52. *Orientation Effects in the Diphenyl Series. Part XIII. The Nitration of the Four 2-Halogeno-4 : 4′-dimethyldiphenyls.*

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THE observation (Shaw and Turner, J., 1932, 285; Marler and Turner, *ibid.*, p. 2391) that nitration of 4 : 4′-dihalogeno- and 4 : 4′-dimethyl-diphenyls tends to occur in the 2-position made it desirable to examine the more complicated cases of the nitration of the four 2-halogeno-4 : 4′-dimethyldiphenyls. The preparation of these compounds entailed an exceptional amount of tedious work, owing partly to the initial difficulty of making reasonable quantities of 4 : 4′-ditolyl and partly to the occurrence of unwanted side reactions during the replacement of a 2-amino-group (from 2-nitro-) by halogen. 2-*Fluoro*- and 2-*chloro*-4 : 4′-*dimethyldiphenyl* melt respectively at 73—74° and 32—33°, but the 2-*bromo*- and 2-*iodo*-compounds are liquids. It may be noted that 2-chlorodiphenyl is a solid, but that the corresponding bromo- and iodo-compounds are liquids. It is possible that with increase in size of the halogen atom from fluorine to iodine the diphenyl molecule is less able to take up a co-planar arrangement, and this would inevitably react on the shape of the crystal and on the melting point.

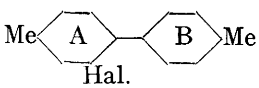
Mononitration of 2-fluoro-4 : 4′-ditolyl was accomplished without difficulty by the use of excess of equal volumes of nitric acid (*d* 1·2) and glacial acetic acid. Only one substance was formed, and this must be 2-*fluoro*-2′-*nitro*-4 : 4′-*dimethyldiphenyl*, since reduction, followed by replacement of the amino-group by fluorine, gave 2 : 2′-*difluoro*-4 : 4′-*dimethyldiphenyl*, identical with the substance obtained by a similar replacement from 2 : 2′-diamino-4 : 4′-dimethyldiphenyl.

In the nitration of the other three 2-halogeno-4 : 4′-ditolyls, difficulty was experienced in finding conditions which avoided both partial absence of nitration and partial dinitration.

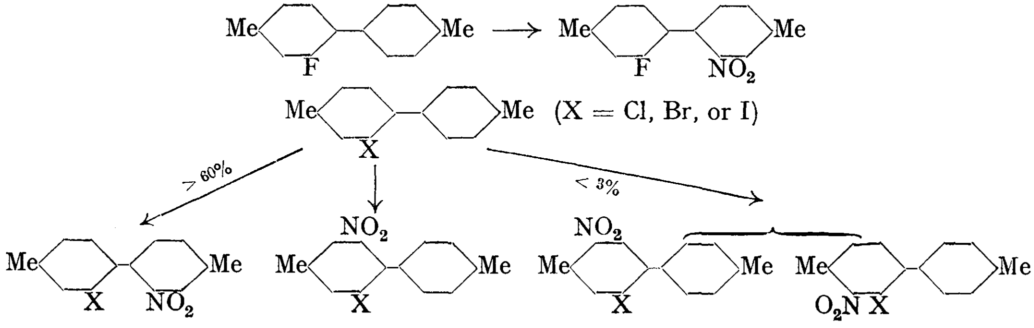
By using 1·5—2 molecular proportions of nitric acid (*d* 1·5) in an equal volume of glacial acetic acid in the warm, the second, more undesirable, difficulty was overcome. In all three cases, mixtures of nitro-compounds were obtained, and these could not be separated as such. Reduction, followed by conversion into mixtures of base hydrochlorides, rendered a partially quantitative separation possible, for one series of bases (α) formed sparingly soluble hydrochlorides, and were thus separable from the accompanying bases (β), which were most conveniently manipulated as their acetyl derivatives. By repeating the nitrations many times, we were able to satisfy ourselves that the figures for the weight proportion β/α for the chloro-, bromo- and iodo-compounds were, respectively, 2·7, 1·7 and 2·4.

The β-chloro- and β-iodo-bases were respectively convertible into 2 : 2′-dichloro- and 2 : 2′-di-iodo-4 : 4′-dimethyldiphenyl, though difficulties were encountered in performing the necessary replacements such as were noted, in similar work, by Mascarelli and his co-workers (*Gazzetta*, 1929, **59**, 858; 1931, **61**, 320) and by Angelletti and Brambilla (*ibid.*, 1930, **60**, 967). 2-Chloro- and 2-iodo-ditolyl are therefore nitrated to the extent of over 60% in position 2′. The constitution of the corresponding bromo-compound could not be proved and is inferred, and here again over 60% of 2′-nitration took place.

In view of the known deactivating effects of the halogens, particularly of fluorine, it would be expected that 2-fluoroditolyl would be mononitrated mainly or entirely in nucleus B. It has already been shown (*loc. cit.*) by the exclusive 2-nitration of 4 : 4′-ditolyl that the directive influence of the *p*-tolyl radical can entirely outweigh that of the methyl group. Apparently the *p*-tolyl radical can still exert its influence even when it contains a fluorine atom in position 2. This persistence of *ortho*-directive power by an aromatic nucleus with fluorine as a substituent has already been shown by the exclusive 2-nitration of 4 : 4′-difluorodiphenyl. For similar reasons, it would be expected that 2-chloro- and 2-bromo-ditolyl should be mononitrated mainly in nucleus B, in the 2′-position, but to a less extent than 2-fluoroditolyl, the electron affinities of these halogens being smaller. 2-Iododitolyl might be expected to undergo partial nitration in nucleus A, since iodine is feebly activating. The experimental fact is, however, that 2-iododitolyl actually gives more 2′-nitro-compound than does 2-bromoditolyl. One explanation of this is that the iodine atom, on account of its size, is near enough to the 2′-positions in nucleus B to have a Bennett " reversed-field " effect upon it.



The structure of the α-bases has not been settled, nor do we think that the elaborate investigation necessary to do this would lead to results of sufficient importance to justify it. That the α-bases are derived from neither a 3- nor a 5-nitro-compound is shown fairly conclusively by the observation that the total mononitration product in no instance responded to a sufficient extent to the hot piperidine test for activated halogen, the deactivating effect of methyl groups notwithstanding. We think that substitution in the 6-position is more likely than in the 3′-position, from a general consideration of the orienting effect of the tolyl group compared with that of the methyl group, in conjunction with the relative deactivating effects of the halogens. The whole of the results now obtained may be summarised in the scheme given below. The observed slight reactivity of the mononitro-mixtures with piperidine, which could be determined with considerable accuracy, fixes the amount of 3- or 5-nitration at not more than 3% :



EXPERIMENTAL.

2-*Amino*-4 : 4′-*dimethyldiphenyl*.—Reduction of 2-nitro-4 : 4′-ditolyl with iron filings and feebly acidified water at 100° was found more convenient than the method previously described (Marler and Turner, *loc. cit.*). The reduction mixture was extracted with boiling acetone, and the latter filtered and evaporated. The residual base was dissolved in hot dilute hydrochloric acid, and the solution filtered from a little tarry dimethylcarbazole. The sparingly soluble hydrochloride was obtained on cooling, in 80% yield.

2-*Fluoro*-4 : 4′-*dimethyldiphenyl*.—20 G. of the preceding base were diazotised in hydrochloric acid and hydrofluoboric acid was added to the resulting solution until precipitation was complete. The precipitate was collected, washed with ether, and dried in a vacuum. The diazonium borofluoride (21 g.) was introduced in small quantities into a large flask heated at 100°. When decomposition was complete, the residue was treated with alkali and distilled in steam. 2-*Fluoro*-4 : 4′-*dimethyldiphenyl* (11 g.) came over and was crystallised from methyl alcohol. It formed needles, m. p. 73—74° (Found : C, 83·3; H, 6·4. $C_{14}H_{13}F$ requires C, 83·9; H, 6·5%).

Nitration of 2-*Fluoro*-4 : 4′-*dimethyldiphenyl*.—6 G. of the fluoro-compound were dissolved in 30 c.c. of glacial acetic acid and 30 c.c. of nitric acid (*d* 1·43) were added. The fluorodimethyldiphenyl was precipitated in the cold, but after 2 minutes at 100° it all redissolved. The solution was poured into excess of water, a yellow oil separating which solidified later (7·2 g.). Crystallisation from alcohol gave 6·3 g. of small, pale yellow prisms, m. p. 89—90°. The theoretical yield of 2-*fluoro*-2′-*nitro*-4 : 4′-*dimethyldiphenyl* is 7·6 g. (Found : N, 5·9. $C_{14}H_{12}O_2NF$ requires N, 5·7%).

Reduction of 2-*Fluoro*-2′-*nitro*-4 : 4′-*dimethyldiphenyl*.—The nitro-compound was reduced with stannous chloride in a mixture of acetic and hydrochloric acids at 100°. The cooled solution was poured into excess of alkali, and the base extracted with ether. The ether was evaporated, and the residue dissolved in hot dilute hydrochloric acid. The hydrochloride separated in leaflets from the cooled solution, and from it was obtained 2-*fluoro*-2′-*amino*-4 : 4′-*dimethyldiphenyl*, which crystallised from aqueous alcohol in rectangular needles, m. p. 105—106° (yield, 96%) (Found : N, 6·5. $C_{14}H_{14}NF$ requires N, 6·5%).

2 : 2′-*Difluoro*-4 : 4′-*dimethyldiphenyl*.—6 G. of 2-fluoro-2′-aminoditolyl were dissolved in 20 c.c. of hydrofluoboric acid and 2 g. of sodium nitrite were added with stirring, the solution being well cooled. The diazonium borofluoride (8 g.) separated and was collected, washed with ether, and dried. It was decomposed at 100° and the product was distilled in steam; the difluoro-compound came over and readily solidified. It crystallised from alcohol in long needles (4 g.), m. p. 97—98°, and was identical with 2 : 2′-*difluoro*-4 : 4′-*dimethyldiphenyl* obtained by decomposition of the bisdiazonium borofluoride prepared by a similar method from 2 : 2′-diamino-4 : 4′-ditolyl (Found : C, 76·9; H, 5·8. $C_{14}H_{12}F_2$ requires C, 77·0; H, 5·5%).

2-*Chloro*-4 : 4′-*dimethyldiphenyl*.—46 G. of the 2-amino-compound were submitted to a Sandmeyer reaction, and the product distilled in steam. Ditolyl (4 g.) came over first and then 24 g. of 2-*chloro*-4 : 4′-*dimethyldiphenyl*. Crystallisation from methyl alcohol gave 20 g. of long needles, m. p. 32—33° (Found : Cl, 16·0. $C_{14}H_{13}Cl$ requires Cl, 16·4%).

Nitration of 2-*Chloro*-4 : 4′-*dimethyldiphenyl*.—5 G. of chloroditolyl were melted and 2 c.c. (1·8 mols.) of nitric acid (*d* 1·5) in 2 c.c. of glacial acetic acid were added slowly. The mixture became hot, but the oil did not all dissolve. It was heated for 5 minutes at 100°; the oil then dissolved, but reappeared on cooling. The mixture was poured into water, the oil extracted with ether, and the ether removed. It was impossible to cause the product to solidify (yield, 95%).

Reduction of Preceding Nitration Product.—This was effected with stannous chloride in acetic–hydrochloric acid at the b. p. The solution was strongly basified with alkali and extracted with ether, the latter then being removed. The residue was extracted several times with hot dilute hydrochloric acid, which left undissolved a little black oil. The filtered extracts on cooling deposited brownish crystals of a base hydrochloride (α), which was hydrolysed by water and was sparingly soluble in dilute hydrochloric acid. The mother-liquor was concentrated to half-volume. On cooling, a brown gum and later small crystals appeared, the whole being treated as base hydrochloride (β). Addition of ammonia, followed by ether extraction, etc., gave a residue, which was dissolved in diluted acetic acid and then treated with acetic anhydride. The *acetyl* derivative of base (β) separated, and crystallised from dilute acetic acid (charcoal) in small needles, m. p. 115—116° (Found : N, 5·2. $C_{16}H_{16}ONCl$ requires N, 5·1%). The hydrochloride of the α-base gave with ammmonia the *base* itself, small rhombohedra, m. p. 75—77°, from alcohol (Found : N, 6·5. $C_{14}H_{14}NCl$ requires N, 6·1%). The *acetyl* derivative of base α crystallised from alcohol or from aqueous alcohol in needles, m. p. 123—124° (Found : N, 5·2%). The m. p. of a mixture of the two acetyl derivatives was 90—105°. Recrystallisation of the hydrochloride of base α gave needles, m. p. 223—224° (decomp.).

Treatment of Nitro-2-chlorodimethyldiphenyl with Piperidine.—7·1160 G. of the crude nitration product were heated in a closed tube with excess of piperidine for 3 hours at 100°. A little alkali was added and then ether. The ethereal layer was separated and well washed with water. The united aqueous extracts were freed from ether, acidified with nitric acid, and treated with silver nitrate. The silver chloride obtained, after being washed with hot chloroform to remove traces of organic matter, weighed 0·0636 g., corresponding to elimination of chlorine from 1·6% of the nitration product.

The results of three typical series of experiments were as follows :

	α-Base, weighed as hydrochloride.	β-Base, weighed as acetyl derivative.	Ratio β/α of free bases.
(1)	Crude, 1·0 g.	2·92 g., m. p. 108—111°	2·8
	Recryst., 0·75 g.	2·20 g., m. p. 114—115°	2·6
(2)	Crude, 0·62 g.	1·82 g., m. p. 108—111°	2·9
(3)	Recovered from piperidine treatment :		
	Crude, 0·54 g.	1·36 g., m. p. 107—112°	2·6
	Recryst., 0·40 g.	1·08 g., m. p. 114—116°	2·6

2 : 2′-*Dichloro*-4 - 4′-*dimethyldiphenyl.*—The base obtained by hydrolysis, with hot concentrated hydrochloric acid, of the above β-chloro-acetamido-derivative, was diazotised, and submitted to a Sandmeyer reaction. Distillation in steam gave the dichloro-compound, which crystallised from alcohol in small plates, m. p. 90°. It was identical with 2 : 2′-*dichloro*-4 : 4′-*dimethyldiphenyl*, prepared in a similar manner from 2 : 2′-diamino-4 : 4′-dimethyldiphenyl (Found : Cl, 28·3. $C_{14}H_{12}Cl_2$ requires Cl, 28·3%).

2-*Bromo*-4 : 4′-*dimethyldiphenyl.*—Direct bromination of dimethyldiphenyl with bromine (2 mols.) in acetic acid in presence of sodium acetate at the b. p., followed by addition of much water, led to a complex mixture of products. 4 : 4′-Dimethyldiphenyl-2-diazonium perbromide was therefore prepared in the usual way from the 2-amino-compound, and decomposed in hot alcohol. The alcohol was removed, and the residue washed with alkali. The dark oil deposited crystals of what appears to be a bromoethoxydimethyldiphenyl, m. p. 67—68° (Found : Br, 26·9. $C_{16}H_{17}OBr$ requires Br, 26·2%). Decomposition of the perbromide in hot glacial acetic acid gave a mixture of solid substances which proved to be the result of unwanted further bromination. The perbromide was finally decomposed by introducing it in small quantities into a flask kept at 100°. The residue was dissolved in carbon tetrachloride, and the solution washed with alkali, dried, and distilled three times at 12 mm. pressure. The 2-*bromo*-4 : 4′-*dimethyldiphenyl*, containing a small amount of a dibromo-compound, from which it could not be separated, had b. p. 183—187°/12 mm. (Found : Br, 32·8. $C_{14}H_{13}Br$ requires Br, 30·7%).

Application of the Sandmeyer reaction to 2-amino-4 : 4′-dimethyldiphenyl gave the 2-bromo-compound, b. p. 182—184°/18 mm., mixed with a small amount of ditolyl, from which it could not be separated (Found : Br, 28·9%).

Nitration of 2-*Bromo*-4 : 4′-*dimethyldiphenyl.*—The bromo-compound was nitrated in a manner similar to that described for the chloro-compound. Treatment with piperidine indicated the presence of 1·3% of labile bromine.

Reduction of Nitration Product.—The oily nitration product was reduced with stannous chloride as described under the chloro-series. Two basic substances, α and β, were obtained, representing 58—62% of the total reduction product, the remainder being insoluble in acid. The less soluble α-hydrochloride crystallised from hydrochloric acid in needles, m. p. 227—229° (decomp.). The free α-base was a gum, but its *acetyl* derivative crystallised from dilute acetic acid in needles, m. p. 146—147° (Found : N, 4·4. $C_{16}H_{16}ONBr$ requires N, 4·4%). The more soluble β-hydrochloride was a gum, but a small amount was obtained in minute hexagonal plates. The β-base was a gum, but its *acetyl* derivative crystallised from dilute acetic acid in clusters of small needles, m. p. 134—135° (Found : N, 4·7%). A mixture of the two acetyl derivatives melted at 120—132°.

The results of four typical series of experiments are as follows :

	α-Base, weighed as hydrochloride.	β-Base, weighed as acetyl derivative.	Ratio, β/α, of free bases.
(1)	Crude, 1·06 g.	1·90 g., m. p. 121—126°	1·8
	Recryst., 0·90 g.	1·60 g., m. p. 132—134°	1·8
(2)	Crude, 0·42 g.	0·70 g.	1·7
	Recryst., 0·25 g.	0·45 g.	
(3)	0·60 g.	1·10 g.	1·8
(4)	Recovered from piperidine treatment, etc.,	0·80 g., m. p. 132—134°, and	1·6
	0·47 g.	0·18 g., m. p. 124—126°	

2 : 2′-*Dibromo*-4 : 4′-*dimethyldiphenyl*.—The gummy base obtained by hydrolysis with hydrochloric acid of the purified acetyl derivative of the β-base was submitted to a Sandmeyer reaction. The mixture was made alkaline and steam-distilled. The oil distilling later solidified, and crystallisation from alcohol gave the dibromo-compound, the m. p. of which was not depressed by admixture with the product, m. p. 114—115°, obtained from 2 : 2′-diamino-4 : 4′-dimethyldiphenyl by the Sandmeyer reaction. During the Carius determination of halogen in these two specimens, the tubes burst, and it was impracticable to prepare more of them. It was therefore not proved that the β-base was 2-bromo-2′-amino-4 : 4′-dimethyldiphenyl, but from the above evidence of m. p. and from the complete parallelism of the products of nitration, reduction, acetylation, etc., in this series with those in the chloro- and iodo-series (below), in which the β-bases were proved to be of the 2 : 2′-type, and also from the fact that the m. p.'s of the acetyl derivatives and hydrochlorides of the bromo-α- and -β-bases lie between those of the corresponding chloro- and iodo-compounds, it is extremely probable that the β-bromo-compounds are derived from the 2′-nitro-compound.

2-*Iodo*-4 : 4′-*dimethyldiphenyl*.—30 G. of 2-amino-4 : 4′-dimethyldiphenyl were suspended in 10 c.c. of concentrated sulphuric acid, diluted with 100 c.c. of water, cooled to 0°, and diazotised. Urea was added, and the solution was poured into an aqueous solution of 35 g. of potassium iodide and 60 g. of hydrated sodium acetate at 30°. The mixture was kept for an hour, warmed, and then distilled in steam. About 1·5 g. of ditolyl came over first, and was followed by an oil, which was manipulated by means of chloroform. It distilled at 198—208°/15 mm. (12 g.), and on redistillation at 200—205°/15 mm. The decomposed diazo-solution was alternatively extracted with carbon tetrachloride, and the latter with alkali. After removal of the carbon tetrachloride and cooling to — 20°, 3 g. of an azo-compound separated, and the mother-liquor was distilled. About 1 g. of ditolyl and 12·5 g. of oil, b. p. 200—210°/15 mm., were obtained, and redistillation, after previous treatment with mercury to remove free iodine, gave 11 g. of 2-*iodo*-4 : 4′-*dimethyldiphenyl*, b. p. 200—205°/15 mm. (Found : I, 40·8. $C_{14}H_{13}I$ requires I, 41·2%).

Nitration of 2-*Iodo*-4 : 4′-*dimethyldiphenyl*.—To the iodo-compound (1 mol.) were added cautiously, with shaking, 2 mols. of nitric acid (*d* 1·5) mixed with 1 vol. of glacial acetic acid. The mixture was heated at 100° for 10 minutes and then poured into excess of water. The reddish oil was worked up in the manner described for the chloro- and bromo-compounds, 98·5—99·7% of the theoretically possible mononitro-mixture resulting. Piperidine treatment indicated 1·4% of labile iodine in the total crude nitration product. Reduction was carried out as described for the chloro- and bromo-compounds. The acid-soluble part of the total reduction product (57—63%) led to two base hydrochlorides, α and β. The α-hydrochloride formed leaflets, m. p. 222—224° (decomp.), and the α-*acetyl* derivative crystallised from dilute acetic acid in small prisms, m. p. 165—166° (Found : N, 4·2. $C_{16}H_{16}ONI$ requires N, 3·9%). The *acetyl* derivative of the β-base crystallised from dilute acetic acid in needles, m. p. 160—161° (Found : N, 3·9%), or 140—152° when mixed with the α-acetyl derivative. Neither of the bases could be obtained crystalline.

The results of six typical series of experiments are as follows :

α-Base, weighed as hydrochloride.	β-Base, weighed as acetyl derivative.	Ratio, β/α, of free bases.
(1) Crude, 1·0 g.	2·2 g., m. p. 141—147°	2·2
Recryst., 0·6 g.	1·36 g., m. p. 158—160°	2·3
(2) Recovered from piperidine treatment, etc. :		
Crude, 0·61 g.	1·35 g., m. p. 140—146°	2·2
Recryst., 0·40 g.	0·91 g., m. p. 159—160°	2·3
(3) 0·36 g.	0·86 g.	2·4
(4) 0·65 g.	1·55 g.	2·4
(5) 0·55 g.	1·10 g.	2·0
(6) 0·45 g.	0·91 g.	2·1

2 : 2′-*Di-iodo*-4 : 4′-*dimethyldiphenyl*.—The base obtained by hydrolysis with hot concentrated hydrochloric acid, containing a little alcohol, of the β-acetyl derivative above was diazotised in hydrochloric acid and the solution was poured into potassium iodide solution. When decomposition was complete in the warm, the product was steam-distilled. The colourless product crystallised from methyl alcohol in large hexagonal plates, m. p. 116—117° (0·4 g. from 2·6 g. of acetamido-compound), and was identical with 2 : 2′-*di-iodo*-4 : 4′-*dimethyldiphenyl* similarly prepared from 2 : 2′-diaminoditolyl (Found : I, 58·4. $C_{14}H_{12}I_2$ requires I, 58·5%). A yellow insoluble powder, which was the main product of the diazo-reaction, was ditolyleneiodonium iodide (cf. Angelletti and Brambilla, *loc. cit.*). This was heated at 240°, and gave a sublimate, m. p. 113°, melting at 115—116° when mixed with the above di-iodo-compound.

2-*Hydroxy*-4 : 4′-*dimethyldiphenyl*.—This compound was formed in the preparation of all the 2-halogeno-compounds, from which it was separated by usual methods. It was also prepared, in 60% yield, by heating an aqueous solution of 4 : 4′-dimethyldiphenyl-2-diazonium sulphate. After filtration of the resulting suspension, acid was added, the *hydroxy*-compound then separating; it crystallised from aqueous alcohol in fine needles, m. p. 57—58°, having a floral odour (Found : C, 84·6; H, 7·1. $C_{14}H_{14}O$ requires C, 84·8; H, 7·1%). The *p*-toluenesulphonate formed long needles, m. p. 130°.

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