

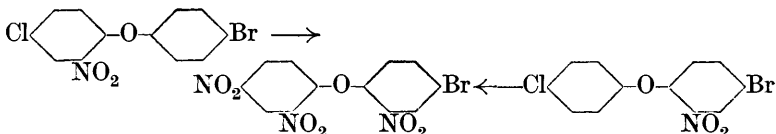
CXLI.—*The Scission of Diaryl Ethers and Related Compounds by Means of Piperidine. Part IV. Elimination of Halogen Atoms and Scission Reactions during Substitution Processes.*

By DOROTHY LILIAN FOX and EUSTACE EBENEZER TURNER.

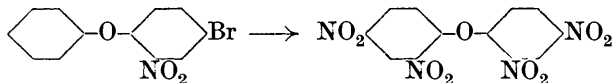
IN earlier investigations in the present series, a number of halogenated diphenyl ethers have been nitrated, with results that can be explained by current theories of aromatic substitution. We have now encountered some cases in which nitration is not of the simple type hitherto met with, but is accompanied by elimination of halogen atoms or disruption of the molecule.

The 2:2'-dinitration of 4:4'-dichloro- and 4:4'-dibromodiphenyl ether proceeds without difficulty (J., 1927, 1168), and the mononitro-derivatives obtained by controlling the conditions of

nitration are readily convertible into the dinitro-compounds. We have now found that under the conditions which favour the formation of these dinitro-derivatives, both the 2- and the 2'-nitro-derivative of 4-chloro-4'-bromodiphenyl ether undergo partial elimination of chlorine, and that when the nitration is performed at 100°, complete elimination of chlorine occurs, with the formation of 4-bromo-2 : 2' : 4' : 4'-trinitrodiphenyl ether :



The same product is formed when the more drastic nitration conditions are applied to 4-chloro-4'-bromo-2 : 2'-dinitrodiphenyl ether. The latter compound may be obtained by nitrating either of the corresponding mononitro-compounds under definite conditions. Prolonged nitration of the bromotrinitro-ether causes very slow removal of the bromine atom. On the other hand, when 4-bromo-2-nitrodiphenyl ether is nitrated, the bromine atom is eliminated more readily, and with prolonged nitration pure 2 : 4 : 2' : 4'-tetranitrodiphenyl ether is produced :

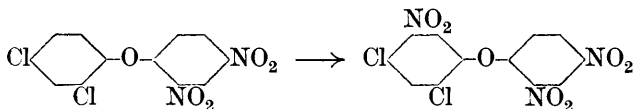


Elimination of chlorine occurs during the prolonged nitration of 4 : 4'-dichloro-2 : 2'-dinitrodiphenyl ether, but, in view of the above facts, it is surprisingly slow, and we have not succeeded in obtaining a pure specimen of the tetranitro-ether by this process. In short, the product of one replacement of chlorine by a nitro-group, namely, 4-chloro-2 : 2' : 4' : 4'-trinitrodiphenyl ether (compare the stability of the analogous bromo-compound) is relatively resistant. It is produced by the nitration of 4-chloro-2'-nitrodiphenyl ether, and, together with 4 : 4'-dichloro-2 : 2'-dinitrodiphenyl ether, by the hot nitration of 4 : 4'-dichloro-2-nitrodiphenyl ether.

There would appear to be three main factors determining such replacements of halogen by a nitro-group: (a) The factor that determines the course of ordinary aromatic substitution. In the present examples halogen and not hydrogen is eliminated. (b) The tendency of a co-valently attached halogen atom to become an ion. (c) The tendency of a halogen atom to remain in co-valent attachment to a carbon atom.

An excellent survey of the literature of atom or group elimination during substitution processes is given by de Lange (*Rec. trav. chim.*,

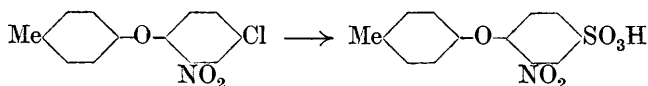
1926, 45, 19), and it is only necessary for present purposes to refer to a few general conclusions. It has usually been found that bromine is more readily eliminated than chlorine during nitration. Thus, for example, Ling (J., 1889, 55, 589) found that 2-chloro-4-bromo-6-nitrophenol was nitrated to give 2-chloro-4 : 6-dinitrophenol, and that 4-chloro-2-bromo-6-nitrophenol lost bromine in the *o*-position rather than chlorine in the *p*-, to give 4-chloro-2 : 6-dinitrophenol. That factor (*a*) is of greater importance than the nature of the halogen atom (factors *b* and *c*) would appear to be shown by the results of Hewitt and Mitchell (J., 1906, 89, 1167), who found that when diazotised *p*-nitroaniline was added to an alkaline solution of 1-chloro-, 1-bromo-, or 1-iodo- $\beta$ -naphthol, the product in each case was 1-benzeneazo- $\beta$ -naphthol. Again, it has already been shown (Parts II and III) that 2 : 4-dichloro- and 2 : 4-dibromo-2' : 4'-dinitrodiphenyl ethers readily undergo 5-nitration :



This occurs in the cold, but we have now submitted the two resulting trinitro-ethers to the action of fuming nitric acid at 100°. Although in both cases slight elimination of halogen occurs, almost the whole of the original substances may be recovered in the pure condition. It therefore seems probable that factor (*a*) is most important in these cases. In 4-chloro-4'-bromo-2- and -2'-nitrodiphenyl ether, the *para*-orienting effect of oxygen is the most powerful influence at work, whereas in 2 : 4-dichloro- and 2 : 4-dibromo-2' : 4'-dinitrodiphenyl ether this effect is more than counterbalanced by the 5-directing influence of the two halogen atoms, so that elimination of halogen does not occur. Again factor (*a*) takes control. The preferential elimination of chlorine from the chloro-bromo-ethers may be attributed to factor (*b*).

To some extent elimination reactions of the type under consideration are governed by mere mass effects in addition. For instance, bromination of 4-chloro-2 : 6-dinitrophenol under certain conditions causes replacement of a nitro-group by bromine, 4-chloro-2-bromo-6-nitrophenol being produced (Gordon, *Chem. News*, 1891, 63, 222), whilst picric acid, when gently warmed with bromine and water, gives 2-bromo-4 : 6-dinitrophenol (Armstrong, *Ber.*, 1873, 6, 650), and it is a common experience that in the chlorination of nitro-compounds at moderately high temperatures, nitrous fumes are occasionally given off, no doubt because partial elimination of the nitro-group has taken place.

A second type of elimination reaction has been observed in which a chlorine atom is replaced by the sulphonic acid group. Thus, when 4-chloro-2-nitro-4'-methyldiphenyl ether is dissolved in cold concentrated sulphuric acid, hydrogen chloride is at once evolved, and 2-nitro-4'-methyldiphenyl ether 4-sulphonic acid is formed :



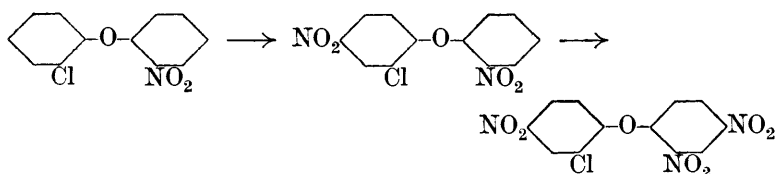
This result is unexpected, for no halogen hydride is produced by the action of cold concentrated sulphuric acid on the isomeric 4-chloro-2'-nitro-4'-methyldiphenyl ether, or on 2:4:4'-trichloro-, 2:4-dichloro-2':4'-dinitro-, or 2:4-dibromo-2':4'-dinitro-diphenyl ether.

A third type of reaction which has to be recorded is that of scission during nitration. By mild nitration, 4-chloro-2-nitro-4'-methyldiphenyl ether may be converted into 4-chloro-2:2'-dinitro-4'-methyldiphenyl ether, but, when it is dissolved in cold fuming nitric acid, the main product is 4-chloro-2:6-dinitrophenol. This phenol is also the main product formed by similarly nitrating 4-chloro-2'-nitro-4'-methyldiphenyl ether. Yet, although it is difficult to avoid concluding that in both nitrations the initial product is 4-chloro-2:2'-dinitro-4'-methyldiphenyl ether, the latter substance does not undergo scission when heated with fuming nitric acid, but suffers partial replacement of chlorine by a nitro-group.

The apparent destruction of a tolyl group during the above nitrations is interesting in view of the fact (Pauly, Gilmour, and Will, *Annalen*, 1914, **403**, 119) that 3-nitro-*p*-cresol is converted by fuming sulphuric acid into  $\beta$ -methyl- $\gamma$ -crotonolactone- $\gamma$ -acetic acid. Incidentally, Reilly, Drumm, and Barrett (J., 1927, 67) have found that di-*p*-tolyl ether also undergoes considerable scission when nitrated.

A fourth set of results concerns the scission of certain ethers by piperidine. Although 4-chloro-2'-nitro-4'-methyldiphenyl ether readily undergoes scission by piperidine, 4-chloro-2-nitro-4'-methyldiphenyl ether is somewhat resistant to this reagent. Since, in general, 2- or 4-nitrodiphenyl ethers permit of facile piperidine scission, it would appear that the chlorine atom in 4-chloro-2-nitro-4'-methyldiphenyl ether acts in opposition to the nitro-group. A similar effect may be produced by a bromine atom; *e.g.*, *o*-bromonitrobenzene readily reacts with potassium phenoxide to give 2-nitrodiphenyl ether, but 2:5-dibromonitrobenzene reacts very indifferently.

The nitration of 2-chloro-2'-nitrodiphenyl ether has been found to proceed according to the following scheme :



The constitution of the chlorodinitro-ether follows from the fact that the ether is not identical with 2-chloro-2':4'-dinitrodiphenyl ether. 2-Bromo-2'-nitrodiphenyl ether is nitrated similarly.

Bromination of 4-bromo-2-nitrodiphenyl ether takes place in the 4'-position, for the product is identical with that obtained by the mononitration of 4:4'-dibromodiphenyl ether.

#### EXPERIMENTAL.

*Preparation of Diphenyl Ethers.*—The general procedure was as follows: Potassium hydroxide (1 mol.) was treated with so much water that a clear melt was obtained on heating to about 250° (about 1/10 to 1/15 mol.). The melt was then allowed to cool until incipient crystallisation began, and at once the phenolic substance (1 mol.) was rapidly added, with shaking. Subsequent procedure depended on the nature of the halogenonitro-compound to be used: (a) Halogenomononitro-compounds such as *o*-chloronitrobenzene, 2:5-dibromonitrobenzene, etc. In such cases, the halogenonitro-compound (1 mol.) was added in one portion to the still hot phenoxide melt, the whole was well shaken, and then heated under a short air-condenser in a metal bath at 160—180° for 3—4 hours. (b) Halogenodinitro-compounds, such as 1-chloro-2:4-dinitrobenzene. The halogenodinitro-compound (1 mol.) was added gradually with vigorous shaking during about 5 minutes. As a rule, potassium halide began to separate almost immediately, and the reaction was rendered complete by an hour's heating at 100°. In all cases, the reaction product was shaken with hot dilute alkali, and the cooled mixture filtered or extracted with ether, according to the nature of the final product.

It has not been found advisable to use copper-bronze as a catalyst in any of the condensations.

4-Chloro-4'-bromo-2'-nitrodiphenyl ether, prepared from *p*-chlorophenol and 2:5-dibromonitrobenzene, was crystallised from glacial acetic acid; it then melted at 100—101°. Raiford and Colbert (*J. Amer. Chem. Soc.*, 1926, **48**, 2652) gave m. p. 100.5°.

4-Chloro-4'-bromo-2-nitrodiphenyl ether, from *p*-bromophenol and 2:5-dichloronitrobenzene, had m. p. 95°. Raiford and Colbert (*loc. cit.*) gave m. p. 93—94°.

*4-Chloro-4'-bromo-2:2'-dinitrodiphenyl Ether*.—4-Chloro-4'-bromo-2'-nitrodiphenyl ether (3 g.) was added to a cold mixture of 15 g. of nitric acid (*d* 1.5) and glacial acetic acid (15 g.). The solution was gently warmed until the solid had dissolved, and then poured into water. The precipitated solid crystallised from glacial acetic acid in very pale yellow, silky needles, m. p. 165° (0.1482 g. gave 0.1350 g. AgCl + AgBr.  $C_{12}H_6O_5N_2ClBr$  requires AgCl + AgBr, 0.1316 g.).

Similar nitration of 4-chloro-4'-bromo-2-nitrodiphenyl ether gave a product which alone or mixed with the above compound melted at 165°.

*4-Bromo-2:2':4'-trinitrodiphenyl Ether*.—(1) 4-Chloro-4'-bromo-2-nitrodiphenyl ether was added to 10 parts of nitric acid (*d* 1.5) and the resulting solution was heated at 100° for 2 hours and then cooled and poured into water. The precipitated solid crystallised from glacial acetic acid in pale yellow, prismatic needles, m. p. 154° (Found: Br, 20.1. Calc.: Br, 20.8%). Raiford and Colbert (*loc. cit.*) gave m. p. 148.5°. We have found that a specimen kept for some months melts at 148—149°. (2) Similar nitration of 4-chloro-4'-bromo-2'-nitrodiphenyl ether gave an identical product.

*4:4'-Dichloro-2:2'-dinitrodiphenyl Ether*.—A solution of 4:4'-dichloro-2-nitrodiphenyl ether in 10 parts of nitric acid (*d* 1.5) was warmed gently for 10 minutes. The cooled solution was poured into water, and the precipitate crystallised from glacial acetic acid. The dinitro-compound melted at 154° (compare Le Fèvre, Saunders, and Turner, J., 1927, 1168).

*4-Chloro-2:2':4'-trinitrodiphenyl Ether*.—(a) 4:4'-Dichloro-2-nitrodiphenyl ether was added to 10 parts of nitric acid (*d* 1.5), and the solution heated at 100° for 2 hours. The whole was cooled and poured into water, and the solid obtained crystallised from glacial acetic acid. It formed yellow prismatic needles, m. p. 155°. Raiford and Colbert (*loc. cit.*) describe the compound as forming yellowish plates, m. p. 154° (Found: Cl, 10.8. Calc.: Cl, 10.5%).

(b) 4-Chloro-2:2':4'-trinitrodiphenyl ether was also prepared by condensing *p*-chlorophenol with 1-chloro-2:4-dinitrobenzene, the product being treated with cold fuming nitric acid. The solution was gently warmed and poured into water. The precipitate, after recrystallisation, had m. p. 155° alone or when mixed with the product from (a).

(c) 4-Chloro-2'-nitrodiphenyl ether, when nitrated in a similar manner, gave a product identical with those from (a) and (b).

*Prolonged Action of Nitric Acid on 2:4-Dichloro- and 2:4-Dibromo-5:2':4'-trinitrodiphenyl Ether*.—The dichloro-ether was heated with 10 parts of nitric acid (*d* 1.5) for 2 hours at 100°. A little hydrogen chloride was slowly evolved. The solution was poured into water,

and the precipitate washed and dried. It had 90% of the weight of the original ether, and melted at 128°, alone or when mixed with the pure trinitro-ether. Similar treatment of the dibromo-ether gave 92% of unchanged ether, m. p. 139—140° alone or mixed with pure ether.

2-Chloro-2'-nitrodiphenyl ether had b. p. 345°, m. p. 47—48°. Roberts and Turner (J., 1925, 127, 1008) gave m. p. 48° (Found : Cl, 14.3. Calc. : Cl, 14.2%).

2-Chloro-2' : 4'-dinitrodiphenyl ether, prepared from *o*-chlorophenol and 1-chloro-2 : 4-dinitrobenzene, crystallised from glacial acetic acid-alcohol in cream-coloured prisms, m. p. 75—76° (Found : Cl, 12.0.  $C_{12}H_7O_5N_2Cl$  requires Cl, 12.05%).

2-Chloro-4 : 2'-dinitrodiphenyl Ether.—2-Chloro-2'-nitrodiphenyl ether was dissolved in 10 parts of nitric acid (*d* 1.4) with warming. The solution was poured into water; the precipitate obtained, after crystallising from glacial acetic acid, had m. p. 126—127° (Found : Cl, 12.0.  $C_{12}H_7O_5N_2Cl$  requires Cl, 12.05%).

2-Chloro-4 : 2' : 4'-trinitrodiphenyl Ether.—A solution of the 4 : 2'-dinitro-ether in 10 parts of nitric acid (*d* 1.5) was heated for 20 minutes at 100° and then poured into water. The resulting precipitate separated from glacial acetic acid in yellow rhombohedra, m. p. 135—136° (Found : Cl, 9.8.  $C_{12}H_6O_7N_3Cl$  requires Cl, 10.5%).

4-Bromo-2-nitrodiphenyl Ether.—A mixture of 6 g. of potassium hydroxide, 0.2 c.c. of water, 9 g. of phenol, and 28 g. of 2 : 5-dibromonitrobenzene was allowed to react for 6 hours under the usual conditions. Although potassium bromide separated, only 14 g. of 4-bromo-2-nitrodiphenyl ether were obtained, as a dark oil, b. p. 228—230°/21 mm. It was found impossible to remove a small quantity of unchanged dibromonitrobenzene (Found : Br, 28.7.  $C_{12}H_8O_3NBr$  requires Br, 27.2%).

Bromination of 4-Bromo-2-nitrodiphenyl Ether.—A solution of 29 g. of this ether and 14.8 c.c. of bromine in 135 c.c. of glacial acetic acid was heated under reflux at 100° until hydrogen bromide was no longer evolved. The solution was poured into water, and the precipitate filtered off. It melted at 94° after crystallisation from glacial acetic acid, and was identical with a specimen of 4 : 4'-dibromo-2-nitrodiphenyl ether obtained by the mononitration of 4 : 4'-dibromodiphenyl ether (Le Fèvre, Saunders, and Turner, *loc. cit.*).

Prolonged Nitration of 4-Bromo-2-nitrodiphenyl Ether.—The ether was dissolved in 10 parts of nitric acid (*d* 1.5), and a clear solution obtained by warming. On pouring the solution into water, and crystallising the precipitate from glacial acetic acid, a product was obtained, m. p. 180—182°. A second similar nitration raised the m. p.

to 191—192°, a third to 195—196°, and a fourth to 196°. The final product did not depress the m. p. of 2 : 4 : 2' : 4'-tetranitrodiphenyl ether. In another experiment, 5 g. of 4-bromo-2-nitrodiphenyl ether were heated with 25 g. of nitric acid (*d* 1.5) for 2 hours at 100°. The gases evolved were absorbed in alkali, and the alkaline solution analysed. It was found that 80% of the bromine originally present had been given off. Pure tetranitrodiphenyl ether was obtained from the nitric acid solution.

*Bromination of 2-Nitrodiphenyl Ether.*—A solution of 20 g. of the ether and 16 g. of bromine in 40 g. of glacial acetic acid was heated under reflux at 100° until the colour of the bromine had disappeared. The solution was poured into alcohol. The solid that separated on standing was crystallised from glacial acetic acid, and then had m. p. 72°. Raiford and Colbert (*loc. cit.*) obtained 4-bromo-2'-nitrodiphenyl ether by a condensation process, and gave m. p. 71°.

*2-Bromo-2' : 4'-dinitrodiphenyl ether*, from *o*-bromophenol and 1-chloro-2 : 4-dinitrobenzene, separated from glacial acetic acid in pale yellow leaflets, m. p. 88—89° (Found : Br, 23.4.  $C_{12}H_7O_5N_2Br$  requires Br, 23.6%).

*Mononitration of 2-Bromo-2' : 4'-dinitrodiphenyl Ether.*—The ether was added to a mixture of 5 parts of glacial acetic acid and 5 parts of nitric acid (*d* 1.5). A clear solution was produced by warming, and after 20 minutes it was poured into water, and the precipitate collected. The *2-bromo-4 : 2' : 4'-trinitrodiphenyl ether* crystallised from glacial acetic acid in small yellow needles, m. p. 127—128° (Found : Br, 21.6.  $C_{12}H_6O_7N_3Br$  requires Br, 20.8%).

*2-Bromo-2'-nitrodiphenyl ether*, from *o*-bromophenol and *o*-chloronitrobenzene, had b. p. 251°/27 mm. It crystallised from glacial acetic acid-alcohol in yellow prisms, m. p. 49—50° (Found : Br, 27.6.  $C_{12}H_8O_3NBr$  requires Br, 27.2%).

*2-Bromo-4 : 2'-dinitrodiphenyl Ether.*—2-Bromo-2'-nitrodiphenyl ether (3 g.) was added to a mixture of 15 g. of glacial acetic acid and 15 g. of nitric acid (*d* 1.5). The whole was warmed until solution was complete, left for 20 minutes, and poured into water. The product separated from glacial acetic acid in rectangular crystals, m. p. 128° (Found : Br, 24.1.  $C_{12}H_7O_5N_2Br$  requires Br, 23.6%).

*Nitration of 4-Bromo-2' : 4'-dinitrodiphenyl Ether.*—A solution of the ether in 10 parts of nitric acid (*d* 1.5) was warmed for a few minutes and poured into water, and the precipitate crystallised from glacial acetic acid; 4-bromo-2 : 2' : 4'-trinitrodiphenyl ether was then obtained, m. p. 154°.

*4-Chloro-2-nitro-4'-methyldiphenyl ether*, prepared from *p*-cresol and 2 : 5-dichloronitrobenzene, crystallised from alcohol in pale brownish plates, m. p. 99° (Found : Cl, 13.8.  $C_{13}H_{10}O_3NCl$  requires Cl, 13.6%).



An attempt was made to nitrate the ether with concentrated sulphuric acid and potassium nitrate. When the ether was dissolved in the acid, hydrogen chloride was evolved, and on warming at 100° a clear solution was obtained, which on cooling and dilution gave white silky needles of 2-nitro-4'-methyldiphenyl ether 4-sulphonic acid, m. p. 129—130°. Crystallisation from light petroleum did not affect this m. p. (Found: S, 11.0.  $C_{13}H_{11}O_6NS$  requires S, 10.4%).

*Action of Piperidine on 4-Chloro-2-nitro-4'-methyldiphenyl Ether.*—The ether was heated for an hour at 100° with its own weight of piperidine. When the solution was made alkaline, a mixture of 4-chloro-2-nitrophenylpiperidine and unchanged ether was precipitated. The mixture was extracted with 50% sulphuric acid; from the acid extract, on treatment with alkali, the pure chloronitrophenylpiperidine was precipitated. In a second experiment, a solution of the ether in excess of piperidine was boiled for several hours, the bulk of the piperidine distilled off, and alkali added; the chloronitrophenylpiperidine which then separated was removed. The filtrate was extracted with benzene until it was colourless, traces of benzene were removed by boiling, and *p*-toluenesulphonyl chloride was added to the heated alkaline solution. After some time, *p*-tolyl *p*-toluenesulphonate separated; after crystallisation from acetic acid-alcohol, it had m. p. 68°, alone or when mixed with an authentic specimen.

*4-Chloro-2 : 2'-dinitro-4'-methyldiphenyl Ether.*—4-Chloro-2-nitro-4'-methyldiphenyl ether was dissolved in an ice-cold mixture of 5 parts of glacial acetic acid and 5 parts of nitric acid (*d* 1.5). The solution was heated at 100° for an hour, cooled, and poured into water. The precipitate crystallised from acetic acid and alcohol in very pale yellow plates, m. p. 115° (Found: Cl, 12.1.  $C_{13}H_9O_5N_2Cl$  requires Cl, 11.5%).

When a solution of the dinitro-ether in nitric acid (*d* 1.5) was heated at 100° for an hour, hydrogen chloride was slowly evolved. When the solution was poured into water, a solid was obtained, m. p. 146—149°. This could not be separated into definite fractions, but was probably a mixture of unchanged material with 2 : 4 : 2'-trinitro-4'-methyldiphenyl ether.

*4-Chloro-2'-nitro-4'-methyldiphenyl ether*, prepared from 4-chloro-3-nitrotoluene and *p*-chlorophenol, crystallised from alcohol in very pale yellow, irregular, rectangular plates, m. p. 52° (Found: Cl, 13.6.  $C_{13}H_{10}O_3NCl$  requires Cl, 13.6%).

When a solution of the ether in 5 parts of glacial acetic acid and 5 parts of nitric acid (*d* 1.5) was heated for an hour at 100°, 4-chloro-2 : 2'-dinitro-4'-methyldiphenyl ether was obtained, identical with the product of nitrating the isomeric 2-nitro-ether.

*Action of Piperidine on 4-Chloro-2'-nitro-4'-methyldiphenyl Ether.*—A solution of the ether in its own weight of piperidine was heated for an hour at 100°. When excess of alkali was added to the cooled solution, 2-nitro-4-methylphenylpiperidine separated, m. p. 69°.

*Nitrative Scission of 4-Chloro-2-nitro-4'-methyl- and of 4-Chloro-2'-nitro-4'-methyl-diphenyl Ether.*—The ethers were dissolved in 10 parts of nitric acid (*d* 1.5) at 0°. After 20 minutes, the solutions were poured into water, and the yellow precipitates collected. After crystallisation they both melted at 74—75°, and were pure specimens of 4-chloro-2 : 6-dinitrophenol.

All the m. p.'s given are corrected.

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