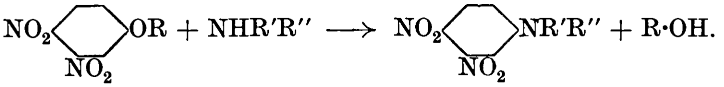
CLXII.—*The Scission of Diaryl Ethers and Related Compounds by means of Piperidine. Part I. The Scope of the Method and its Use in determining the Constitution of some Nitro-derivatives.*

By RAYMOND JAMES WOOD LE FÈVRE, SYDNEY LEONARD MORGAN SAUNDERS, and EUSTACE EBENEZER TURNER.

IT has been known for some time that ethers of nitrophenols react with ammonia, and with some of its mono- and di-substitution products, to give an alcohol (phenol) and a nitro-base :



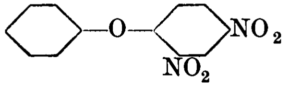
The extent to which substituents affect the course of this reaction is, however, a matter requiring investigation. Further, when R is a substituted aryl group, there is a possibility that a base such as piperidine may, in effecting the scission, which may now be written : $R{\cdot}O{\cdot}R' + C_5H_{10}NH \longrightarrow R{\cdot}NC_5H_{10} + R'{\cdot}OH$, give rise to more than two products. It should be possible, therefore, to use such reactions to compare the effects of different groups, or similar groups in different positions, on the strengths of attachment of the oxygen atom to the two benzene nuclei.

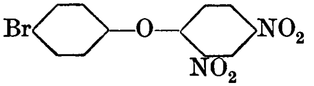
In order to determine the scope of the method, we have first investigated the behaviour towards piperidine of a number of substituted diphenyl ethers, some of which have been prepared for the purpose.

Diphenyl ether itself does not react with piperidine at 100°. 2- and 4-Nitrodiphenyl ether, and 2′-, 3′-, and 4′-chloro-2-nitrodiphenyl ether react slowly with piperidine at this temperature. On the other hand, 2 : 4-dinitrodiphenyl ether (I), 4′-bromo-2 : 4-dinitrodiphenyl ether (II), 2′ : 4′-dibromo-2 : 4-dinitrodiphenyl ether, and 2 : 4 : 2′ : 4′-tetranitrodiphenyl ether give colorations in the cold with piperidine, which at 100° converts them in the course of a few minutes into mixtures of 2 : 4-dinitrophenylpiperidine

(Lellmann and Geller, *Ber.*, 1888, **21**, 2283) (III) and phenol, *p*-bromo-, 2 : 4-dibromo-, and 2 : 4-dinitro-phenol, respectively.

(I.)





(II.)

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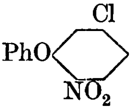

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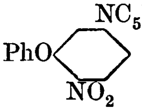

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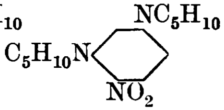
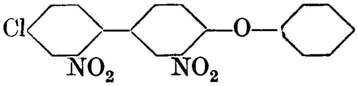


(VI.)

In 5-chloro-2-nitrodiphenyl ether (IV), the chlorine atom is more reactive than the phenoxyl radical, and by adjusting the conditions it is therefore possible to convert the ether first into 5-*piperidino-2-nitrodiphenyl ether* (V) and then into 1-nitro-2 : 4-dipiperidinobenzene (VI).

The considerable reactivity of diaryl ethers is well illustrated by the fact that we now find that 4-chloro-2 : 3′-dinitro-4′-phenoxydiphenyl (VII) and the corresponding 4-bromo-compound, both comparatively complex, are rapidly and quantitatively converted by piperidine at 100° into 4-chloro- (VIII) and 4-bromo-2 : 3′-dinitro-4′-piperidinodiphenyl respectively (compare Dennett and Turner, J., 1926, 476; Le Fèvre and Turner, *ibid.*, p. 1759).



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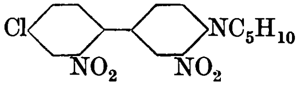


(VIII.)

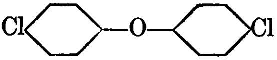
Similarly, 3 : 3′-dinitro-4 : 4′-diphenoxydiphenyl is converted, though apparently more slowly, into 3 : 3′-dinitro-4 : 4′-dipiperidinodiphenyl.

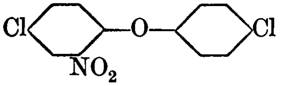
2 : 4-Dinitrodiphenyl ether, when brominated, gave the 4′-bromo-derivative, the constitution of which follows (1) from its synthesis from 1-chloro-2 : 4-dinitrobenzene and potassium *p*-bromophenoxide, and (2) from its conversion, by piperidine, into *p*-bromophenol and 2 : 4-dinitrophenylpiperidine.

Hoffmeister (*Annalen*, 1871, **159**, 210), by the bromination of diphenyl ether, obtained a dibromo-derivative, m. p. 53—55°, which was regarded by Mailhe and Murat (*Bull. Soc. chim.*, 1912, **11**, 33), without supporting experimental evidence, as the 4 : 4′-compound. This constitution for the substance has now been established by synthesis. 4-Bromo-4′-nitrodiphenyl ether, obtained from potassium *p*-bromophenoxide and *p*-chloronitrobenzene, on reduction gave 4-*bromo*-4′-*aminodiphenyl ether*, from which the 4 : 4′-dibromo-derivative was readily prepared. It melted at 60·5°, but repetition of Hoffmeister's experiments gave an identical substance.

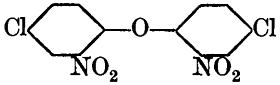
4 : 4′-Dichlorodiphenyl ether (IX), synthesised in a similar manner, was converted by excess of cold fuming nitric acid into a dinitro-compound. The latter was shown to be (XI), since it reacted with piperidine to give a mixture of 4-chloro-2-nitrophenol and 4-chloro-2-nitropiperidinobenzene.

(IX.)





(X.)



(XI.)

Mononitration of the dichlorodiphenyl ether was also effected, and the product (X), when further nitrated, was quantitatively converted into (XI). No 3-nitration appears to occur, demonstrating again that oxygen has a much greater directive influence than chlorine (compare the nitration of *o*-fluoroanisole by Holmes and Ingold, J., 1926, 1328). The present experiments incidentally establish the constitution of the product of direct chlorination of diphenyl ether (Mailhe and Murat, *loc. cit.*).

2-Nitrodiphenyl sulphide is unaffected by piperidine under conditions sufficing to effect partial scission of 2-nitrodiphenyl ether. Similarly, 2 : 4-dinitro- and 2 : 4 : 6-trinitro-*N*-ethyldiphenylamine do not react with piperidine. *p*-Nitrophenol is unaffected when boiled for some time with piperidine. It is hoped to investigate such cases in greater detail.

EXPERIMENTAL.

Action of Piperidine on 2- and 4-Nitrodiphenyl Ether and 2′-, 3′-, and 4′-Chloro-2-nitrodiphenyl Ether.—These ethers were heated for 30 minutes at 100° with an excess of piperidine. In each case, slight reaction occurred, as was evidenced by the odour of phenol, phenol, *o*-, *m*-, and *p*-chlorophenols, respectively, after acidification. Interaction was, however, insufficiently complete to allow of the isolation of any definite piperidino-derivative from the reddish, oily products.

4-*Bromo*-2 : 4′-*dinitrodiphenyl Ether.*—When 10 g. of 2 : 4-dinitrodiphenyl ether were heated with 12·3 g. of bromine in glacial acetic acid in presence of sodium acetate at 100°, 12·5 g. of the bromodinitro-compound, m. p. 134—136·5°, were obtained. One crystallisation from glacial acetic acid raised the m. p. to 136—137·5°. Raiford and Colbert (*J. Amer. Chem. Soc.*, 1926, **48**, 2652) give m. p. 138·5°.

2 : 4-*Dibromo*-2′ : 4′-*dinitrodiphenyl ether* was prepared by heating

a mixture of 10 g. of 2 : 4-dibromophenol, 1·1 g. of potassium hydroxide, and 4 g. of 1-chloro-2 : 4-dinitrobenzene at 100° for 1·5 hours. After being extracted with alkali and with water, the product separated from glacial acetic acid in pale yellow crystals (9·5 g.), m. p. 131° (Found: Br, 38·3. $C_{12}H_6O_5N_2Br_2$ requires Br, 38·3%).

Action of Piperidine on 2 : 4-*Dinitro-* (I), 4′-*Bromo*-2 : 4-*dinitro-* (II), 2′ : 4′-*Dibromo*-2 : 4-*dinitro-*, *and* 2 : 4 : 2′ : 4′-*Tetranitro-diphenyl Ether.*—Each of these ethers gave a yellow to red coloration with cold piperidine, and on warming, a vigorous reaction set in. The resulting solution, on dilution with water, gave almost pure 2 : 4-dinitrophenylpiperidine (Lellmann and Geller, *loc. cit.*). This, after one crystallisation from alcohol, had m. p. 92°. The four aqueous filtrates, when acidified, etc., gave phenol, *p*-bromophenol, 2 : 4-dibromophenol, and 2 : 4-dinitrophenol, respectively.

Action of Piperidine on 5-*Chloro*-2-*nitrodiphenyl Ether.*—(1) *Two mols. of piperidine.* To a solution of 2·5 g. (1 mol.) of the ether in 10 c.c. of chloroform were added 2·2 c.c. of piperidine (2·25 mols.) dissolved in 5 c.c. of chloroform. The mixture was boiled for 2 minutes, the chloroform removed by evaporation, and the residual oil left in a vacuum for a week, then washed with light petroleum, and crystallised from alcohol–light petroleum. 5-*Piperidino*-2-*nitrodiphenyl ether* was thus obtained in yellow needles, m. p. 86—86·5° (Found: N, 9·5. $C_{17}H_{18}O_3N_2$ requires N, 9·4%). (2) *Excess of piperidine.* On addition of the chloronitro-ether (2 g.) to 5 c.c. of piperidine and gentle warming, a definite reaction occurred; the solution soon set to a magma of crystals. The whole was heated for ½ hour; a clear reddish-brown solution then resulted. Dilution gave an oil, which, after being washed, was extracted with benzene. The extract was dried over sodium sulphate and evaporated, and the solid residue crystallised from alcohol. The orange crystals obtained melted at 67° and were identical (mixed melting point) with the product of interaction of 2 : 4-dichloro-1-nitrobenzene with piperidine (Le Fèvre and Turner, this vol., 1113).

4-*Bromo*-4′-*nitrodiphenyl Ether.*—*p*-Bromophenol, *p*-chloronitrobenzene, and potassium hydroxide, the last dissolved in the minimal quantity of water, were allowed to condense in the usual manner. After extraction and distillation in a vacuum, the *bromonitro-ether* crystallised from alcohol in colourless prisms, m. p. 60°, b. p. 230°/15 mm. (Found: Br, 27·3. $C_{12}H_8O_3NBr$ requires Br, 27·2%).

4-*Bromo*-4′-*aminodiphenyl Ether and* 4 : 4′-*Dibromodiphenyl Ether.*—The preceding nitro-compound, when reduced with water, iron powder, and ferric chloride, gave an 84% yield of the crude amino-compound, which was at once diazotised and converted into the diazo-perbromide. This, when decomposed in hot glacial acetic acid, gave dibromodiphenyl ether, which, after crystallisation from alcohol, melted at 60°. This compound did not depress the m. p. of the product (m. p. 60·5°; b. p. 210°/11 mm.) obtained by direct bromination of diphenyl ether by Hoffmeister's method (*loc. cit.*).

Dinitration of 4 : 4′-*Dibromodiphenyl Ether.*—A solution of the dibromo-compound in 10 parts of nitric acid (*d* 1·5) was heated at 100° for ½ hour and then poured into water. The precipitated solid separated from glacial acetic acid in small needles, m. p. 167° (Found : Br, 38·0. $C_{12}H_6O_5N_2Br_2$ requires Br, 38·3%).

Mononitration of 4 : 4′-*Dibromodiphenyl Ether.*—A solution of 20 g. of dibromodiphenyl ether in glacial acetic acid was treated with one of 8 g. of potassium nitrate in concentrated sulphuric acid. The solution was warmed at 100° for an hour, then cooled, and kept. The crystalline deposit separated from glacial acetic acid in small prisms, m. p. 90—91° (Found : Br, 42·5. $C_{12}H_7O_3NBr_2$ requires Br, 42·9%).

4-*Chloro*-4′-*nitrodiphenyl Ether.*—Condensation, by the usual process, of *p*-chloronitrobenzene, *p*-chlorophenol, and potassium hydroxide gave a product which, after alkali-washing and distillation in a vacuum, was crystallised from alcohol; it then had m. p. 75·5—76° and b. p. 215°/12 mm.

4-*Chloro*-4′-*aminodiphenyl Ether.*—Reduction of the preceding nitro-compound with iron, water, and ferric chloride gave an almost theoretical yield of crude amine. The latter crystallised from alcohol in colourless prisms, m. p. 100° (Found : Cl, 16·0. $C_{12}H_{10}ONCl$ requires Cl, 16·2%).

4 : 4′-*Dichlorodiphenyl Ether.*—The amino-compound was diazotised and submitted to the Sandmeyer reaction; after the usual procedure, the dichloro-compound separated from alcohol in colourless needles, m. p. 30°.

Nitration of 4 : 4′-*Dichlorodiphenyl Ether.*—The dichloro-compound was dissolved in 10 parts of nitric acid (*d* 1·5), and the solution warmed gently for 15 minutes. On cooling, crystals separated. These crystallised from glacial acetic acid in slender, white needles, m. p. 152° (Found : Cl, 21·4. $C_{12}H_6O_5N_2Cl_2$ requires Cl, 21·6%).

The dinitro-compound was dissolved in excess of piperidine, and the solution was boiled for 10 minutes. Dilution and filtration gave a solid, which, after being crystallised from glacial acetic acid, melted at 48° and was identical with 4-chloro-2-nitropiperidinobenzene (Le Fèvre and Turner, *loc. cit.*).

The filtrate from the above solid was acidified, and submitted to steam distillation; 4-chloro-2-nitrophenol then passed over. Its identity was established by comparison with a sample prepared by heating 2 : 5-dichloronitrobenzene with 50% aqueous potassium hydroxide at the b. p. for 2 hours. Both specimens, and a mixture, melted at 87—88°.

Mononitration of 4 : 4′-*Dichlorodiphenyl Ether*.—To a solution of the dichloro-ether in glacial acetic acid was added a solution of 1·25 mols. of potassium nitrate in concentrated sulphuric acid. The mixture was warmed on the water-bath for an hour and diluted, and the precipitate was collected. It crystallised from alcohol in wads of short, white needles, m. p. 75°. Its m. p. was unaffected by admixture with a specimen prepared as follows : *p*-Chlorophenol, 2 : 5-dichloronitrobenzene, and potassium hydroxide were condensed together in the usual manner, and gave a product which, after extraction with alkali, boiled at 215—220°/15 mm. After crystallisation from alcohol, it had m. p. 75°.

Nitration of 4 : 4′-*Dichloro*-2-*nitrodiphenyl Ether*.—A solution of the nitro-compound in 10 parts of fuming nitric acid (*d* 1·5) was warmed for 10 minutes and then diluted. Filtration, followed by crystallisation from glacial acetic acid, gave the dinitro-compound, m. p. 152°, identical (mixed m. p.) with that obtained above from 4 : 4′-dichlorodiphenyl ether.

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EAST LONDON COLLEGE,
UNIVERSITY OF LONDON.

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