XV.—*Substitution Products of 2-Aminodiphenyl.*

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The orientation of substituents in 2-acetamido- and in 2-aminodiphenyl forms the second part of a series of investigations on the substitution products of the monoacid bases of the diphenyl series, of which the first part (J., 1926, 557) deals with the products of chlorination and bromination of 4-acetamido- and of 4-aminodiphenyl.

The only substitution product of 2-aminodiphenyl on record is a chlorinated base obtained by Hübner (*Annalen*, 1881, **209**, 339) on reduction of 2-nitrodiphenyl with tin and hydrochloric acid. The salts of this base were analysed, but no attempt was made to assign to it a definite structure. Later investigators, using less drastic methods for the reduction, have been unable to confirm the formation of such a base.

The scope of the present work was, first, a reinvestigation of the methods used in the reduction of 2-nitrodiphenyl, and, secondly, the preparation of the chloro-, bromo-, and nitro-derivatives of 2-acetamido- and of 2-amino-diphenyl.

On reduction of 2-nitrodiphenyl under normal conditions, substitution products of the base were not formed, but on reduction with tin and hydrochloric acid under conditions favourable to indirect chlorination (compare Blanksma, *Rec. trav. chim.*, 1906, **25**,

365) a mixture of approximately 60% of 5-chloro-2-aminodiphenyl and 40% of 2-aminodiphenyl was produced.

Direct chlorination of 2-aminodiphenyl in carbon tetrachloride solution proceeded smoothly and gave a quantitative yield of 3 : 5-dichloro-2-aminodiphenyl hydrochloride. Direct chlorination of the acetylated base invariably yielded gummy products, from which were isolated mixtures of 5-chloro-2-acetamidodiphenyl and unchanged 2-acetamidodiphenyl; and a prolonged action of chlorine yielded a tar from which a pure substance could not be isolated.

2-Acetamidodiphenyl yielded a stable *N*-chloroamine, which could be converted, on treatment with alcohol and acetic acid, into a mixture of 5-chloro-2-acetamidodiphenyl and 2-acetamidodiphenyl. This partly chlorinated mixture could not be separated into its components on account of the very slight differences in solubility of the two substances in all the usual organic solvents. By treating the mixture with sodium hypochlorite, a *N*-chloroamine was formed by both substances, and on conversion with acetic acid in alcohol pure 5-chloro-2-acetamidodiphenyl was obtained. Free chlorine was observed during the conversion, and this fact may be taken as an indication that *N* : 5-dichloro-2-acetamidodiphenyl cannot be transformed into a dichloro-derivative substituted in either ring. This behaviour is the same as that of *N* : 3-dichloro-4-acetamidodiphenyl (*loc. cit.*).

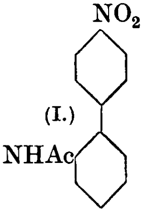
Bromination of the free base in carbon tetrachloride solution yielded 5-bromo-2-aminodiphenyl hydrobromide; bromination in acetic acid solution resulted in a quantitative yield of 3 : 5-dibromo-2-aminodiphenyl, provided that care was taken to remove from the reaction mixture the hydrogen bromide formed. Direct bromination of the base under various conditions did not give a more highly brominated product which could be isolated.

2-Acetamidodiphenyl yielded an impure *N*-bromo-derivative which could not be purified by crystallisation from non-hydroxylic solvents. The impure product on treatment with acetic acid was transformed partly into 5-bromo-2-acetamidodiphenyl and partly into 2-acetamidodiphenyl with the liberation of free bromine.

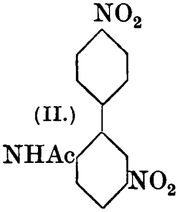
Direct bromination of the acetyl derivative in acetic acid solution at room temperature yielded 5-bromo-2-acetamidodiphenyl; more highly brominated products were obtained in very small yields only on prolonged exposure to sunlight. On bromination at 100°, 3 : 5-dibromo-2-aminodiphenyl was obtained either by the further bromination of the monobromoacetyl derivative and subsequent hydrolysis, or by bromination of 5-bromo-2-aminodiphenyl after hydrolysis had taken place.

On nitration of 2-acetamidodiphenyl in a mixture of acetic acid and sulphuric acid at 0°, an approximately 50% yield of 4′-nitro-2-acetamidodiphenyl (I) was obtained; the residue was a yellow gum from which a crystalline product could not be isolated. By the further nitration of 4′-nitro-2-acetamidodiphenyl, or of the residual gum, a dinitro-2-acetamidodiphenyl was obtained. This product on hydrolysis and deamination yielded 3 : 4′-dinitrodiphenyl (IV), and must therefore have the constitution of a 5 : 4′-dinitro- (II) or of a 3 : 4′-dinitro-2-acetamidodiphenyl (III).

(I.)



(II.)



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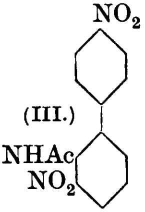

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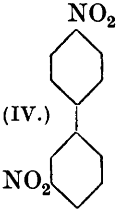

A conclusive proof of the structure of this dinitro-compound could not be obtained owing to the symmetry of the molecule, but if consideration is given to the chlorination and bromination products of 2-acetamidodiphenyl, it would appear that the most probable structure is 5 : 4′-dinitro-2-acetamidodiphenyl (II).

The structures of the substitution products of 2-aminodiphenyl and of its acetyl derivative are in agreement with those to be expected from an application of the tentative rules for substitution in the diphenyl series which were suggested in the previous communication (*loc. cit.*).

Although it may be seen that the amino-group and groups derived therefrom tend to promote substitution in the same nucleus, yet the nitration of 2-acetamidodiphenyl to yield a product substituted in the 4′-position gives a second instance of substitution in the opposite nucleus when conditions for indirect substitution are not favourable. This anomalous effect can hardly be ascribed to steric influences, since the para-position to the acetamido-group is available, and this position is not adjacent to any large hindering group as was the case in the bromination of 4-acetamidodiphenyl.

EXPERIMENTAL.

2-*Aminodiphenyl*.—(*a*) 25 G. of 2-nitrodiphenyl (van Hove, *Bull. Acad. Roy. Belg.*, 1922, **8**, 505) were added to a solution of 105 g. of stannous chloride in 500 c.c. of ether obtained by passing in dry hydrogen chloride. After 24 hours, the ether was removed and the base was liberated with sodium hydroxide and distilled in a vacuum (compare Dimroth, *Ber.*, 1907, **40**, 2378).

(*b*) 37 G. of 2-nitrodiphenyl, dissolved in 300 c.c. of alcohol, were added slowly to a solution of 240 g. of stannous chloride in 240 c.c. of concentrated hydrochloric acid. The alcohol was removed after refluxing for 3 hours, and the base liberated and purified as described above.

2-Aminodiphenyl was thus obtained as a white solid, b. p. 170°/15 mm., m. p. 49—50°. Previously recorded values of the m. p. vary between 44° and 49°.

2-*Acetamidodiphenyl* was prepared by adding 1·5 mols. of acetyl chloride drop by drop to a solution of the base in dry pyridine (5 parts) at 0°. After 20 minutes, the mixture was poured into an excess of ice-cold dilute hydrochloric acid. The substance crystallised from dilute alcohol or light petroleum (b. p. 60—80°) in white needles, m. p. 121° (corr.). Previously recorded values of the m. p. vary between 117·5° and 119°. Acetylation of the base by heating with acetic acid or a mixture of acetic acid and acetic anhydride was unsatisfactory, the oily product crystallising only with difficulty and with considerable loss. Samples of 2-aminodiphenyl contaminated with a little 4-aminodiphenyl were acetylated, and the mixed acetyl derivatives treated, in a Soxhlet apparatus, with light petroleum (b. p. 40—60°), in which the 4-acetamidodiphenyl is insoluble.

Chlorination on Reduction of 2-Nitrodiphenyl.—A solution of 10 g. of 2-nitrodiphenyl in 100 c.c. of alcohol and 200 c.c. of concentrated hydrochloric acid was boiled under reflux, and granulated tin (10 g.) was added, each piece after the preceding one had dissolved. The alcohol was distilled off and the bases were liberated with sodium hydroxide. The product, isolated and dried in ether, distilled at 170—190°/15 mm. and partly solidified on cooling (Found: Cl, 10·4%, which corresponds with 60% of a monochloro-base). The mixed bases were benzoylated and 5-chloro-2-benzamidodiphenyl, m. p. 142°, was isolated by fractional crystallisation.

3 : 5-*Dichloro-2-aminodiphenyl.*—A slight excess of a saturated solution of chlorine in carbon tetrachloride was added to an ice-cold 5% solution of 2-aminodiphenyl in the same solvent. The white precipitate which separated was collected after an hour, washed with carbon tetrachloride, and dried in the air; 3 : 5-*dichloro-2-aminodiphenyl hydrochloride* was then obtained, m. p. 140—145° (decomp.) (Found: HCl, 13·4. $C_{12}H_9NCl_2,HCl$ requires HCl, 13·3%). Warming with dilute ammonia gave 3 : 5-*dichloro-2-aminodiphenyl*, which crystallised from dilute alcohol in white needles, m. p. 51° (Found : Cl, 29·6. $C_{12}H_9NCl_2$ requires Cl, 29·8%). On benzoylation (Schotten–Baumann) 3 : 5-*dichloro-2-benzamidodiphenyl* was obtained, which crystallised from alcohol in long needles, m. p. 207° (Found: Cl, 20·7. $C_{19}H_{13}ONCl_2$ requires Cl, 20·7%).

Chlorination in acetic acid solution yielded tar-like products from which crystalline compounds could not be obtained.

3 : 5-*Dichlorodiphenyl*, obtained from 3 : 5-dichloro-2-aminodiphenyl hydrochloride by the elimination of the amino-group in the usual manner, was a pale yellow oil, b. p. 180°/15 mm. On oxidation with chromic anhydride in glacial acetic acid solution, it yielded 3 : 5-dichlorobenzoic acid, m. p. 188°.

N-*Chloro-2-acetamidodiphenyl*.—To a suspension of 10·6 g. of 2-acetamidodiphenyl in a solution of 20 g. of sodium bicarbonate in 200 c.c. of water, 150 c.c. of *N*-sodium hypochlorite were added during 2 hours. The precipitate was collected after 12 hours, washed with cold water, dried, and fractionally crystallised from light petroleum (b. p. 40—60°), the more soluble fraction being preserved. The *chloroamine* was thus obtained in colourless needles, m. p. 86° (Found : available Cl, 13·9. $C_{14}H_{12}ONCl$ requires Cl, 14·4%).

Conversion of the N-*Chloroamine*.—A mixture of 5 g. of the chloroamine, 100 c.c. of alcohol, and 5 c.c. of glacial acetic acid was warmed gently until it gave no reaction with potassium iodide. Water was then added to start precipitation, and the solid matter which separated on cooling was crystallised fractionally from light petroleum (b. p. 60—80°), and also from dilute aqueous solutions of alcohol, acetone, and acetic acid. The product formed white crystals which melted over the range 110—120° according to the specimen, but it was not possible to separate the constituents : m. p. after two crystallisations, 116° (Found: Cl, 11·6%); m. p. after six crystallisations, 120° (Found : Cl, 12·2%); m. p. of another preparation, 118° (Found : Cl, 10·4%). $C_{14}H_{12}ONCl$ requires Cl, 14·4%.

By treatment of the mixture with sodium hypochlorite, followed by conversion with dilute acetic acid as previously described, chlorine was evolved and pure *5-chloro-2-acetamidodiphenyl* was obtained, which crystallised from dilute alcohol or light petroleum in long needles, m. p. 122·5° (Found : Cl, 14·6. $C_{14}H_{12}ONCl$ requires Cl, 14·4%). From this substance, *5-chloro-2-benzamidodiphenyl* was obtained, which crystallised from dilute alcohol in colourless needles, m. p. 142—143° (Found : Cl, 11·6. $C_{19}H_{14}ONCl$ requires Cl, 11·5%).

The yield of crystalline solids in both *N*-chloroamine transformations was small, as the residues from the crystallisation were dark oils from which pure substances could not be separated.

Direct Chlorination of 2-Acetamidodiphenyl.—A 2% solution of 2-acetamidodiphenyl in glacial acetic acid, containing a large excess of anhydrous sodium acetate, was cooled in water and a mixture of chlorine and carbon dioxide was passed in slowly until the gain in weight corresponded to the formation of a monochlorinated compound; the mixture was then poured on to ice and water. A yellow gum separated which became semi-solid and crystallised from light petroleum as a white powder consisting of 5-chloro-2-acetamidodiphenyl and 2-acetamidodiphenyl. A similar mixture was obtained by chlorination in carbon tetrachloride solution. A solid could not be separated if the chlorination was carried on to a higher stage of substitution.

2 : 5-*Dichlorodiphenyl.*—5 G. of 5-chloro-2-acetamidodiphenyl were hydrolysed by boiling for a day with 10% alcoholic hydrochloric acid. The hydrochloride of the base, which separated after the removal of the alcohol, was converted into the corresponding dichlorodiphenyl by the Sandmeyer reaction. A light yellow oil (2 g.) was obtained, b. p. 171°/15 mm. (Found : Cl, 31·25. $C_{12}H_8Cl_2$ requires Cl, 31·8%). This crude product was oxidised by chromic anhydride in glacial acetic acid solution to 2 : 5-dichlorobenzoic acid, m. p. 154°.

N-*Bromo-2-acetamidodiphenyl* was prepared in a similar manner to the corresponding chloro-compound. It was a pale yellow powder, easily soluble in non-hydroxylic solvents, and could not be obtained of a greater purity than about 70%. On treatment with alcohol and acetic acid, it decomposed with the liberation of bromine, and yielded a mixture of 5-bromo-2-acetamidodiphenyl, m. p. 130°, and 2-acetamidodiphenyl.

5-*Bromo-2-acetamidodiphenyl.*—A cold 10% solution of 2-acetamidodiphenyl in glacial acetic acid was treated with bromine (1 mol.) as a 10% solution in the same solvent. After 1 day, the mixture was poured into water; the brominated compound, which was precipitated in an almost quantitative yield, crystallised from dilute alcohol in white needles, m. p. 130° (Found : Br, 27·7. $C_{14}H_{12}ONBr$ requires Br, 27·6%).

By the hydrolysis of this acetyl derivative with 10% alcoholic hydrobromic acid 5-*bromo-2-aminodiphenyl* was obtained. It crystallised from dilute alcohol in white needles, m. p. 57·5° (Found : Br, 32·0; C, 58·1; H, 4·15. $C_{12}H_{10}NBr$ requires Br, 32·1; C, 58·1; H, 4·0%). This base on benzoylation (Schotten–Baumann) gave 5-*bromo-2-benzamidodiphenyl*, which crystallised from alcohol in white needles, m. p. 162° (Found : Br, 22·9. $C_{19}H_{14}ONBr$ requires Br, 22·7%).

2 : 5-*Dibromodiphenyl*, obtained from 5-bromo-2-aminodiphenyl by the Sandmeyer reaction, was a yellow oil, b. p. 209°/15 mm., which became very viscous but did not solidify on cooling to 0° (Found : Br, 51·4. $C_{12}H_8Br_2$ requires Br, 51·3%). On oxidation

with chromic anhydride in glacial acetic acid solution it yielded 2 : 5-dibromobenzoic acid, m. p. 156°.

5-*Bromo*-2-*aminodiphenyl Hydrobromide*.—A 10% solution of 2-aminodiphenyl in carbon tetrachloride was treated with slightly more than one molecular equivalent of bromine as a 5% solution in the same solvent. The light yellow precipitate which formed was filtered off after an hour, washed with carbon tetrachloride, and dried in the air. It had a m. p. of 226°, but it could not be crystallised on account of the ease with which it was hydrolysed (Found : HBr, 24·4. $C_{12}H_{10}NBr,HBr$ requires HBr, 24·6%). On treatment with ammonia, it yielded the corresponding base as a viscous oil. This, on benzoylation, gave 5-bromo-2-benzamidodiphenyl, which alone or mixed with a specimen prepared by the alternative method melted at 161—162°.

3 : 5-*Dibromo*-2-*aminodiphenyl*.—To 5 g. of 2-aminodiphenyl, dissolved in 50 c.c. of glacial acetic acid, 5 g. of powdered anhydrous sodium acetate were added and the mixture was cooled in ice-water while 100 c.c. of a 10% solution of bromine in glacial acetic acid were run in slowly until the bromine was no longer decolorised. The mixture was poured on to ice and water. The brown oil thrown down soon solidified and crystallised from dilute alcohol in needles, m. p. 51—52° (Found : Br, 48·8. $C_{12}H_9NBr_2$ requires Br, 48·9%). The yield is quantitative, but if no sodium acetate be added to remove the hydrogen bromide produced by the reaction only viscous black oils can be obtained.

The *benzoyl* derivative crystallised from alcohol in white needles, m. p. 218° (Found : Br, 37·0. $C_{19}H_{13}ONBr_2$ requires Br, 37·1%). On eliminating the amino-group from the base in the usual manner 3 : 5-*dibromodiphenyl*, b. p. 208°/15 mm., was obtained (compare J., 1926, 561). It was oxidised to 3 : 5-dibromobenzoic acid, m. p. 212°.

Further Bromination of 5-*Bromo*-2-*acetamidodiphenyl*.—Only small traces of more highly brominated products could be obtained by exposing a solution of 5-bromo-2-acetamidodiphenyl and bromine, containing a little iodine as a catalyst, to sunlight for more than a week. On heating the mixture to 100°, bromination occurred together with hydrolysis of the acetyl derivative, for, on pouring the product into water, a dark oil separated which, on benzoylation, yielded 3 : 5-dibromo-2-benzamidodiphenyl; this melted at 218°, alone or mixed with a sample prepared by the alternative method.

Nitration of 2-*Acetamidodiphenyl*.—15 G. of 2-acetamidodiphenyl, dissolved in 15 c. c. of glacial acetic acid and 30 c.c. of concentrated sulphuric acid at 0°, were slowly treated with a mixture of 6 c.c. of fuming nitric acid and 14 c.c. of glacial acetic acid. After an hour, the product was poured on to ice; the yellow solid was filtered off, washed with dilute sodium carbonate solution, and fractionally crystallised from alcohol; 8 g. of pale yellow needles, m. p. 199°, were thus obtained, consisting of *4′-nitro-2-acetamidodiphenyl* (Found: N, 10·8. $C_{14}H_{12}O_3N_2$ requires N, 10·9%). The residual alcoholic solutions, on evaporation, yielded a reddish-yellow gum from which it was not possible to isolate any other substitution product.

By the hydrolysis of the acetyl derivative with 10% alcoholic hydrochloric acid, *4′-nitro-2-aminodiphenyl* was obtained. It crystallised from alcohol in orange-red needles, m. p. 158° (Found: N, 13·3. $C_{12}H_{10}O_2N_2$ requires N, 13·1%).

4′-Nitro-2-bromodiphenyl, obtained from the base by the Sandmeyer reaction, crystallised from alcohol in bright yellow needles, m. p. 82·5° (Found: Br, 28·5. $C_{12}H_8O_2NBr$ requires Br, 28·7%). On oxidation with chromic anhydride in glacial acetic acid solution, bromine was evolved and *p*-nitrobenzoic acid was produced, m. p. 240—241°.

Dinitration of 2-Acetamidodiphenyl.—The nitration was carried out under conditions similar to those given above, but with the use of a double quantity of nitric acid, and the mixture was kept for 24 hours before the products were separated. The solid product was extracted with alcohol, and the insoluble residue was crystallised from benzene; it then formed pale yellow prisms, m. p. 211°, of 5(or 3) : *4′-dinitro-2-acetamidodiphenyl* (Found: N, 14·1. $C_{14}H_{11}O_5N_3$ requires N, 14·0%). This substance yielded *p*-nitrobenzoic acid (m. p. 240—241°) on oxidation with chromic and glacial acetic acids, showing that one of the nitro-groups was in the 4′-position.

The same dinitro-compound could be isolated by further nitration of the gum produced in the less drastic nitration reaction, but in no case was the total yield more than 60%. The residue consisted of the usual, more soluble, oily products. On hydrolysis with alcoholic hydrochloric acid, the *base* corresponding to the acetyl derivative was obtained. It separated from alcohol as a bright yellow powder, m. p. 238° (Found: N, 16·35. $C_{12}H_9O_4N_3$ requires N, 16·2%).

By eliminating the amino-group from this compound by the usual method, *3 : 4′-dinitrodiphenyl* was obtained; it melted at 189°, alone or mixed with a specimen obtained by the elimination of the amino-group from 3 : 4′-dinitro-4-aminodiphenyl.

All the m. p.'s recorded in this paper have been corrected, and where necessary the identity of a substituted benzoic acid has been established by the "mixed m. p." method.

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