XII.—*Substituted Diaryl Ethers. Part I. Di*-p-*tolyl Ether.*

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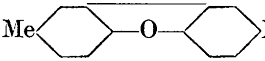
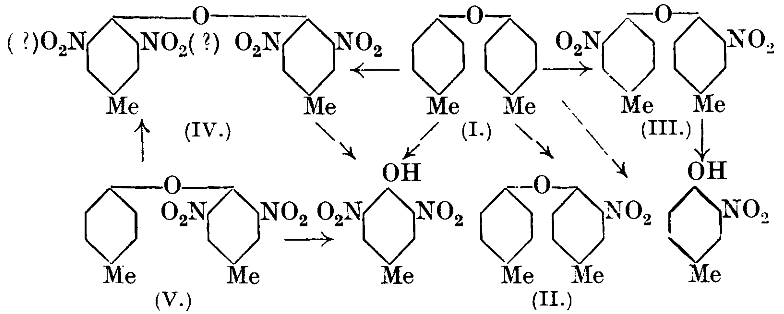
WHILST the mixed ethers such as anisole and phenetole have been extensively studied, the substituted diaryl ethers derived from alkylphenols have received scarcely any attention, although from the newer aspects of chemical theory their reactions and the orientation of their derivatives are of interest.

Di-*p*-tolyl ether was selected as typical of the class of substances indicated. The only two references to this compound in the literature are the following : Busch (*Ber.*, 1884, **17**, 2638) claimed to have prepared ditolyl ether by heating *p*-cresol with zinc chloride to 300° and gave the melting point as 165°, whilst Gladstone and Tribe (J., 1882, **41**, 9), by distilling aluminium *p*-tolyloxide, isolated, in small amounts, a substance of m. p. 50° which, from analogy with diphenyl ether, they called *p*-cresyl ether. In the present work, di-*p*-tolyl ether (I) was prepared in very good yield from *p*-cresol and *p*-bromotoluene, and the work of Gladstone and Tribe confirmed. Sabatier and Mailhe (*Compt. rend.*, 1910, **151**, 494), by the catalytic dehydration of *p*-cresol with thoria at 470°, obtained a compound similar to that of Busch to which they assigned the constitution  *i.e.*, di-*p*-tolylene ether. The present work supports the views of Sabatier and Mailhe. It would appear, therefore, that the only authentic reference in the literature to di-*p*-tolyl ether is that of Gladstone and Tribe (*loc. cit.*).

Di-*p*-tolyl ether behaves normally on oxidation, forming an ether acid which on distillation with soda-lime gives phenol and diphenyl ether.

Di-*p*-tolyl ether condenses with acetyl and benzoyl chlorides and phthalic anhydride in the presence of aluminium chloride to give monoketonic and not diketonic derivatives as might be expected. These develop characteristic colours with sulphuric acid, accompanied by fluorescence in the case of the last two compounds. These compounds behave abnormally with phenylhydrazine and hydroxylamine and will form the subject of a further communication.

The behaviour of di-*p*-tolyl ether on nitration is in many ways different from that of diphenyl ether and hitherto no nitration products of this substance have been described. Diphenyl ether nitrates smoothly to nitrodiphenyl ethers with very little decomposition to nitrophenols (Ryan and Drumm, *Proc. Roy. Soc. Dublin*, 1924, **17**, 313). Di-*p*-tolyl ether, on the other hand, under the different conditions of nitration described below, gave mono- and dinitro-*p*-cresols as the main product, the nature of the by-product, consisting of small quantities of various nitrodi-*p*-tolyl ethers, depending on the experimental conditions. Amongst the new nitro-products isolated and identified by synthesis were 2-*nitrodi*-p-*tolyl ether* (II), 2 : 2′-*dinitrodi*-p-*tolyl ether* (III), and a tetranitro-compound which is probably 2 : 6 : 2′ : 6′-*tetranitrodi*-p-*tolyl ether* (IV). 2 : 6-Dinitrodi-*p*-tolyl ether (V) was obtained by the condensation of *p*-cresol with 3 : 5-dinitro-*p*-bromotoluene. In addition, 3-nitro- and 3 : 5-dinitro-*p*-cresols were isolated in certain cases. The actual scheme of nitration may be indicated as follows:



2-Nitrodi-*p*-tolyl ether is readily reduced to 2-aminodi-*p*-tolyl ether, and the latter diazotises and gives azo-dyes. These substances, together with the amino-compounds from the other nitro-derivatives of di-*p*-tolyl ether, are being further examined.

EXPERIMENTAL.

*Di-*p*-tolyl Ether.*—In the preliminary experiments, *p*-cresol, *p*-bromotoluene, powdered potassium hydroxide, and a trace of copper bronze were heated at 200—250° for 3 to 4 hours, the procedure used in the case of diphenyl ether being followed. The product, on distillation in steam, gave much unchanged bromotoluene, followed by a small quantity of oil, which solidified (yield, 20—25%). By altering the method as follows, the yield was increased to 87%. Potassium *p*-tolyloxide (dried at 150° in a vacuum) (35 g.), *p*-bromotoluene (commercial *p*-bromotoluene purified by standing in contact with sulphuric acid to remove traces of isomerides; m. p. of purified product, 28·5°) (41 g.), copper bronze (Naturkupfer C; washed with ether to remove oily impurities) (0·3 g.), and *p*-cresol (20 g.) (solvent) were slowly heated in a dried flask fitted with an air condenser. Reaction commenced at 200°, with separation of potassium bromide. The heating was continued for 2 hours at 230—240°. The dark product was made alkaline with aqueous potassium hydroxide and distilled in steam. Unchanged bromotoluene passed over, followed by an oil which quickly solidified; this crystallised from ethyl alcohol in colourless prisms, m. p. 50° (Found: C, 84·5; H, 7·3; *M*, cryoscopic in naphthalene, 191. Calc. for $C_{14}H_{14}O$: C, 84·8; H, 7·1%; *M*, 198).

Di-*p*-tolyl ether is very soluble in acetone, ether, or benzene, readily soluble in hot alcohol or warm glacial acetic acid, and insoluble in water. It has a pleasant odour, similar to, but fainter than, that of diphenyl ether.

Di-p-*tolylene Oxide.*—*p*-Cresol (25 g.) and litharge (50 g.) were intimately mixed and heated (oil-bath) at 110—120° for 10 hours. The product, after cooling, was powdered and distilled. At first, unchanged *p*-cresol passed over. The fraction, b. p. above 300°, set to a crystalline solid and separated from boiling light petroleum (b. p. 70—100°) in glistening, pearly plates, m. p. 165°. Prepared in a manner analogous to that of diphenylene oxide from phenol, this substance is obviously di-*p*-tolylene oxide. Its further investigation is in progress.

Oxidation of Di-p-*tolyl Ether.*—A solution of chromic acid in glacial acetic acid was gradually added, with stirring, to an acetic acid solution of di-*p*-tolyl ether at 40° until oxidation was apparently completed. The gelatinous precipitate that formed on dilution with water was separated from the liquid by the streamline filter, washed with water, and repeatedly dissolved in aqueous ammonia and precipitated with hydrochloric acid. The collected solid was converted into the silver salt in the usual manner (Found : Ag, 45·4. $C_{14}H_8O_5Ag_2$ requires Ag, 45·7%). Di-*p*-carboxydiphenyl ether is a white, amorphous solid which does not melt. It is easily soluble in alkalis and is precipitated therefrom by acids. The silver salt, sparingly soluble in water, is readily soluble in ammonia.

An intimate mixture of the above acid (1 part) with dry soda-lime (4 parts) was strongly heated in a retort. The small amount of oil, smelling strongly of phenol, that distilled was extracted with ether, and the ethereal layer well washed with aqueous sodium hydroxide to remove phenolic substances. On evaporation of the ether an oil remained which gradually solidified in a freezing mixture. This substance, m. p. 28°, was identified as diphenyl ether by the method of mixed melting point.

Action of Nitric Acid on Di-p-*tolyl Ether under Various Conditions.*—*In acetic acid solution.* To a well-cooled solution of nitric acid (12 c.c.; *d* 1·5) in glacial acetic acid (50 c.c.), di-*p*-tolyl ether (5 g.) was slowly added, with constant stirring. The temperature was allowed to rise slowly to 30°, and the red solution was then poured on to crushed ice. The precipitated yellow oil in ethereal solution was washed with dilute potassium hydroxide solution and with water and dried. The residual oil, cooled in a freezing mixture, set to a crystalline solid (2 g.) which was dried on a porous tile and crystallised from ethyl alcohol, colourless prisms, m. p. 50°, being obtained (Found: N, 5·6. $C_{14}H_{13}O_3N$ requires N, 5·7%). This substance (A) is therefore one of the mononitro-derivatives of di-*p*-tolyl ether and its constitution was determined later by direct synthesis. The dark red potash extract was acidified with dilute hydrochloric acid, and the yellow precipitate collected and distilled in steam. From the distillate a yellow solid separated (1 g.). This, after crystallisation from dilute aqueous ethyl alcohol, melted at 33° and showed no depression of melting point when mixed with 3-nitro-*p*-cresol. From the residue after distillation was isolated a crystalline substance (2 g.), m. p. 85°, which was identified as 3 : 5-dinitro-*p*-cresol by the mixed melting-point method.

Direct nitration. Cold nitric acid of concentrations up to *d* 1·4 is without appreciable action on di-*p*-tolyl ether. On heating the mixture a very vigorous reaction, which was difficult to control, commenced at 70°, with copious evolution of nitrous fumes. With nitric acid of a higher density, under the following conditions, a dinitrodi-*p*-tolyl ether was isolated. Di-*p*-tolyl ether (5·5 g.) was added during 1 hour to nitric acid (10 c.c.; *d* 1·5) at $-10°$ to $-5°$. In the absence of very efficient external cooling the reaction tends to become rather violent. The resulting dark red solution was poured on to crushed ice. The precipitated oily solid was washed in ethereal solution with dilute aqueous sodium hydroxide, until this showed no coloration, then with water, and dried. The residue from the ethereal solution was re-extracted with light petroleum (b. p. 70—100°). From the latter, a yellow substance (B) (1 g.) slowly separated which crystallised from alcohol in slender plates, m. p. 126° (Found : N, 9·9. $C_{14}H_{12}O_5N_2$ requires N, 9·7%). The constitution of this dinitrodi-*p*-tolyl ether was determined later by direct synthesis. From the alkaline extract 3 : 5-dinitro-*p*-cresol (4 g.) was isolated in the usual way.

With a mixture of sulphuric and nitric acids. Finely powdered di-*p*-tolyl ether (5 g.) was added slowly to a mixture of 98% sulphuric acid (25 g.) and nitric acid (25 g.; *d* 1·5) at $-10°$ with thorough stirring and cooling in a freezing mixture. The resulting highly-coloured solution was poured on to crushed ice. The precipitated light brown oil was extracted with ether, and the ether extract freed from nitrocresols in the usual way. From the ether was obtained a yellow solid (1 g.) which was separated into two fractions by means of boiling light petroleum (b. p. 70—100°); the soluble part consisted of a dinitrodi-*p*-tolyl ether identical with that obtained by direct nitration; the insoluble portion (C) separated from boiling ethyl alcohol in colourless, rectangular plates, m. p. 246° (Found : N, 14·6. $C_{14}H_{10}O_9N_4$ requires N, 14·8%). This analysis agrees with that for a tetranitrodi-*p*-tolyl ether and the orientation of two of the nitro-groups has been ascertained as described later.

*Action of Gaseous Nitrogen Peroxide on Di-*p*-tolyl Ether.*—Dry liquid nitrogen peroxide, prepared from dry lead nitrate, and di-*p*-

tolyl ether were placed in two shallow containers left side by side under a bell-jar. Initially the absorption of the nitrogen peroxide was rapid and it needed renewal from time to time. The tolyl ether lost its crystalline form and after a week appeared as an intumescent, brown syrup. The method of working up employed was the same as that for the products of direct nitration. From it was isolated, in addition to 3 : 5-dinitro-*p*-cresol, a dinitrodi-*p*-tolyl ether (1·2 g.), m. p. 126°, identical in every respect with the dinitro-product obtained by direct nitration.

Syntheses of Nitrodi-p-*tolyl Ethers.*—2-*Nitrodi*-p-*tolyl ether.* Potassium *p*-tolyloxide (7 g., dried at 150° in a vacuum), 4-bromo-3-nitrotoluene (9 g.), copper bronze (0·1 g.), and *p*-cresol (20 g.) (solvent) were slowly heated (oil-bath), with stirring, in a flask fitted with an air condenser. At 160°, reaction set in with separation of potassium bromide. Heating was continued for 3 hours at 210—220°. The dark product was extracted with ether and the ethereal layer was washed with dilute sodium hydroxide solution until the latter was colourless, and then with water. On fractionation of the dried ethereal extract under diminished pressure, a pale yellow oil (3 g.) distilled at 220°/15 mm. The oil solidified to a mass of light yellow crystals, m. p. 46—48°, and separated from alcohol in colourless prisms, m. p. 50° (Found : N, 5·6. $C_{14}H_{13}O_3N$ requires N, 5·7%). 2-Nitrodi-*p*-tolyl ether is freely soluble in benzene, ether, or chloroform, and less soluble in light petroleum (b. p. 70—100°) or ethyl alcohol. It is not hydrolysed by boiling with potassium hydroxide solution (20%), as evidenced by the negligible amount of colour developed in solution after 10 hours. The nitro-group was reduced by tin and hydrochloric acid; the resulting amino-compound diazotised and then coupled with alkaline β-naphthol to give a scarlet azo-dye. 2-Nitrodi-*p*-tolyl ether agrees in every respect, including mixed melting point, with the mononitro-derivative (A) obtained by nitration, in acetic acid solution, of di-*p*-tolyl ether.

2 : 2′-*Dinitrodi*-p-*tolyl ether.* Potassium 3-nitro-*p*-tolyloxide (6 g., dried at 100° in a vacuum), 4-bromo-3-nitrotoluene (6 g., prepared by diazotisation in dilute sulphuric acid of 3-nitro-*p*-toluidine with subsequent conversion into the diazonium perbromide and decomposition of this with a small amount of absolute ethyl alcohol), 3-nitro-*p*-cresol (15 g.) (solvent) and copper bronze (0·2 g.) were heated (oil-bath), with stirring, very slowly to 190°, and then, after 1 hour, to 210° during 3 hours. The highly coloured product was powdered and repeatedly extracted with ether, and the ethereal layer was freed from nitrocresol in the usual way. The residue left after removal of the ether was extracted with boiling light petroleum

(b. p. 70—100°), from which a yellow, crystalline solid slowly separated. This solid crystallised from ethyl alcohol in pale yellow, slender laminæ, m. p. 126° (Found: N, 9·9. $C_{14}H_{12}O_5N_2$ requires N, 9·7%).

2 : 2′-Dinitrodi-*p*-tolyl ether is colourless when pure, but gradually assumes a yellow colour in contact with air. It is very soluble in ether or benzene and readily soluble in hot light petroleum (b. p. 70—100°) or hot ethyl alcohol. It is slowly hydrolysed by boiling potassium hydroxide solution (20%), more readily by alcoholic potassium hydroxide, with formation of 3-nitro-*p*-cresol. It is identical with the dinitro-derivative (B) obtained by direct nitration of di-*p*-tolyl ether.

2 : 6-*Dinitrodi*-p-*tolyl ether*. Potassium *p*-tolyloxide (6 g.) and 3 : 5-dinitro-*p*-bromotoluene (prepared by the method of Jackson and Ittner, *J. Amer. Chem. Soc.*, 1897, **19**, 7) (7·5 g.) were heated in alcoholic solution on the steam-bath for 4 hours. The solution became orange-coloured and potassium bromide separated almost immediately. The solution was filtered hot and, on cooling, deposited faintly yellow crystals, m. p. 98—100°. The pure substance was obtained from alcohol in colourless, slender prisms, m. p. 107° (Found: N, 9·9. $C_{14}H_{12}O_5N_2$ requires N, 9·7%).

2 : 6-Dinitrodi-*p*-tolyl ether is easily soluble in ether, chloroform, or acetone and sparingly soluble in cold ethyl alcohol or cold light petroleum. It is readily hydrolysed by boiling alcoholic potassium hydroxide with formation of *p*-cresol and 3 : 5-dinitro-*p*-cresol. In contact with air, it gradually assumes a yellow colour.

Nitration of 2 : 6-*Dinitrodi*-p-*tolyl Ether*.—To nitric acid (12 c.c.; *d* 1·5) was slowly added 2 : 6-dinitrodi-*p*-tolyl ether (2·6 g.), the temperature being maintained at —5°. The solution was then poured on to ice, and the yellow precipitate freed from small amounts of nitrocresols as before. The residue crystallised from glacial acetic acid in colourless plates, m. p. 246° (Found: N, 14·6. $C_{14}H_{10}O_9N_4$ requires N, 14·8%). The tetranitrodi-*p*-tolyl ether is freely soluble in acetone, much less soluble in ether, chloroform, or benzene, and practically insoluble in cold glacial acetic acid or light petroleum. It is readily hydrolysed by hot alcoholic potassium hydroxide with formation of 3 : 5-dinitro-*p*-cresol. It agrees in melting point and other properties with the tetranitro-compound (C) obtained by the nitration of di-*p*-tolyl ether in a mixture of nitric and sulphuric acids.

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