257. *Substitution in Compounds containing Two or More Phenyl Groups. Part I. The Nitration of 4-Methyldiphenyl.*

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THERE is abundant evidence that the methyl group, in general, induces increased reactivity in reactions of certain types, and in considering the bearing of this property on substitution reactions in polycyclic systems it has been pointed out (Ingold, *Ann. Reports*, 1926, 134; *Rec. trav. chim.*, 1929, **48**, 805) that, whereas in naphthalene and anthraquinone, for example, the activating effect of a methyl group leads to further substitution in the ring already substituted, the deactivating influence of a substituent such as the nitro-group causes further substitution to take place in the other ring (compare, also, Lapworth and Robinson, *Mem. Proc. Manchester Lit. Phil. Soc.*, 1928, **72**, 43). Further examples of this behaviour are to be found in other polynuclear systems, *e.g.*, in substituted diphenyl ethers (Fox and Turner, J., 1930, 1853; Reilly, Drumm, and Daly, *Proc. Roy. Irish Acad.*, 1931, **40** *B*, 90) and in substituted azobenzenes (Burns, McCombie, and Scarborough, J., 1928, 2928). There appears, however, to be no information available on substitution in the monomethyldiphenyls, apart from the fact that Carnelley (J., 1876, **29**, 20) nitrated 4-methyldiphenyl and obtained 4-nitro-4′-methyldiphenyl. This result seemed unusual in view of the universal homonuclear substitution found in the methylnaphthalenes, coupled with the fact that all the nuclear positions in toluene have been shown to be activated by the methyl group (Ingold, Lapworth, Rothstein, and Ward, J., 1931, 1959). It would seem likely that some homonuclear nitration might also be expected to take place to give 2- and/or 3-nitro-4-methyldiphenyl.

Carnelley used impure 4-methyldiphenyl and obtained a mononitration product, m. p. 141°, but the greater portion of his product consisted of a yellow oil. Kliegl and Huber (*Ber.*, 1920, **53**, 1655) assigned to the solid mononitration product the probable constitution of 4-nitro-4′-methyldiphenyl, and complete proof was given by Gomberg and Pernert (*J. Amer. Chem. Soc.*, 1926, **48**, 1372), but the constitution of the oil does not appear to have been investigated. It is now shown that the nitration of 4-methyldiphenyl proceeds under milder conditions than are required for the nitration of diphenyl, thus indicating an increased reactivity of the molecule as a whole, and that the product consists of 4-nitro-4′-methyldiphenyl (40—45%), 2-nitro-4′-methyldiphenyl, and 2-nitro-4-methyldiphenyl.

After removal of the solid 4-nitro-4′-methyldiphenyl from the nitration product, a yellow oil remained, which when oxidised with chromic acid or potassium permanganate gave 2-*nitrodiphenyl-4′-carboxylic acid.* The identity of this acid was proved (a) by further nitration, which gave 2 : 2′-dinitrodiphenyl-4-carboxylic acid (Gull and Turner, J., 1929, 491), and (b) by synthesis, effected by the addition of *p*-toluenediazonium chloride to nitrobenzene in the presence of aqueous sodium hydroxide, a reaction which gave 4-nitro-4′-methyldiphenyl and 2-nitro-4′-methyldiphenyl (Gomberg and Bachmann, *J. Amer. Chem. Soc.*, 1924, **46**, 2339, and Gomberg and Pernert, *loc. cit.*, record the formation of the former only), the latter being oxidised to 2-nitrodiphenyl-4′-carboxylic acid by means of chromic acid. Reduction of the liquid nitration product gave a base from which, on acetylation, an *acetamido*-4-*methyldiphenyl*, m. p. 145°, was isolated. 2-*Acetamido*-4′-*methyldiphenyl*, prepared by reduction and acetylation of the synthetic 2-nitro-4′-methyldiphenyl already mentioned, melted at 103°, while by the action of diazotised 2-nitro-4-aminotoluene on benzene in the presence of aqueous sodium hydroxide, followed by reduction and acetylation of the product, 3-*acetamido*-4-*methyldiphenyl*, m. p. 150°, was obtained. Neither of these derivatives was therefore identical with the acetamido-compound isolated from the liquid nitration product. Attempts to obtain 2-acetamido-4-methyldiphenyl from diazotised 3-nitro-4-aminotoluene and benzene, and from iodobenzene, 4-chloro-3-nitrotoluene, and copper-bronze, were unsuccessful. It was possible, however, to obtain 2-*nitrodiphenyl*-4-*carboxylic acid* from ethyl 4-bromo-3-nitrobenzoate, iodobenzene, and copper-bronze (compare Gull and Turner, *loc. cit.*; Lesslie and Turner, J., 1930, 1758) and hydrolysis of the resulting ester, which acid was then reduced and acetylated to give 2-*acetamidodiphenyl*-4-*carboxylic acid*. This acid was identical with that obtained on oxidation with neutral permanganate of the acetamido-4-methyldiphenyl obtained from the liquid nitration product, thus proving its constitution. Since the liquid nitration product was thus shown to contain (at least) two isomerides, it seemed that milder oxidation should give some 2-nitrodiphenyl-4-carboxylic acid in addition to 2-nitrodiphenyl-4′-carboxylic acid, and on repeating the chromic acid oxidation under less vigorous conditions a small quantity of the former acid was found.

Previous work on the dinitration of 4-methyldiphenyl is confined to the sole observation of Carnelley (*loc. cit.*) that nitration of impure 4-methyldiphenyl with concentrated nitric and sulphuric acids gave a substance, m. p. 153—156°, which from analysis appeared to be a dinitro-4-methyldiphenyl. Since mononitration has now been shown to give (at least) three isomerides, it appeared to be unprofitable to study the direct dinitration of 4-methyldiphenyl, but further nitration of 4-nitro-4′-methyldiphenyl gave a mixture of presumably two dinitro-derivatives, from which a dinitro-4-methyldiphenyl, m. p. 178°, was isolated. Preliminary experiments on the mononitration of 4-methyldiphenyl had also yielded this compound when too vigorous conditions were used. It is regarded as 2(*or* 3) : 4′-*dinitro*-4-*methyldiphenyl*.

The nitration of 4-methyldiphenyl, giving rise to both homonuclear and heteronuclear substitution, is not in disagreement with theoretical prediction, the substitution being primarily controlled by the similar strongly ortho-para directing groups C_6H_5 and p-$CH_3{\cdot}C_6H_4$.

EXPERIMENTAL.

Nitration of 4-*Methyldiphenyl.*—A mixture of glacial acetic acid (100 c.c.) and nitric acid (150 c.c.; *d* 1·42) was added gradually to 4-methyldiphenyl (Gomberg and Pernert, *J. Amer. Chem. Soc.*, 1926, **48**, 1372) (30 g.) in glacial acetic acid (100 c.c.). After 24 hours, the yellow crystalline solid was removed (6·5 g.; m. p. 120—125°), and the filtrate diluted with water. From the oil produced, which was isolated, washed (aqueous alkali) and dried (calcium chloride) in ether and recovered (28 g.), 3 g. of solid separated on standing (m. p. 120—125°). The liquid, distilled under reduced pressure, gave (i) a reddish oil (16 g.), b. p. 180—186°/8 mm., (ii) a pale yellow oil (6·5 g.), b. p. 186—210°/8 mm., which on standing at − 10° deposited 3 g. of solid, m. p. 120—125°, and (iii) a fraction, b. p. 225—265°/20 mm., which solidified (2 g., m. p. 120—125°). The total solid product (14·5 g.) on recrystallisation from alcohol gave pure 4-nitro-4′-methyldiphenyl, m. p. 140°. The total liquid product (19—20 g.), consisting of isomeric mononitro-4-methyldiphenyls, comprised approximately 57% of the total nitration product.

Nitration of 4-*Nitro*-4′-*methyldiphenyl.*—The substance (4 g.) was heated for 5 minutes with fuming nitric acid and then poured into water. Repeated crystallisation of the product from glacial acetic acid and finally from alcohol gave 2(or 3) : 4′-*dinitro*-4-*methyldiphenyl* in minute prisms, m. p. 178° (Found : C, 60·5; H, 4·1. $C_{13}H_{10}O_4N_2$ requires C, 60·5; H, 3·9%), and a second isomeride, m. p. below 150°.

Nitration of 4-methyldiphenyl with concentrated nitric and acetic acids on the steam-bath, fuming nitric and acetic acids or concentrated nitric and sulphuric acids at room temperature also gave considerable quantities of 2(or 3) : 4′-dinitro-4-methyldiphenyl.

Oxidation of 4-*Nitro*-4′-*methyldiphenyl.*—A hot solution of 4-nitro-4′-methyldiphenyl (1 g.) in glacial acetic acid was treated gradually with chromic anhydride (2 g.) in acetic acid (30 c.c.), heated on the steam-bath for 10 hours, and diluted with water. The white solid, crystallised from absolute alcohol, gave 4-*nitrodiphenyl*-4′-*carboxylic acid* * in small needles, m. p. 340° (Found : C, 64·4; H, 4·0. $C_{13}H_9O_4N$ requires C, 64·2; H, 3·7%), and almost insoluble in

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* The literature contains a reference to "4-nitrodiphenyl-4′-carboxylic acid, m. p. 222—225°" (Kuhling, *Ber.*, 1895, **28**, 525; 1896, **29**, 166), but this acid must be 4-nitrodiphenyl-2′-carboxylic acid, since it was obtained by oxidation of a nitromethyldiphenyl later shown by Kliegl and Huber (*loc. cit.*) to be 4-nitro-2′-methyldiphenyl.

benzene and light petroleum. The use of a larger quantity of chromic anhydride (15 g.) and prolonged boiling (30 hours) produced *p*-nitrobenzoic acid, m. p. and mixed m. p. 239°, which was isolated in ether.

Reduction of 4-nitro-4′-methyldiphenyl with stannous chloride (Schlenk and Weickel, *Annalen*, 1909, **368**, 303) gave 4-amino-4′-methyldiphenyl, m. p. 97° (acetyl derivative, m. p. 219°) (compare Kliegl and Huber, *Ber.*, 1920, **53**, 1646).

Nitration of 4-*Nitrodiphenyl*-4′-*carboxylic Acid.*—The acid (0·5 g.) was dissolved in cold fuming nitric acid, heated on the steam-bath for 10 minutes, and poured into water. The white solid, crystallised from alcohol, gave 2 : 4′-dinitrodiphenyl-4-carboxylic acid, m. p. 255—256° both alone and when mixed with an authentic specimen (Gull and Turner, *loc. cit.*). The present results support the view, expressed by these authors, that the deactivating effect of the nitro-group exceeds that of the carboxyl group.

Oxidation of the Liquid Nitration Product from 4-*Methyldiphenyl.*—(a) *With potassium permanganate.* The liquid (5 g.) and water (30 c.c.) were heated under reflux while a concentrated solution of potassium permanganate (7·5 g.) was gradually added. After 20 hours' boiling (a little oil still remained), the mixture was treated with sulphur dioxide and filtered, the residue treated with aqueous sodium hydroxide and extracted with ether to remove unchanged oil, and the extract added to the filtrate. Acidification of the aqueous layer gave a white precipitate, which on crystallisation from alcohol gave 2-*nitrodiphenyl*-4′-*carboxylic acid*, m. p. 250°, in small fine needles (Found : C, 64·1 ; H, 4·2. $C_{13}H_9O_4N$ requires C, 64·2 ; H, 3·7%). The ethereal extract, containing unchanged nitration product, was reduced as described later to give 2-amino-4-methyldiphenyl.

(b) *With chromic acid.* A hot solution of chromic anhydride (25 g.) in glacial acetic acid (25 c.c.) and water (5 c.c.) was gradually added to a boiling solution of the liquid nitration product (5·5 g.) in glacial acetic acid (25 c.c.), and the mixture boiled under reflux for 16 hours and then poured into much water. The oxidation product was removed, dissolved in alkali, filtered, precipitated by acid, and crystallised from absolute alcohol, 2-nitrodiphenyl-4′-carboxylic acid (m. p. 250°) separating (1 g.). Evaporation of the mother-liquor gave a second product, m. p. (after repeated crystallisation from alcohol) 185—188°, raised on admixture with 2-nitrodiphenyl-4-carboxylic acid (m. p. 191°).

Nitration of 2-*Nitrodiphenyl*-4′-*carboxylic Acid.*—The acid was nitrated in the same way as the 4-nitro-acid, and 2 : 2′-dinitrodiphenyl-4-carboxylic acid obtained, m. p. 194—195°, not depressed on admixture with the authentic acid (m. p. 201°) prepared by the method of Gull and Turner (*loc. cit.*). Slightly higher temperatures were used than those given by these authors.

Reduction of the Liquid Nitration Product.—The liquid (2 g.) in alcohol (25 c.c.) and stannous chloride (12 g.) in hot concentrated hydrochloric acid (25 c.c.) were mixed and heated on the steam-bath for 2 hours, and the cooled solution made alkaline (sodium hydroxide). Ether extracted a reddish-brown oil, which was treated with acetic anhydride; crystallisation from alcohol gave 2-*acetamido*-4-*methyldiphenyl* in small transparent plates, m. p. 145° (Found: C, 79·5; H, 6·6; N, 6·3. $C_{15}H_{15}ON$ requires C, 80·0; H, 6·7; N, 6·2%). A portion of the reduction product, benzoylated by the Schotten–Baumann method, gave 2-*benzamido*-4-*methyldiphenyl*; fine white plates, m. p. 221°, from alcohol (Found: C, 83·5; H, 5·6. $C_{20}H_{17}ON$ requires C, 83·6; H, 5·9%).

Synthesis of 2-*Acetamido*-4′-*methyldiphenyl.*—*p*-Toluidine (107 g.) in 192 c.c. of hydrochloric acid (*d* 1·16) was diazotised at 0—5° with aqueous sodium nitrite and added slowly to a well-stirred mixture of nitrobenzene (600 c.c.) and 40% sodium hydroxide solution (275 c.c.) below 5°. After 5 hours, the nitrobenzene layer was separated, washed (hydrochloric acid; water), and dried (calcium chloride), the nitrobenzene distilled, the dark residue heated under reflux with benzene and light petroleum (b. p. 60—80°), and the clear solution decanted from the tar and distilled under reduced pressure after removal of the solvent, three fractions being collected: (a) b. p. 160—180°/17 mm., mainly nitrobenzene with a small quantity of a higher fraction; fraction (b), b. p. 180—210°/20 mm., deposited a yellow solid. This was added to fraction (c), b. p. 210—250°/20 mm., which had solidified almost completely. Recrystallisation of the solid from alcohol gave pure 4-nitro-4′-methyldiphenyl, m. p. and mixed m. p. 140°. The higher fraction from (a) and the liquid fraction from (b) both consisted of 2-nitro-4′-methyldiphenyl, since on oxidation with chromic acid both gave 2-nitrodiphenyl-4′-carboxylic acid, m. p. and mixed m. p. 250°. Attempts to prepare 2-nitro-4′-methyldiphenyl by the action of diazotised *o*-nitroaniline on toluene by the Gomberg method and by heating *o*-chloronitrobenzene with *p*-iodotoluene in the presence of copper-bronze were unsuccessful. Reduction of the 2-nitro-4′-methyldiphenyl in the manner already described for the reduction of the liquid nitration product gave a liquid base which on acetylation with acetic anhydride and subsequent crystallisation from 95% alcohol gave 2-*acetamido*-4′-*methyldiphenyl* in white needles, m. p. 103° (Found: C, 79·6; H, 6·7; N, 6·4. $C_{15}H_{15}ON$ requires C, 80·0; H, 6·7; N, 6·2%).

Synthesis of 3-*Acetamido*-4-*methyldiphenyl.*—This was effected as that of 2-acetamido-4′-methyldiphenyl (2-nitro-4-aminotoluene, 61 g., concentrated hydrochloric acid, 78 c.c., sodium nitrite solution; benzene, 300 c.c., sodium hydroxide, 44 g. in 150 c.c., at 5—10°). The oil obtained from the benzene–light petroleum was reduced with stannous chloride, and the liquid base acetylated. Recrystallisation from aqueous alcohol gave 3-*acetamido*-4-*methyldiphenyl* in small white needles, m. p. 150° (Found: C, 80·4; H, 6·7; N, 6·6. $C_{15}H_{15}ON$ requires C, 80·0; H, 6·7; N, 6·2%).

Oxidation of 2-*Acetamido*-4-*methyldiphenyl.*—2-Acetamido-4-methyldiphenyl (1·3 g., prepared from the liquid nitration product of 4-methyldiphenyl) was suspended in boiling water (100 c.c.) containing magnesium sulphate (2·5 g.), and potassium permanganate (1·8 g.) added during 2 hours. The mixture was boiled for 4 hours, treated when cold with sulphur dioxide, and the solid recrystallised from aqueous alcohol, 2-*acetamidodiphenyl*-4-*carboxylic acid* being obtained in small white prisms, m. p. 222° (Found: C, 70·5; H, 4·95; N, 5·65. $C_{15}H_{13}O_3N$ requires C, 70·6; H, 5·1; N, 5·5%).

Synthesis of 2-*Nitrodiphenyl*-4-*carboxylic Acid.*—Ethyl 4-bromo-3-nitrobenzoate (40 g.), iodobenzene (32 g.), and copper-bronze (40 g.) were heated for 1 hour at 235—245°. The cold solid mass was extracted with chloroform, evaporation of which left a dark sticky residue; this was heated with concentrated sodium hydroxide solution, diluted, and filtered. The filtrate on acidification deposited a solid. Both this solid and that obtained from the alkaline filtration were heated with concentrated hydrochloric acid; a hot absolute alcoholic extract of the residue deposited, on cooling, a crystalline solid, m. p. 189—191°. Recrystallisation from alcohol gave pale buff-yellow needles of 2-*nitrodiphenyl*-4-*carboxylic acid*, m. p. 191° (Found: C, 64·5; H, 4·1. $C_{13}H_9O_4N$ requires C, 64·2; H, 3·7%). The less soluble material consisted of 2 : 2′-dinitrodiphenyl-4 : 4′-dicarboxylic acid.

Reduction of 2-*Nitrodiphenyl*-4-*carboxylic Acid.*—The acid (2 g.) was heated on the steam-bath with tin (4 g.) and concentrated hydrochloric acid (25 c.c.). After 2 hours, the liquid was diluted with water and the solid was collected, dried, and acetylated (acetic anhydride and one drop of concentrated sulphuric acid); ether extracted from the diluted solution a crystalline substance which, recrystallised from aqueous alcohol, gave 2-acetamidodiphenyl-4-carboxylic acid, m. p. 222°, both alone and when mixed with that obtained from the liquid nitration product of 4-methyldiphenyl.

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