LXXII.—*Some Substitution Products of 2-Nitro- and 2-Acetamido-diphenyl Ethers and the Corresponding Diphenylene Oxides.*

By Hamilton McCombie, William George Macmillan, and Harold Archibald Scarborough.

The investigation of the products of bromination of 2-nitro- and of 2-acetamido-diphenyl ethers has been extended to include the products of chlorination, iodination, and nitration of these compounds; and further, the conversion of the substituted amino-compounds into the corresponding diphenylene oxides.

The chlorination of 2-nitrodiphenyl ether proceeded smoothly, yielding 4-chloro-2′-nitrodiphenyl ether; further chlorination by passage of dry chlorine into the molten chloronitro-compound yielded a thick red gum. Similarly, on iodination with iodine monochloride, 2-nitrodiphenyl ether yielded 4-*iodo*-2′-*nitrodiphenyl* *ether.* The bromination of 4-chloro-2-nitrodiphenyl ether yielded 4-chloro-4′-bromo-2-nitrodiphenyl ether.

The structures of 2-chloro-, 4-*chloro*-, 4′-chloro-, 4 : 4′-dichloro-, and 4-chloro-4′-bromo-2-nitrodiphenyl ethers follow from their syntheses from the corresponding *o*-halogenonitrobenzene and the sodium or potassium halogenophenoxide. Attempts were made to determine the structure of 4-iodo-2′-nitrodiphenyl ether by reduction and deamination, but a pure specimen of 4-iododiphenyl ether was not obtained.

The chlorination of 2-acetamidodiphenyl ether was attempted by direct treatment with chlorine, by the use of a chlorate and hydrochloric acid, and by the preparation of the *N*-chloro-derivative and the conversion of this compound into a ring-substituted product; all three methods failed to yield a product which could be obtained in a state of purity. Similarly, iodination of 2-acetamidodiphenyl ether with iodine monochloride yielded a semi-solid black oil.

The nitration of 2-acetamidodiphenyl ether was found to depend largely on the experimental conditions : in acetic acid or in a mixture of acetic anhydride and acetic acid at various temperatures, the ether either remained unchanged or was converted into a mixture of nitration products which were separable only with great loss. Nitration in ice-cold fuming nitric acid solution was too violent, and, in addition to the formation of a mixed nitration product, hydrolysis to the amine occurred. Nitration of both the substituted and the unsubstituted acetamido-compounds was, however, effected quite smoothly by suspending the compound in 7 or 8 times its weight of nitric acid (*d* 1·42) and cautiously adding fuming nitric acid until solution was completed. 2-Acetamidodiphenyl ether, 2′-*chloro*-, 4′-*chloro*-, 4 : 4′-*dichloro*-, and 4′-*bromo*-2-*acetamidodiphenyl ethers* were thus converted into mononitro-derivatives. In the presence of an excess of fuming nitric acid certain of the mononitro-derivatives were converted into dinitro-derivatives.

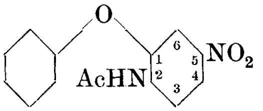
The structures of the mononitro-substituted 2-acetamidodiphenyl ethers were based on the following observations : 2-acetamidodiphenyl ether yielded 5-*nitro*-2-*acetamidodiphenyl ether* (I), which on deacetylation, deamination, and ring closure with elimination of nitrogen yielded 2-nitrodiphenylene oxide * (II). Again 4′-*bromo*-5-*nitro*-2-*acetamidodiphenyl ether* on deacetylation and deamination

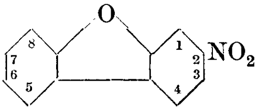
---

* Borsche and Bothe (*Ber.*, 1908, **41**, 1940) ascribed to this compound the structure of 3-nitrodiphenylene oxide. Mayer and Krieger (*Ber.*, 1922, **55**, 1659) showed that this view was incorrect, but it remained for Cullinane (J., 1930, 2267) to prove conclusively that the main product of nitration of diphenylene oxide was 2-nitrodiphenylene oxide by conversion into the corresponding 2-chlorodiphenylene oxide and synthesis from 5-chloro-2-aminodiphenyl ether.

yielded 4-bromo-3′-nitrodiphenyl ether; and finally 4′-bromo-5-nitro-2-acetamidodiphenyl ether was obtained either by the bromination of 5-nitro-2-acetamidodiphenyl ether or by the nitration of 4′-bromo-2-acetamidodiphenyl ether.

(I.)





(II.)

The position taken by the second entering nitro-group has not been established and the formulæ assigned are based on the general effects of the directive influences observed in this series of compounds.

The conversion of the substituted 2-aminodiphenyl ethers into the corresponding diphenylene oxides by treating the diazotised amine with boiling 50% sulphuric acid was successful in the cases of 2-nitro-, 3-*chloro*-, 3-*chloro*-7-*nitro*-, 3 : 6-*dichloro*-, 2-*bromo*-, 3-bromo-, 2 : 6-*dibromo*-, and 3 : 6-*dibromo-diphenylene oxides*; but an attempt to prepare 1-chlorodiphenylene oxide from the appropriate amine was not successful. The structures of these compounds follow from their method of synthesis.

The results show that chlorination and iodination of 2-nitrodiphenyl ether follow the same path as bromination but that in these cases the introduction of more than one substituent atom is not attained. The most striking result is the behaviour of 2-acetamidodiphenyl ether on nitration : this compound yielded a nitro-derivative in which the nitro-group is in the same ring as the acetamido-group when the reaction was carried out in mineral acid solution. In other series, particularly the diphenyl series (compare J., 1927, 1133 *et seq.*), nitration could be effected in the ring containing the acetamido-group only when the reaction was carried out in acetic acid solution, and the use of a mineral acid as solvent invariably effected nitration in the other ring. The work is being extended to the preparation of certain di- and tri-nitrodiphenyl ethers in order to establish the structure of the dinitro-2-acetamidodiphenyl ethers and also to an examination of the substitution products of diphenylene oxide.

EXPERIMENTAL.

5-*Nitro*-2-*acetamidodiphenyl ether* was prepared by keeping a solution of 2-acetamidodiphenyl ether in nitric acid (*d* 1·42) at room temperature for 15 minutes. The product, precipitated when the mixture was poured on ice, crystallised from methyl alcohol in yellow rhombs, m. p. 180° (Found : N, 10·35. $C_{14}H_{12}O_4N_2$ requires N, 10·3%). The nitro-derivative was refluxed for 6 hours with ethyl-alcoholic hydrogen chloride and poured on ice, and the base liberated with dilute aqueous ammonia. 5-*Nitro-2-aminodiphenyl ether*, thus obtained, separated from dilute methyl alcohol in yellow plates, m. p. 116° (Found : N, 12·1. $C_{12}H_{10}O_3N_2$ requires N, 12·2%). The base was dissolved in dilute hydrochloric acid and diazotised, and the diazo-solution allowed to drop slowly into hot 50% sulphuric acid. The sulphuric acid solution was refluxed for 3 hours and distilled with superheated steam; 2-nitrodiphenylene oxide, thus obtained, separated from acetic acid in faintly yellow needles, m. p. 186°, and was identical with the product obtained by direct nitration of diphenylene oxide (Borsche and Bothe, *loc. cit.*).

5 : 4′(?)-*Dinitro-2-acetamidodiphenyl ether* was obtained when 2-acetamido- or 5-nitro-2-acetamido-diphenyl ether was dissolved in a mixture of 2 parts of nitric acid (*d* 1·42) and 1 part of nitric acid (*d* 1·5). It separated from ethyl alcohol in faintly yellow needles, m. p. 190° (Found : N, 13·15. $C_{14}H_{11}O_6N_3$ requires N, 13·25%). The base, 5 : 4′-*dinitro-2-aminodiphenyl ether*, prepared by the hydrolysis of the acetyl derivative with ethyl-alcoholic hydrogen chloride, crystallised from ethyl alcohol in yellow plates, m. p. 192° (Found : N, 15·2. $C_{12}H_9O_5N_3$ requires N, 15·25%).

2-Chloro-2′-nitrodiphenyl ether was obtained in almost theoretical yield when potassium *o*-chlorophenoxide was condensed with *o*-chloronitrobenzene for 18 hours at 170°. The melt was distilled in steam, the residue taken up in ether, the ethereal solution dried, and the ether removed. The product crystallised from methyl alcohol in yellow rhombs, m. p. 49° (Found : Cl, 14·25. Calc. for $C_{12}H_8O_3NCl$: Cl, 14·2%). The nitro-compound was reduced with stannous chloride in ethereal hydrogen chloride solution, and the base liberated with 30% sodium hydroxide solution. 2-Chloro-2′-aminodiphenyl ether was obtained as a pale yellow oil, b. p. 203°/15 mm., which slowly solidified and then crystallised from light petroleum (b. p. 40—60°) in prisms, m. p. 45° (Found : Cl, 16·1. Calc. for $C_{12}H_{10}ONCl$: Cl, 16·15%).

2-*Chloro-2′-acetamidodiphenyl ether* was obtained by refluxing the base with a mixture of 1 part of acetic anhydride and 5 parts of acetic acid for 24 hours. The acetyl derivative separated from light petroleum (b. p. 60—80°) in heavy clustered needles, m. p. 104° (Found : Cl, 13·55. $C_{14}H_{12}O_2NCl$ requires Cl, 13·6%). An attempt to prepare the corresponding diphenylene oxide was not successful.

2-*Chloro-5′-nitro-2′-acetamidodiphenyl Ether.*—2-Chloro-2′-acetamidodiphenyl ether was suspended in 9 parts of nitric acid (*d* 1·42) and brought into solution by the addition of 1·5 parts of nitric acid (*d* 1·5), and the solution kept for 15 minutes. The *product* crystallised from methyl alcohol in yellow needles, m. p. 142° (Found : Cl, 11·6; N, 9·2. $C_{14}H_{11}O_4N_2Cl$ requires C, 11·6; N, 9·15%).

The base, 2-*chloro*-5′-*nitro*-2′-*aminodiphenyl ether*, was obtained when the acetyl derivative was hydrolysed in the usual manner; it separated from dilute methyl alcohol in yellow needles, m. p. 125° (Found : Cl, 13·4. $C_{12}H_9O_3N_2Cl$ requires Cl, 13·45%).

2-*Chloro*-4(?) : 5′-*dinitro*-2′-*acetamidodiphenyl ether* was obtained when 2-chloro-2′-acetamido- or 2-chloro-5′-nitro-2′-acetamido-diphenyl ether was dissolved in a mixture of equal parts of nitric and fuming nitric acids. The product separated from ethyl alcohol in small orange prisms, m. p. 176° (Found : Cl, 10·0; N, 11·9. $C_{14}H_{10}O_6N_3Cl$ requires Cl, 10·1; N, 11·95%). The hydrolysis of the acetyl derivative yielded 2-*chloro*-4(?) : 5′-*dinitro*-2′-*aminodiphenyl ether*, which separated from ethyl alcohol in yellow needles, m. p. 202° (Found : Cl, 11·45. $C_{12}H_8O_5N_3Cl$ requires Cl, 11·45%).

4-*Chloro*-2-*nitrodiphenyl ether* was obtained when 2 : 5-dichloronitrobenzene was condensed with sodium phenoxide, for 5 hours, at 170—180°. It was a pale yellow oil, b. p. 211°/20 mm. (Found : Cl, 14·3. $C_{12}H_8O_3NCl$ requires Cl, 14·2%). On reduction with stannous chloride in ethereal hydrogen chloride solution in the usual manner it gave 4-*chloro*-2-*aminodiphenyl ether*, a light yellow oil, b. p. 215°/20 mm., which slowly solidified and then separated from light petroleum (b. p. 60—80°) in prisms, m. p. 44° (Found : Cl 16·05. $C_{12}H_{10}ONCl$ requires Cl, 16·15%). The *hydrochloride* of the base separated from a dilute hydrochloric acid solution in needles, m. p. 192° (Found : HCl, 14·1. $C_{12}H_{10}ONCl,HCl$ requires HCl, 14·25%). The acetyl derivative of the base was obtained as a semi-solid mass which could not be further purified. 3-*Chlorodiphenylene oxide* was prepared from the base by diazotisation in the usual manner; it crystallised from light petroleum (b. p. 60—80°) in leaves, m. p. 106° (Found : Cl, 17·65. $C_{12}H_7OCl$ requires Cl, 17·5%).

4-Chloro-2′-nitrodiphenyl ether was prepared (*a*) by treating an acetic acid solution of 2-nitrodiphenyl ether with a slight excess of chlorine, also in acetic acid solution, and keeping the mixture for 24 hours; or (*b*) by condensing potassium *p*-chlorophenoxide with *o*-chloronitrobenzene. It crystallised from methyl alcohol in faintly yellow needles, m. p. 46° (Found : Cl, 14·25. Calc. for $C_{12}H_8O_3NCl$: Cl, 14·2%). The reduction of the nitro-compound in the usual manner yielded 4-chloro-2′-aminodiphenyl ether as a yellow oil, b. p. 215°/20 mm. The *hydrochloride* of the base separated from a dilute hydrochloric acid solution in long needles, m. p. 181° (Found : HCl, 14·2. $C_{12}H_{10}ONCl,HCl$ requires HCl, 14·25%). The base was converted into 3-chlorodiphenylene oxide in the usual manner.

4-*Chloro*-2′-*acetamidodiphenyl ether* was prepared by refluxing the base with a mixture of acetic anhydride (1 part) and acetic acid

(5 parts) for 24 hours. The product, a mixture of the mono- and the di-acetyl derivative, was purified by alternate crystallisations from light petroleum (b. p. 60—80°) and methyl alcohol and separated from the former solvent in needles, m. p. 99° (Found : Cl, 13·5. $C_{14}H_{12}O_2NCl$ requires Cl, 13·6%). The base, on being refluxed with a mixture of acetic anhydride (1 part) and acetic acid (3 parts) for 36 hours, yielded 4-*chloro*-2′-*diacetamidodiphenyl ether*, which separated from light petroleum (b. p. 60—80°) in needles, m. p. 106° (Found : Cl, 11·75. $C_{16}H_{14}O_3NCl$ requires Cl, 11·7%). 4-*Chloro*-5′-*nitro*-2′-*acetamidodiphenyl ether* was prepared by dissolving 4-chloro-2′-acetamidodiphenyl ether in a mixture of 1 part of nitric acid (*d* 1·5) and 6 parts of nitric acid (*d* 1·42) and keeping the solution at room temperature for 15 minutes; the nitration product then separated. It crystallised from ethyl alcohol in yellow prisms, m. p. 203° (Found : Cl, 12·65; N, 9·1. $C_{14}H_{11}O_4N_2Cl$ requires Cl, 11·6; N, 9·15%). Hydrolysis of the acetyl derivative in ethyl-alcoholic solution yielded 4-*chloro*-5′-*nitro*-2′-*aminodiphenyl ether*, which crystallised from methyl alcohol in yellow needles, m. p. 123° (Found : Cl, 13·35. $C_{12}H_9O_3N_2Cl$ requires Cl, 13·45%). The base was converted into 3-*chloro*-7-*nitrodiphenylene oxide* in the manner previously described. This oxide separated from light petroleum (b. p. 60—80°) in pale yellow needles, m. p. 226° (Found : Cl, 14·45. $C_{12}H_6O_3NCl$ requires Cl, 14·35%). 4-*Chloro*-2(?) : 5′-*dinitro*-2′-*acetamidodiphenyl ether* was formed in small quantity, compared with the mononitro-derivative, when 4-chloro-2′-acetamidodiphenyl ether was suspended in 3 parts of nitric acid (*d* 1·42) and brought into solution with 1 part of nitric acid (*d* 1·5) and the solution kept for 15 minutes at room temperature. It separated from acetone–methyl alcohol in needles, m. p. 198° (Found : Cl, 10·1. $C_{14}H_{10}O_6N_3Cl$ requires Cl, 10·1%).

4 : 4′-Dichloro-2-nitrodiphenyl ether was obtained when potassium *p*-chlorophenoxide was condensed with 2 : 5-dichloronitrobenzene, for 2 hours, at 170°. It separated from methyl alcohol in yellow prisms, m. p. 78° (Found : Cl, 24·95. Calc. for $C_{12}H_7O_3NCl_2$: Cl, 25·0%). Reduction of the nitro-compound, in the usual manner, yielded 4 : 4′-dichloro-2-aminodiphenyl ether. The base was obtained as a pale yellow oil, b. p. 235°/25 mm., which solidified and then crystallised from light petroleum (b. p. 60—80°) in needles, m. p. 66° (Found : Cl, 27·8. Calc. for $C_{12}H_9ONCl_2$: Cl, 27·95%). The *hydrochloride* of the base separated from dilute hydrochloric acid solution in needles, m. p. 145° (Found : HCl, 12·5. $C_{12}H_9ONCl_2,HCl$ requires HCl, 12·4%). Acetylation of the base with a mixture of 1 part of acetic anhydride and 5 parts of acetic acid, for 24 hours, yielded 4 : 4′-*dichloro*-2-*acetamidodiphenyl ether*. This derivative

crystallised from light petroleum (b. p. 60—80°) in needles, m. p. 109° (Found : Cl, 23·9. $C_{14}H_{11}O_2NCl_2$ requires Cl, 24·0%). 3 : 6-*Dichlorodiphenylene oxide*, obtained in the usual manner from the base, crystallised from light petroleum (b. p. 60—80°) in needles, m. p. 190° (Found : Cl, 29·95. $C_{12}H_6OCl_2$ requires Cl, 30·05%).

4 : *4′-Dichloro-5-nitro-2-acetamidodiphenyl Ether*.—4 : 4′-Dichloro-2-acetamidodiphenyl ether was dissolved in a mixture of 1 part of nitric acid (*d* 1·5) and 3 parts of nitric acid (*d* 1·42) and the *product* commenced to separate immediately. It crystallised from methyl alcohol in feathery needle clusters, m. p. 150° (Found : Cl, 20·8; N, 8·1. $C_{14}H_{10}O_4N_2Cl_2$ requires Cl, 20·8; N, 8·2%). A small quantity of 4 : *4′-dichloro-2′*(?) : *5-dinitro-2-acetamidodiphenyl ether* was also isolated in this reaction. It separated from acetone–methyl alcohol in fine needles, m. p. 212° (Found : Cl, 18·3. $C_{14}H_9O_6N_3Cl_2$ requires Cl, 18·4%).

4′-Bromo-5-nitro-2-acetamidodiphenyl ether was obtained when (a) 4′-bromo-2-acetamidodiphenyl ether was dissolved in a mixture of 1 part of nitric acid (*d* 1·5) and 6 parts of nitric acid (*d* 1·42) and the solution kept for 15 minutes; and (b) 5-nitro-2-acetamidodiphenyl ether was treated, in acetic acid solution, with an excess of bromine, also in acetic acid solution. The nitro-compound separated from ethyl alcohol in yellow rhombs, m. p. 208° (Found : N, 8·1; Br, 22·8. $C_{14}H_{11}O_4N_2Br$ requires N, 8·0; Br, 22·8%). The base, *4′-bromo-5-nitro-2-aminodiphenyl ether*, obtained from the acetyl derivative by hydrolysis in ethyl-alcoholic hydrogen chloride solution, separated from methyl alcohol in yellow needles, m. p. 133° (Found : Br, 25·8. $C_{12}H_9O_3N_2Br$ requires Br, 25·9%). The base was deaminated in the usual manner; the product, crystallised from light petroleum (b. p. 60—80°) and finally from methyl alcohol, formed yellow rhombs, m. p. 63°. This product did not lower the m. p. of a specimen of 4′-bromo-3-nitrodiphenyl ether obtained by the deamination of 4′-bromo-3-nitro-4-aminodiphenyl ether (Scarborough, J., 1929, 2366).

2-Bromodiphenylene oxide was obtained when 5-bromo-2-aminodiphenyl ether was diazotised in hydrochloric acid solution, the diazo-solution decomposed with boiling 50% sulphuric acid, and the product distilled in superheated steam; it separated from methyl alcohol in plates, m. p. 120° (Found : Br, 32·3. $C_{12}H_7OBr$ requires Br, 32·4%).

3-Bromodiphenylene oxide was prepared from 4-bromo- or 4′-bromo-2-aminodiphenyl ether in the usual manner. The product distilled in superheated steam and crystallised from methyl alcohol or light petroleum (b. p. 60—80°) in plates, m. p. 110° (Found : Br, 32·25. Calc. for $C_{12}H_7OBr$: Br, 32·4%). The same product was obtained by bromination of diphenylene oxide in carbon disulphide solution (Mayer and Kriege, *Ber.*, 1922, **55**, 1659). 2 : 6-*Dibromodiphenylene oxide* was prepared from 4′ : 5-dibromo-2-aminodiphenyl ether. The product distilled in superheated steam and crystallised from light petroleum (b. p. 60—80°) in needles, m. p. 176° (Found : Br, 49·2. $C_{12}H_6OBr_2$ requires Br, 49·1%).

3 : 6-*Dibromodiphenylene oxide* was prepared from 4 : 4′-dibromo-2-aminodiphenyl ether in the usual manner. The product, separated by means of superheated steam, crystallised from light petroleum (b. p. 60—80°) in plates, m. p. 195° (Found : Br, 49·25. $C_{12}H_6OBr_2$ requires Br, 49·1%). The same product was obtained by the bromination of diphenylene oxide in carbon disulphide solution (compare Hoffmeister, *Annalen*, 1871, **149**, 191).

4-Chloro-4′-bromo-2-nitrodiphenyl ether was obtained when (a) 4-chloro-2-nitrodiphenyl ether was treated with an excess of bromine in acetic acid solution, and the solution kept for 12 hours; (b) potassium *p*-bromophenoxide was condensed with 2 : 5-dichloronitrobenzene. The product crystallised from ethyl alcohol in pale yellow needles, m. p. 96° (Found : 0·1516 g. gave 0·1510 g. Ag halides. Calc. for $C_{12}H_7O_3NClBr$: 0·1529 g.).

4-*Iodo-2′-nitrodiphenyl ether* resulted when 2-nitrodiphenyl ether, in acetic acid solution, was treated with a slight excess of iodine monochloride, and the solution kept for 12 hours. The product separated from methyl alcohol in faintly yellow needles, m. p. 86° (Found : I, 37·25. $C_{12}H_8O_3NI$ requires I, 37·25%).

4-*Iodo-2′-nitrodiphenyl ether dichloride* was prepared by treating an ice-cold carbon tetrachloride solution of the nitro-compound with an excess of chlorine in carbon tetrachloride solution. The product separated from the reaction mixture in matted needles, m. p. 96° (decomp.) (Found : Cl, 16·95. $C_{12}H_8O_3NCl_2I$ requires Cl, 17·2%). The dichloride was stable.

4-Iodo-2′-aminodiphenyl ether was prepared from the nitro-compound by reduction with stannous chloride in ethereal hydrogen chloride solution. The base, liberated and extracted in the usual manner, was a viscid oil, b. p. 240°/20 mm. The *hydrochloride* of the base separated from dilute hydrochloric acid solution in needles, m. p. 219° (Found : HCl, 10·45. $C_{12}H_{10}ONI,HCl$ requires HCl, 10·5%). The base was acetylated by refluxing it, for 18 hours, with a mixture of 1 part of acetic anhydride and 5 parts of acetic acid; 4-*iodo-2′-acetamidodiphenyl ether* resulted as the main product. The monoacetyl derivative was separated from the diacetyl derivative by alternate crystallisations from methyl alcohol and light petroleum (b. p. 60—80°); it separated from the latter solvent in needles, m. p. 115° (Found : I, 35·8. $C_{14}H_{12}O_2NI$ requires I, 35·9%). 4-*Iodo-2′-diacetamidodiphenyl ether* was obtained when the base was refluxed, for 24 hours, with a mixture of 1 part of acetic anhydride and 3 parts of acetic acid. It crystallised from light petroleum in needles, m. p. 94° (Found : I, 32·25. $C_{16}H_{14}O_3NI$ requires I, 32·15%).

One of the authors (W. G. M.) begs to thank the Carnegie Trustees for a Fellowship which has enabled him to collaborate in this work.

THE UNIVERSITY CHEMICAL LABORATORIES,
CAMBRIDGE.

[*Received, January* 15*th*, 1931.]