. These authors draw an analogy between the Fries rearrangement of phenyl benzoate, which gives rise to *p*-hydroxybenzophenone, and that of 4-benzoyloxydiphenyl, which is stated to give rise in similar manner to 4-hydroxy-4′-benzoyldiphenyl. Proof of the identity of this compound was claimed by the fact that on methylation it gave a benzoyl-4-methoxydiphenyl identical with that obtained from the action of benzoyl chloride on 4-methoxydiphenyl in the presence of aluminium chloride. This argument, however, is unsatisfactory, since by whichever method the benzoylmethoxydiphenyl is prepared the position of attachment of the benzoyl group is uncertain. Further, many instances are on record of the production of a different aromatic hydroxy-ketone by a Fries rearrangement from that obtained by means of a Friedel–Crafts reaction on the appropriate phenol or its methyl ether (Witt and Braun, *Ber.*, 1914, **47**, 3216; Fries, *Ber.*, 1921, **54**, 709; 1925, **58**, 2835; von Auwers and Mauss, *Ber.*, 1928, **61**, 1495; *Annalen*, 1928, **464**, 293; Mosettig and Burger, *J. Amer. Chem. Soc.*, 1933, **55**, 2981). The two reactions, therefore, do not necessarily follow the same course. Other examples of the application of the Fries rearrangement to esters of polynuclear phenols have been recorded. For example, Witt and Braun (*loc. cit.*) obtained a 5% yield of 6-acetyl-2-naphthol by the action of zinc chloride on β-naphthyl acetate, although with aluminium chloride in place of zinc chloride Fries (*loc. cit.*) obtained 1-acetyl-2-naphthol. In the reactions studied by Mosettig and Burger (*J. Amer. Chem. Soc.*, 1933, **55**, 2981; 1934, **56**, 1745) in the phenanthrene series, by Wojahn (*Arch. Pharm.*, 1933, **271**, 417) in the diphenylmethane series, and by Harris and Christiansen (*J. Amer. Pharm. Assoc.*, 1934, **23**, 530) on various esters of 2- and 3-hydroxydiphenyl, only products formed by homonuclear migration were encountered. Instances of heteronuclear migration in the Fries reaction are thus very rare and it therefore seemed not improbable that the product of the rearrangement studied by Blicke and Weinkauff (*loc. cit.*) is not 4-hydroxy-4′-benzoyldiphenyl but rather 4-hydroxy-3-benzoyldiphenyl.

A reinvestigation of the Fries rearrangement of 4-benzoyloxydiphenyl (I), as carried out by Blicke and Weinkauff, was therefore undertaken. Instead of the one product (m. p. 193—195°) claimed by these authors, we obtained two, namely, 4-hydroxydiphenyl (m. p. 165°) and 4-*hydroxy*-3-*benzoyldiphenyl* (II) (m. p. 89°), the latter yielding 4-*methoxy*-3-*benzoyldiphenyl* (III) (m. p. 93°) on methylation. The presence of 4-hydroxydiphenyl in the product is not unexpected, since the free phenol is often formed as a by-product in the rearrangement of phenolic esters in the presence of aluminium chloride (cf. Cox, *J. Amer. Chem. Soc.*, 1930, **52**, 352). The action of benzoyl chloride on 4-methoxydiphenyl (IV) in the presence of aluminium chloride, under the conditions of Blicke and Weinkauff, also gives rise to two products, namely, 4-*methoxy*-4′-*benzoyldiphenyl* (V) (m. p. 166°), probably identical with the sole product of Blicke and Weinkauff, and a second compound which is regarded as 4-*methoxy*-3 : 4′-*dibenzoyldiphenyl* (m. p. 170°).

The identity of the 4-methoxy-3-benzoyldiphenyl (III), and hence of the corresponding hydroxy-compound (II) obtained from the Fries rearrangement, was established by its synthesis in two ways: (1) Bromination of 4-hydroxydiphenyl yielded 3-bromo-4-hydroxydiphenyl (VI) (Bell and Robinson, J., 1927, 1132), which was converted into 3-bromo-4-methoxydiphenyl (VII); the Grignard compound prepared from this, treated with benzaldehyde, gave a secondary alcohol (VIII), which on oxidation yielded 4-methoxy-3-benzoyldiphenyl (III). (2) Application of the Reimer–Tiemann reaction to 4-hydroxydiphenyl gave 4-hydroxy-3-aldehydodiphenyl (IX) (cf. Bell and Kenyon, J., 1926, 3044), from which 3-*aldehydo-4-methoxydiphenyl* (X) was obtained on methylation; addition of the methoxy-aldehyde to an ethereal solution of phenylmagnesium bromide led to the secondary alcohol (VIII), which on oxidation gave 4-methoxy-3-benzoyldiphenyl (III).

The identity of the 4-methoxy-4′-benzoyldiphenyl (V) obtained by the action of benzoyl chloride on 4-methoxydiphenyl in the presence of aluminium chloride could not be established in a similar way, because neither 4′-bromo- nor 4′-iodo-4-methoxydiphenyl could be induced to react with magnesium. However, nitration of 4-benzoyldiphenyl (XI) gave 4-*nitro*-4′-*benzoyldiphenyl* (XII), the position of the nitro-group in which was proved (a) by oxidation to *p*-nitrobenzoic acid and (b) by contrast with 4-p-*nitrobenzoyldiphenyl* and with 4-m-*nitrobenzoyldiphenyl*, prepared from the appropriate nitrobenzoyl chloride and diphenyl in the presence of aluminium chloride. Reduction of 4-nitro-4′-benzoyldiphenyl yielded 4-*amino*-4′-*benzoyldiphenyl* (XIII), which was converted successively into 4-hydroxy-4′-benzoyldiphenyl (XIV) and 4-methoxy-4′-benzoyldiphenyl (V).



Experimental.

4-Hydroxydiphenyl (m. p. 165°) was purchased or prepared either by the method of Norris, Macintire, and Corse (*Amer. Chem. J.*, 1903, **29**, 120) or from 4-aminodiphenyl by means of the diazo-reaction (cf. Raiford and Colbert, *J. Amer. Chem. Soc.*, 1925, **47**, 1456). Benzoylation was effected either by Blicke and Weinkauff's method (*loc. cit.*) or by the usual Schotten–Baumann process. The benzoate crystallised from absolute alcohol in white needles, m. p. 150—151° (cf. Raiford and Colbert, *loc. cit.*; Kaiser, *Annalen*, 1890, **257**, 101).

Action of Aluminium Chloride on 4-Benzoyloxydiphenyl.—The following is typical of several experiments carried out under the conditions of Blicke and Weinkauff (*loc. cit.*). A solution of 4-benzoyloxydiphenyl (25 g.) in dry tetrachloroethane (125 c.c.) was heated with aluminium chloride (15 g.) at 140° (oil-bath) for 1 hour. The cold product was treated with ice and hydrochloric acid and distilled with steam to remove tetrachloroethane. The residue was extracted several times with hot aqueous sodium hydroxide and the solid precipitated on acidification of the filtered extract was dried and extracted with hot benzene. A little tar was removed by addition of ligroin. Concentration of the benzene solution deposited some 4-hydroxydiphenyl (m. p. and mixed m. p. 165° after crystallisation from aqueous alcohol). Further evaporation yielded an oily residue, which solidified on trituration with light petroleum (b. p. 40—60°). Repeated crystallisation from 95% alcohol gave 4-*hydroxy*-3-*benzoyldiphenyl* (II) in yellow needles, m. p. 89° (Found : C, 83·3; H, 5·5. $C_{19}H_{14}O_2$ requires C, 83·2; H, 5·1%). No trace of an alkali-soluble product, m. p. 193—195°, as claimed by Blicke and Weinkauff, could be detected. The *benzoyl* derivative, prepared by the Schotten–Baumann method, crystallised from aqueous alcohol in white needles, m. p. 95—96° (Found : C, 82·8; H, 5·05. $C_{26}H_{18}O_3$ requires C, 82·5; H, 4·8%). The *acetyl* derivative, obtained from the hydroxy-ketone (1 g.), acetic anhydride (5·6 g.), and anhydrous sodium acetate (3·8 g.) at 180—190° and crystallised from light petroleum (b. p. 40—60°), melted at 136—137° (Found : C, 79·9; H, 5·0. $C_{21}H_{16}O_3$ requires C, 79·7; H, 5·1%).

4-*Methoxy*-3-*benzoyldiphenyl* (III).—To a boiling solution of 4-hydroxy-3-benzoyldiphenyl (0·5 g.) in alcoholic potassium hydroxide (0·8 g. in the least quantity of absolute alcohol), an excess of methyl iodide was added in portions. When the colour was discharged (3 hours), the bulk of the solvent was evaporated, and water added to the residue, which was then extracted with ether. Removal of the ether from the dried extract left an oil which solidified. Recrystallisation from light petroleum (b. p. 60—80°) gave 4-*methoxy*-3-*benzoyldiphenyl* (III) in colourless transparent blades, m. p. 93° (Found : C, 83·2; H, 5·5. $C_{20}H_{16}O_2$ requires C, 83·3; H, 5·55%). The 2 : 4-*dinitrophenylhydrazone*, prepared by Brady's method (J., 1931, 756), separated from ethyl acetate in small orange-red crystals, m. p. 218—219° (Found : N, 12·1. $C_{26}H_{20}O_5N_4$ requires N, 12·0%).

Action of Benzoyl Chloride on 4-*Methoxydiphenyl in Presence of Aluminium Chloride* (cf. Blicke and Weinkauff, *loc. cit.*).—Benzoyl chloride (7 g.) was added gradually to a solution of 4-methoxydiphenyl (9 g., m. p. 88—89°; prepared by Werner and Rekner's method, *Annalen*, 1902, **322**, 167) in carbon disulphide (40 c.c.) to which finely powdered aluminium chloride (8 g.) had been added. After 24 hours the carbon disulphide was decanted from the brown viscous layer, ice and hydrochloric acid added, the mixture extracted with benzene, and the extract washed with aqueous sodium hydroxide and with water, dried, and evaporated. The residual oil after solidifying was fractionally crystallised from benzene–light petroleum (b. p. 60—80°), giving (a) 4-*methoxy*-4′-*benzoyldiphenyl* (V) in colourless needles, m. p. 166° (Found : C, 83·2; H, 5·6. $C_{20}H_{16}O_2$ requires C, 83·3; H, 5·55%), and (b) colourless needles, m. p. 170°, regarded as 4-*methoxy*-3 : 4′-*dibenzoyldiphenyl* (Found : C, 82·9; H, 4·9. $C_{27}H_{20}O_3$ requires C, 82·6; H, 5·1%). The 2 : 4-*dinitrophenylhydrazone* of the former, prepared by Brady's method, separated from ethyl acetate in small red crystals, m. p. 221° (Found : N, 11·65. $C_{26}H_{20}O_5N_4$ requires N, 12·0%). Treatment of the product (b) in a similar manner yielded a 2 : 4-*dinitrophenylhydrazone* which separated from ethyl acetate in small red crystals, m. p. 221° (Found : N, 9·9. $C_{33}H_{24}O_6N_4$ requires N, 9·8%). The two hydrazones, and also the two parent compounds, depressed each other's m. p.

Synthesis of 4-*Methoxy*-3-*benzoyldiphenyl* (III).—(a) A solution of 3-bromo-4-hydroxydiphenyl (VI) (10 g.) (Bell and Robinson, J., 1927, 1132) in 10% aqueous sodium hydroxide (20 c.c.) was shaken with methyl sulphate (6·3 g.), diluted with water (20 c.c.), and, after ½ hour, heated on the steam-bath for 15 minutes. The granular solid which separated on cooling yielded 3-bromo-4-methoxydiphenyl (VII), m. p. 76—77° (from alcohol) (cf. Bell, J., 1930, 1075). To the Grignard solution prepared smoothly at 30° from 3-bromo-4-methoxydiphenyl (7·5 g.) and magnesium (0·7 g.) in dry ether (100 c.c.), benzaldehyde (3 g.) in dry ether was added gradually, and the mixture was finally boiled under reflux for ½ hour. After addition of ice and dilute sulphuric acid, the ethereal layer was separated, dried, and evaporated, leaving a viscous oil (9 g.), from which, on trituration with absolute alcohol, unchanged 3-bromo-4-methoxydiphenyl separated. The residual secondary alcohol (VIII) (5 g.) was added slowly to a stirred mixture of potassium dichromate (7·5 g.), concentrated sulphuric acid (6 c.c.), and water (38 c.c.) and after 2 hours the temperature was raised to 40—50° for ½ hour. The mixture was diluted with water and extracted with ether, and the extract washed with dilute alkali solution to remove a little benzoic acid, and dried. The viscous residue obtained on removal of the solvent solidified on long standing and, after trituration with light petroleum (b. p. 40—60°), the product was crystallised from light petroleum (b. p. 60—80°). 4-Methoxy-3-benzoyldiphenyl (III) was obtained in colourless needles, m. p. 93° alone and on admixture with the compound obtained on methylation of the product of the Fries rearrangement of 4-benzoyloxydiphenyl.

(b) A mixture of 4-hydroxy-3-aldehydodiphenyl (IX) (6 g.) (Bell and Kenyon, J., 1926, 3047), powdered potassium hydroxide (11·5 g.), and absolute alcohol (150 c.c.) was boiled under reflux with the periodic addition of methyl iodide. After 10 hours the mixture was poured into water, and the precipitated solid extracted with ether. Acidification of the aqueous layer precipitated some unchanged 4-hydroxy-3-aldehydodiphenyl. The solid residue obtained on evaporation of the dried ethereal extract, after crystallisation from light petroleum (b. p. 60—80°), gave 3-*aldehydo*-4-*methoxydiphenyl* (X) in pale yellow needles, m. p. 79° (Found : C, 79·2; H, 5·7. $C_{14}H_{12}O_2$ requires C, 79·25; H, 5·7%). A solution of the methoxy-aldehyde (0·6 g.) in dry ether was added slowly to an ethereal solution of phenylmagnesium bromide prepared from bromobenzene (2 g.) and magnesium (0·3 g.) in dry ether (25 c.c.). Reaction was completed by heating on the water-bath for ½ hour. After addition of ice and dilute sulphuric acid, the ethereal layer was separated, dried, and evaporated, leaving the crude secondary alcohol (VIII) as a yellow viscous oil (1·5 g.), which on oxidation with dichromate mixture yielded 4-methoxy-3-benzoyldiphenyl (III), m. p. and mixed m. p. 93°.

Synthesis of 4-*Methoxy*-4′-*benzoyldiphenyl* (V).—4-Benzoyldiphenyl (XI) was prepared by the action of benzoyl chloride (50 g.) on a solution of diphenyl (27·5 g.) in benzene (65 c.c.) in presence of aluminium chloride (38·5 g.) (cf. Grieve and Hey, J., 1933, 970). One crystallisation from benzene–ligroin yielded 4-benzoyldiphenyl (35 g.), m. p. 100—102°, and distillation of the mother-liquor yielded benzophenone (cf. Montagne, *Rec. trav. chim.*, 1908, **27**, 357). Finely powdered 4-benzoydiphenyl (5 g.) was added in portions to well-stirred nitric acid (*d* 1·46; 100 c.c.) at 0—5° (cf. Grieve and Hey, *loc. cit.*). After 15 minutes the nitrating mixture, containing suspended solid, was poured into water and the precipitated product was crystallised several times from absolute alcohol, from which 4-*nitro*-4′-*benzoyldiphenyl* (XII) separated in pale yellow needles m. p. 154—156° (Found : N, 4·8. $C_{19}H_{13}O_3N$ requires N, 4·6%) (cf. I.G., E.P. 390556 and F.P. 735846). A portion of the nitro-compound (1 g.) was oxidised with chromic anhydride (5 g.) in boiling acetic acid (15 c.c.). After dilution with water, ether extracted *p*-nitrobenzoic acid (m. p. and mixed m. p. 238°). Powdered 4-nitro-4′-benzoyldiphenyl (5 g.) was added gradually to a hot solution of stannous chloride (18 g.) in concentrated hydrochloric acid (25 c.c.) and heating was continued for 1 hour on the steam-bath (cf. Gabriel and Stelzner, *Ber.*, 1896, **29**, 1303). The double salt, which separated when cold, was suspended in water and decomposed with an excess of sodium hydroxide. The liberated base was extracted with benzene and dried. Removal of the solvent left a solid residue (3 g.), which, on crystallisation from aqueous alcohol, gave 4-*amino*-4′-*benzoyldiphenyl* (XIII) in yellow blades, m. p. 143—144° (Found : N, 5·4. $C_{19}H_{15}ON$ requires N, 5·1%). Treatment with acetic anhydride yielded 4-*acetamido*-4′-*benzoyldiphenyl*, which separated from alcohol in white needles, m. p. 206—207° (Found : N, 4·5. $C_{21}H_{17}O_2N$ requires N, 4·4%). An ice-cold suspension of 4-amino-4′-benzoyldiphenyl (2·8 g.) in dilute sulphuric acid (*d* 1·4; 20 c.c.) was diazotised with aqueous sodium nitrite (0·8 g. in 5 c.c.) and the mixture was kept at room temperature for 1 hour, heated on the steam-bath, made alkaline with aqueous sodium hydroxide, filtered hot, and acidified. The precipitated product was extracted with benzene, evaporation of which yielded 4-hydroxy-4′-benzoyldiphenyl (XIV) (1 g.), which separated from benzene–light petroleum (b. p. 40—60°) in faintly yellow, translucent leaves, m. p. 195° (cf. Blicke and Weinkauff, *loc. cit.*). The 4-hydroxy-4′-benzoyldiphenyl (0·4 g.) was shaken with methyl sulphate (0·8 g.) and 5% aqueous sodium hydroxide (5 c.c.) and finally heated for 15 minutes on the steam-bath; the solid which separated on cooling, recrystallised from absolute alcohol, gave 4-methoxy-4′-benzoyldiphenyl (V) in white leaflets, m. p. 166° alone and on admixture with the product obtained from the action of benzoyl chloride on 4-methoxydiphenyl in the presence of aluminium chloride.

4-p-*Nitrobenzoyldiphenyl.*—A concentrated solution of *p*-nitrobenzoyl chloride (100 g.) in benzene was added in portions to a solution of diphenyl (35 g.) in the least quantity of benzene required for solution in the presence of powdered aluminium chloride (49 g.); the viscous product had to be warmed on the steam-bath before the addition was complete. When evolution of hydrogen chloride ceased, the mixture was treated with ice and the product was separated in benzene from insoluble brown material, dried, recovered (25 g.), and crystallised from benzene–light petroleum (b. p. 40—60°), 4-p-*nitrobenzoyldiphenyl* separating in pale yellow needles, m. p. 165° (Found : N, 4·8. $C_{19}H_{13}O_3N$ requires N, 4·6%).

4-m-*Nitrobenzoyldiphenyl* (12 g. crude), prepared similarly from *m*-nitrobenzoyl chloride (25 g.), diphenyl (9 g.), benzene (45 c.c.), and aluminium chloride (12 g.), separated from absolute alcohol in white nacreous leaves, m. p. 130° (Found : N, 4·7%) (cf. Dilthey *et al.*, *J. pr. Chem.*, 1931, **129**, 189).

4-*Bromo- and* 4-*Iodo*-4′-*methoxydiphenyl*.—Since difficulty was experienced in obtaining a sufficient quantity of 4-bromo-4′-methoxydiphenyl by bromination of 4-methoxydiphenyl by Bell's method (J., 1930, 1075), an alternative process was adopted. 4-Nitrodiphenyl was brominated, and the resulting 4-bromo-4′-nitrodiphenyl reduced to the amino-compound (Le Fèvre and Turner, J., 1926, 2045), which was converted into 4-bromo-4′-hydroxydiphenyl (Bell and Robinson, J., 1927, 1131). Methylation with methyl sulphate and aqueous sodium hydroxide yielded 4-bromo-4′-methoxydiphenyl, which separated from alcohol in white blades, m. p. 144° (cf. Bell, *loc. cit.*). 4-Iodo-4′-aminodiphenyl was obtained (a) from diazotised benzidine and aqueous potassium iodide (Täuber, *Ber.*, 1894, **27**, 2627; Gelmo, *Ber.*, 1906, **39**, 4179), and (b) from the reduction of 4-iodo-4′-nitrodiphenyl, m. p. 210—211°, prepared by the method of Guglialmelli and Franco (*Anal. Asoc. Quím. Argentina*, 1931, **19**, 5), who record m. p. 202—206°. The reduction, effected by the method used by Le Fèvre and Turner (*loc. cit.*) for the corresponding bromo-compound, gave 4-iodo-4′-aminodiphenyl (85% yield), which separated from alcohol in white leaflets, m. p. 166° (cf. Guglialmelli and Franco, *loc. cit.*; Kawai, *Sci. Papers Inst. Phys. Chem. Res., Tokyo*, 1930, **13**, 260). 4-Iodo-4′-hydroxydiphenyl (m. p. 193°) was prepared from diazotised 4-iodo-4′-aminodiphenyl (cf. van Alphen, *Rec. trav. chim.*, 1931, **50**, 1111; Angeletti and Gatti, *Gazzetta*, 1928, **58**, 630) and methylated with methyl sulphate and aqueous sodium hydroxide. 4-Iodo-4′-methoxydiphenyl crystallised from benzene in white leaflets, m. p. 183°.

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