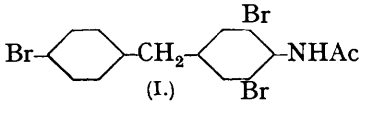
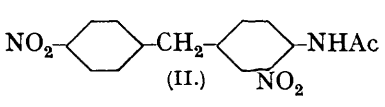
252. *Some Substitution Reactions of 4-Aminodiphenylmethane.*

By WILLIAM A. WATERS.

A VERY close analogy may be traced between the substitution reactions of the diphenyl and the diphenylmethane series (cf., *inter alia*, Scarborough and Waters, J., 1926, 557; 1927, 1133; Bell; Turner). For instance, in each type of compound, initial substitution of a phenyl group occurs in the *o*- or *p*-position to the linking bond, no matter what substituent group may be present in the other ring. Further, a group such as amino- or acetamido-, which greatly activates particular positions within one ring, has no more than a slight general activating influence upon the other. This influence is even less pronounced in the case of diphenylmethane than in that of diphenyl, probably on account of the additional difficulty of polar induction through the saturated methylene group, although the analogy between the two cases has been successfully demonstrated both in bromination and in nitration reactions, with each of which substitution can be effected in both rings. For example, the ultimate product of bromination of 4-acetamidodiphenylmethane in cold glacial acetic acid solution is 3 : 5 : 4′-*tribromo*-4-*acetamidodiphenylmethane* (I), and the principal product of nitration of the same substance in cold glacial acetic and concentrated sulphuric acids is 3 : 4′-*dinitro*-4-*acetamidodiphenylmethane* (II). Similarly, each of the



(I.)



(II.)

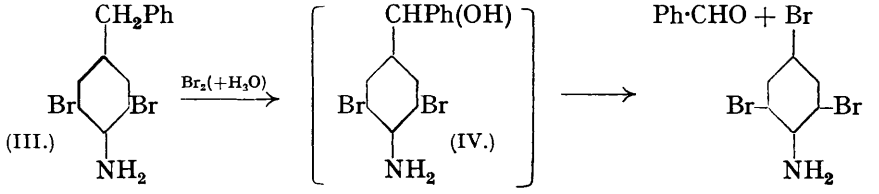
three isomeric mononitrodiphenylmethanes gives, on further nitration, the 4′-disubstituted product, the earlier work on this subject (Staedel, *Annalen*, 1878, **194**, 307; 1894, **283**, 149) being confirmed.

* This was wrongly given as 60·22% (*loc. cit.*, p. 891).

Monosubstitution of 4-acetamidodiphenylmethane has proved difficult. No evidence has been obtained to suggest that such reaction ever commences in the ring not containing the acetamido-group, as can happen in the diphenyl series. In cold glacial acetic acid solution, 4-acetamidodiphenylmethane is brominated quantitatively to *3-bromo-4-acetamidodiphenylmethane*, m. p. 91°, but at a higher temperature the same compound can be isolated only in much poorer yields from viscous mixtures. In one bromination, carried out at 100°, but not successfully repeated, there was isolated an isomeric monobromo-compound of m. p. 194°, which would appear to be the *2-bromo-4-acetamidodiphenylmethane*. It has been shown that one of the factors interfering with high-temperature substitution is the conversion of the reactant into an inert diacetyl derivative by the acetic acid used as solvent (cf. J., 1927, 1135); another is the disruption of the diphenylmethane ring system as in the case of the free bases (see below).

4-Benzamido- and *4'-bromo-4-benzamido-diphenylmethanes* are brominated only in the adjacent 3 position. Iodination of 4-acetamidodiphenylmethane, with the use of dichloramine-T and potassium iodide, appears to follow the same course as does bromination, since there have been isolated traces of low m. p. and high m. p. monoiodo-derivatives. These, however, are formed only in minute yields even after prolonged reaction. Definite chlorination products of 4-acetamidodiphenylmethane have not been isolated.

In contrast to its acetyl derivative, 4-aminodiphenylmethane undergoes halogenation very rapidly in both the positions adjacent to the amino-group, but, when further substitution is attempted, there occurs a fission of the whole molecule. Thus, *3 : 5-dibromo-4-aminodiphenylmethane* (III) on being warmed with bromine in glacial acetic acid yields 2 : 4 : 6-tribromoaniline. When this reaction is carried out in warm chloroform or carbon tetrachloride solution, hydrogen bromide is evolved and benzaldehyde can be isolated. The methylene group must therefore be a point of reactivity in the base (III), which may perhaps be converted into the corresponding hydrol (IV) before the actual fission, since the latter compound has been shown by Clarke and Esselen (*J. Amer. Chem. Soc.*, 1911, **33**, 1135) to undergo this same type of fission with bromine.



This fission of diphenylmethane bases affords a simple method of ascertaining the correct orientation of higher substitution derivatives; it has been applied, in test, also to *3 : 5 : 4'-tribromo-4-aminodiphenylmethane*.

Di-iodination of 4-aminodiphenylmethane occurs rapidly at 0°, the best yields being obtained by treating a strongly acid alcoholic solution of the base with a solution of sodium iodate and iodide, iodine monochloride being formed, $NaIO_3 + 2NaI + 6HCl = 3ICl + 3NaCl + 3H_2O$. The iodinating agent can be run in from a burette at such a rate that the iodo-compound forms instantly, there being present at no time enough free iodine chloride to cause oxidation or tarring. Under these conditions, aniline gives 2 : 4-di-iodoaniline in practically quantitative yield. Bromination, similarly, can be effected smoothly by the corresponding bromate–bromide mixture.

3-Bromo-5-iodo-4-aminodiphenylmethane, prepared by the iodination of 3-bromo-4-aminodiphenylmethane, has nearly the same m. p. as 3 : 5-dibromo-4-aminodiphenylmethane, and, further, the two compounds exhibit no appreciable depression of m. p. on admixture. This is similar to the case previously reported by the author with the exactly corresponding compounds of the benzophenone series (J., 1929, 2107; 1931, 2151).

With bromine, *3 : 5-di-iodo-4-aminodiphenylmethane* undergoes the customary fission to yield benzaldehyde. Some iodine is, however, replaced by bromine during the reaction. Under similar experimental conditions, too, iodine is liberated from di-iodoaniline. Similar

instances of halogen replacement have been described by Orton and his colleagues (cf. J., 1901, **79**, 822; 1907, **91**, 1543).

The structures of the substitution derivatives of the diphenylmethane series have, in general, been established by eliminating the amino-group and then oxidising the product to the corresponding substituted benzophenone, which was available for direct comparison as the result of a previous investigation (J., 1929, 2106) wherein structures had been rigorously proved.

Experimental.

Except where otherwise stated, bromination was effected by means of bromine in acetic acid–sodium acetate, and oxidation by chromic anhydride in acetic acid.

4-Nitro-, 3-nitro-, and 4-nitro-4′-bromo-diphenylmethanes were prepared from the corresponding benzyl chlorides by the Friedel–Crafts reaction, and were reduced to the amines by tin and hydrochloric acid in alcoholic solution. 4-Aminodiphenylmethane was purified by vacuum distillation (b. p. 198°/15 mm.), and the acetyl derivative was crystallised from dilute aqueous methyl alcohol, forming plates, m. p. 127° (King, J., 1920, **117**, 988, gives 128—129°, corr.). 4-*Benzamidodiphenylmethane* crystallised from alcohol in needles, m. p. 161° (Found: N, 4·9. $C_{20}H_{17}ON$ requires N, 4·9%). 4′-Bromo-4-aminodiphenylmethane had b. p. 226—230°/15 mm.; its *benzoyl* derivative crystallised from alcohol in needles, m. p. 181° (Found: Br, 21·8. $C_{20}H_{16}ONBr$ requires Br, 21·8%).

3 : 5-*Dibromo-4-aminodiphenylmethane.*—(*a*) 4-Aminodiphenylmethane in cold acetic acid was treated, with cooling, with 2 mols. of bromine in the same solvent. The dark solid precipitated by pouring into sodium sulphite solution was recrystallised from alcohol.

(*b*) 2 Equivs. of a *N*-solution of brominating reagent (28 g. $KBrO_3$ and 37·25 g. NaBr in 500 c.c. H_2O) were added to a mixture of equal volumes of *N*-base in alcohol and concentrated hydrochloric acid at 0°, which was kept cold in crushed ice. The product formed a light brown precipitate, easily separated in quantitative yield on dilution with ice–water. The *base* crystallised from alcohol in long needles, m. p. 92° (Found: Br, 46·8. $C_{13}H_{11}NBr_2$ requires Br, 46·9%). Its *diacetyl* derivative crystallised from alcohol in plates, m. p. 116° (Found: Br, 37·85. $C_{17}H_{15}O_2NBr_2$ requires Br, 37·65%), and its *benzoyl* derivative from alcohol in needles, m. p. 222° (Found: Br, 36·1. $C_{20}H_{15}ONBr_2$ requires Br, 36·0%).

3 : 5-*Dibromodiphenylmethane*, prepared by deamination of the base by the usual method, crystallised from methyl alcohol in needles, m. p. 61°, b. p. 201°/15 mm. (Found: Br, 49·3. $C_{13}H_{10}Br_2$ requires Br, 49·1%). On oxidation, it gave 3 : 5-dibromobenzophenone (m. p. and mixed m. p. 74—75°).

Bromine fission of 3 : 5-*dibromo-4-aminodiphenylmethane.* (*a*) The dibromo-base in acetic acid was kept for 8 hours at 100°, bromine being added from time to time to remain in excess. On dilution with water, 2: 4 : 6-tribromoaniline was formed, m. p. 119°, alone or mixed with an authentic specimen.

(*b*) The dibromo-base was refluxed for 2 hours with excess bromine in chloroform, hydrogen bromide being evolved. After evaporation of the solvent the dark sticky residue was steam-distilled, whereupon benzaldehyde separated (phenylhydrazone, m. p. 156°). Reaction in carbon tetrachloride was exactly similar.

3 : 5 : 4′-*Tribromo-4-aminodiphenylmethane*, prepared from 4′-bromo-4-aminodiphenylmethane by the usual method of bromination, the product being poured into water, formed plates, m. p. 141° from alcohol (Found: Br, 57·1. $C_{13}H_{10}NBr_3$ requires Br, 57·1%). Further bromination with dry bromine in boiling carbon tetrachloride yielded tribromoaniline, m. p. 119°, and *p*-bromobenzaldehyde, recognised, after steam-distillation, by formation of its phenylhydrazone, m. p. 113° (Gattermann, *Annalen*, 1912, **393**, 215, gives 112—113°).

3-*Bromo-4-acetamidodiphenylmethane.*—22·5 G. of 4-acetamidodiphenylmethane and 25 g. of anhydrous sodium acetate were dissolved in 400 c.c. of stable acetic acid, 17 g. of bromine were added, and the mixture set aside for 3 days. The product, isolated by pouring the mixture into water, crystallised from methyl alcohol in plates or prisms, m. p. 91° (Found: Br, 26·2. $C_{15}H_{14}ONBr$ requires Br, 26·3%). The yield was nearly 100% : in boiling acetic acid it was only 20—25%. Hydrolysis of the *acetyl* compound with hydrobromic acid in alcohol yielded the *hydrobromide* of 3-bromo-4-aminodiphenylmethane, crystallising from dilute hydrobromic acid in needles, m. p. 216° (decomp.) (Found: HBr, 23·7. $C_{13}H_{12}NBr,HBr$ requires HBr, 23·6%). The free base was an oil, b. p. 204—208°/15 mm., which was brominated quantitatively in cold acetic acid to 3 : 5-dibromo-4-aminodiphenylmethane, thus establishing its structure. Its *benzoyl* derivative crystallised from alcohol in needles, m. p. 97° (Found: Br, 22·2.

$C_{20}H_{16}ONBr$ requires Br, 21·9%), and was obtained both from the free base with benzoyl chloride and also by brominating 4-benzamidodiphenylmethane in acetic acid at room temperature.

On brominating 3-bromo-4-acetamidodiphenylmethane for several hours at 100° by the normal procedure, a sticky product resulted from which could be isolated only 3-*bromo*-4-*diacetamidodiphenylmethane*; fine plates, m. p. 112°, from methyl alcohol (Found: Br, 22·4. $C_{17}H_{16}O_2NBr$ requires Br, 22·45%). This same compound has also been obtained by direct bromination of 4-acetamidodiphenylmethane at 100°. By keeping 3-bromo-4-acetamidodiphenylmethane for several months with excess bromine in the usual solution, there was produced in small yield (*ca.* 10%) 3 : 5 : 4′-*tribromo*-4-*acetamidodiphenylmethane*, which forms needles from methyl alcohol, m. p. 209° (Found: Br, 51·9. $C_{15}H_{12}ONBr_3$ requires Br, 51·95%). Hydrolysis gives the corresponding base, m. p. 140—141°, alone or mixed with an authentic specimen.

2-*Bromo*-4-*acetamidodiphenylmethane* was obtained, in one preparation only, by brominating 4-acetamidodiphenylmethane at 100° for 3 hours. It was usually formed only in traces. It crystallised from alcohol in needles, m. p. 194° (Found: Br, 26·3. $C_{15}H_{14}ONBr$ requires Br, 26·3%). Hydrolysis gave the free base as a thick oil which did not solidify on freezing. The *benzoyl* derivative crystallised from alcohol in needles, m. p. 166° (Found: Br, 22·1. $C_{20}H_{16}ONBr$ requires Br, 21·9%). The free base evolved bromine when oxidised; when heated with excess bromine in carbon tetrachloride it gave, on steam-distillation after removal of the solvent, benzaldehyde (phenylhydrazone, m. p. 155°) and a residue, probably bromoanil, which crystallised from acetone in bright yellow needles, m. p. 300°. The bromine is therefore in the same ring as the acetamido-group, and position 2 is inferred for it in absence of an alternative, although no *direct* proof of structure has been obtained.

3 : 4′-*Dibromo*-4-*benzamidodiphenylmethane* was formed quantitatively by brominating 4′-bromo-4-benzamidodiphenylmethane at room temperature. It crystallised from alcohol in plates, m. p. 135° (Found: Br, 35·95. $C_{20}H_{15}ONBr_2$ requires Br, 35·95%). Hydrolysis gave a gum, which, by treatment with bromine in cold acetic acid, gave 3 : 5 : 4′-tribromo-4-aminodiphenylmethane (m. p. 140°, alone or mixed with an authentic specimen), contaminated with a little tribromoaniline.

3 : 5-*Di-iodo*-4-*aminodiphenylmethane*.—4-Aminodiphenylmethane (10 g.) in alcohol (300 c.c.) and concentrated hydrochloric acid (50 c.c.) was kept cold in crushed ice whilst 2 equivs. of *N*/2-iodinating reagent (33 g. $NaIO_3$ + 55 g. KI per litre of water) were slowly run in. A little tar was deposited; the main yield was separated by pouring into ice–water containing a little sodium sulphite. Yield 62%. The *compound* crystallised from alcohol in needles, m. p. 137° (Found: I, 58·3. $C_{13}H_{11}NI_2$ requires I, 58·35%). Its *benzoyl* derivative crystallises from alcohol in needles, m. p. 257° (Found: I, 46·9. $C_{20}H_{15}ONI_2$ requires I, 47·1%). Deamination by the usual method yielded 3 : 5-*di-iododiphenylmethane*, needles, m. p. 73° (Found: I, 60·6. $C_{13}H_{10}I_2$ requires I, 60·45%), from alcohol–ether. On oxidation it gave 3 : 5-di-iodobenzophenone, m. p. and mixed m. p. 90—91°.

When heated with bromine in carbon tetrachloride, 3 : 5-di-iodo-4-aminodiphenylmethane evolved hydrogen bromide and darkened with liberation of iodine. After evaporation of the solvent, the residue was steam-distilled, and gave free iodine and also benzaldehyde (phenylhydrazone, m. p. 156°). The dark residue on crystallisation from alcohol gave needles, m. p. 73°. In acetic acid solution a similar reaction occurred, the residual mixed bases having m. p. 60—100°.

2 : 4-Di-iodoaniline, m. p. 95°, was obtained when aniline was iodinated by a similar process. On treatment with bromine in acetic acid at 100°, it gave free iodine and a residue of acetylated bases, m. p. 215—220°.

3-*Bromo*-5-*iodo*-4-*aminodiphenylmethane* was obtained by a similar iodination of 3-bromo-4-aminodiphenylmethane. It crystallised from alcohol in needles, m. p. 91°, not depressed on admixture with 3 : 5-dibromo-4-aminodiphenylmethane in varying proportions (Found: 0·2038 g. gave 0·2231 g. AgBr + AgI. Calc.: AgBr + AgI, 0·2221 g.).

Iodination of 4-*Acetamidodiphenylmethane*.—20 G. of 4-acetamidodiphenylmethane in 200 c.c. were treated with iodinating reagent [20 g. powdered KI added to 24 g. dichloramine-T (80%) in 200 c.c. acetic acid] and kept at room temperature for 3 days. The mixture was warmed to 100° for 3 hours and then poured into dilute sodium sulphite solution. The precipitate was washed with dilute sodium hydroxide, and repeated crystallisation from methyl alcohol afforded much original material together with small quantities of two isomeric monoiodo-4-acetamidodiphenylmethanes: A (2-*iodo*-?) crystallised in needles, m. p. 201°, and B (3-*iodo*-?)

in plates, m. p. 113° [Found: I, (A), 36·26; (B), 35·8. $C_{15}H_{14}ONI$ requires I, 36·16%]. Several iodinations at room temperature were completely unsuccessful; iodination at 100° produced decomposition.

Chlorination of 4-acetamidodiphenylmethane with dichloramine-T in acetic acid was attempted, but, from the gummy reaction product, no crystalline substance could be isolated.

Nitration of 4-Acetamidodiphenylmethane.—4-Acetamidodiphenylmethane in acetic acid at 15—30° was not attacked by nitric acid, except on warming, which caused oxidation and decomposition. Dinitration was effected by adding nitric acid (*d* 1·5; 25 c.c.) to a solution of 4-acetamidodiphenylmethane (40 g.) in a mixture of equal volumes (200 c.c. of each) of concentrated sulphuric acid and glacial acetic acid, maintaining the mixture at 30—40° for ½ hour, and then pouring it on ice. There resulted 3 : 4′-*dinitro*-4-*acetamidodiphenylmethane* (21 g.), yellow needles, m. p. 150°, from methyl alcohol (Found: N, 13·4. $C_{15}H_{13}O_5N_3$ requires N, 13·3), together with more soluble, low-melting products which could not be purified.

3 : 4′-*Dinitro*-4-*aminodiphenylmethane*, obtained by hydrolysis of the acetyl derivative, crystallised from aqueous alcohol in orange-red needles, m. p. 122° (Found: N, 15·4. $C_{13}H_{11}O_4N_3$ requires N, 15·4%). Oxidation afforded *p*-nitrobenzoic acid (m. p. and mixed m. p. 240°). This established the orientation of the nitro-group as being in the ring not containing the amino-group. Deamination of the dinitro-base by the usual method yielded 3 : 4′-dinitrodiphenylmethane, m. p. 102° (Found: N, 11·1. Calc.: N, 10·9%), which was oxidised as usual to 3 : 4′-dinitrobenzophenone, m. p. 172° (Found: N, 10·5. Calc.: N, 10·3). These results are in accordance with the observations of Staedel (*loc. cit.*). In confirmation, his nitration of *m*-nitrodiphenylmethane was repeated, equal volumes of nitric and sulphuric acids being used at room temperature, and 3 : 4′-dinitrodiphenylmethane, m. p. 102°, alone or mixed with the deamination product was formed. This confirms the orientation of the other nitro-group.

On treating 3 : 4′-dinitro-4-aminodiphenylmethane with bromine in cold acetic acid, a monobromo-derivative, almost certainly 5-*bromo*-3 : 4′-*dinitro*-4-*aminodiphenylmethane*, was obtained; it crystallised from acetone in orange needles, m. p. 181° (Found: Br, 22·7. $C_{13}H_{10}O_4N_3Br$ requires Br, 22·7%), and was not decomposed by refluxing with bromine in chloroform.

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