240. *The Relative Directive Powers of Groups of the Forms* RO *and* RR′N *in Aromatic Substitution. Part X. The Nitration of* 4-tert.-*Butoxyanisole and* 4-iso*Propoxyanisole.*

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In Parts III (Robinson and Smith, J., 1926, 392), VIII (Clarke, Robinson, and Smith, J., 1927, 2647), and IX (Smith, J., 1931, 251) the relative directive powers of alkoxy-groups in the quinol series were shown to be in the order $C_{16}H_{33}O$ (cetyloxy) $>$ *n*-BuO $>$ Pr$^{\alpha}$O $>$ EtO $>$ MeO. The values of the relative directive powers of the *tert.*-butoxy- and the *iso*propoxy-group have now been determined and found to be in accord with the theoretical principles discussed in Part IV (Allan, Oxford, Robinson, and Smith, J., 1926, 401), the successive replacement of hydrogen atoms in the ethoxy-group by methyl groups being accompanied by successive large increases of directive power. For the purpose of comparison, these values are shown below, together with those of the other alkoxy-groups of the series :

MeO	100	Pr$^{\beta}$O	229	Bu$^{\gamma}$O	328
EtO	164	*n*-BuO	186	$C_{16}H_{33}O$	212
Pr$^{\alpha}$O	180				

Since the products of the nitration of 4-tert.-*butoxy*- and 4-iso*propoxy-anisole* could not be induced to crystallise even at — 20°, their analysis was carried out by a chemical method in preference to the thermo-analytical method used in the previous investigations. The method chosen was suggested by the observation that 2 : 6-dinitro-4-methoxyphenol is formed in small amount during the nitration of 4-*tert.*-butoxyanisole, presumably by further nitration of 2-nitro-4-methoxyphenol resulting from ‘ acid ’ hydrolysis of the 3-nitro-4-*tert.*-butoxyanisole in the mixture of nitro-isomerides. It seemed probable that conditions might be found under which the *tert.*-butyl group in each of the nitro-isomerides would be removed, whilst the methyl group would remain unaffected. The resulting mixture of isomeric nitro-4-methoxyphenols could then be separated owing to their great differences in solubility and steam-volatility. This expectation was realised, complete hydrolysis in the desired way being rapidly effected by concentrated hydrochloric acid in glacial acetic acid at room temperature. In an analogous manner the products of the nitration of 4-*iso*propoxyanisole were found to undergo hydrolysis by the same reagents at 100°. There were indications that under these conditions hydrolysis of the methoxy-group in the *o*-position to the nitro-group took place to a slight extent, but this does not invalidate the calculation of the relative directive power based on the yield of 2-nitro-4-methoxyphenol. Although the values of the relative directive powers found in this way cannot be regarded as having the same degree of accuracy as those previously determined by the thermo-analytical method, they are sufficiently accurate to indicate unmistakably the positions of the *tert.*-butoxy- and the *iso*propoxy-group relative to one another and to the other alkoxy-groups of the series.

EXPERIMENTAL.

The glacial acetic acid used was purified by repeated crystallisation and had m. p. 16·5°. The propionic acid was a redistilled fraction, b. p. 136·5—138·0°/756 mm. The nitric acid had *d* 1·42 and was colourless.

4-tert.-*Butoxyanisole*.—This substance is of interest because no *tert.*-butyl ether of a phenolic compound has hitherto been described. Its preparation in good yield was difficult owing to the ease with which the *tert.*-butyl halides give *iso*butylene in the presence of alkalis. The usual methods for the preparation of aryl ethers were unsatisfactory, and methods involving the use of, *e.g.*, dimethylamine and pyridine, by which certain aliphatic *tert.*-butyl ethers have been prepared, gave negative results. An attempt to prepare the substance by the method of Ullmann from *p*-bromoanisole was also unsuccessful. Eventually, the following method was adopted, by which the substance was obtained in 20% yield calculated on the quinol monomethyl ether employed. A mixture of the pure ether (39·6 g.), prepared as described in Part III (*loc. cit.*), *tert.*-butyl bromide (46·0 g.), potassium carbonate (49·0 g.), and acetone (50 c.c.) was refluxed for 7 hours in an apparatus provided with a series of wash-bottles containing hydrobromic acid for absorption of the *iso*butylene evolved. The acetone was removed on the water-bath, and the residue after the addition of water was extracted with ether. Unchanged quinol monomethyl ether was extracted from the ethereal solution by shaking with potash. The ethereal solution after being dried gave on distillation 11·5 g. of a colourless oil, b. p. 112°/10 mm., 220°/737 mm. (Found: C, 73·4; H, 9·0. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·9%).

Nitration of 4-tert.-*Butoxyanisole*.—4-*tert.*-Butoxyanisole (5·334 g.) was dissolved in 12·6 c.c. of a mixture of propionic acid (20 c.c.) and acetic acid (80 c.c.).* To this solution, cooled to − 10° and stirred mechanically, a solution of nitric acid (2·67 g.; 1 mol.) in the same mixed solvent (6·3 c.c.) was added during 2 hours through a fine capillary tube. When about one-third of the nitric acid had been introduced, the yellow colour of the solution suddenly gave place to a reddish tint, and the temperature rose rapidly from − 10° to + 5°; within a few minutes it fell to − 10°, at which value it was maintained during the rest of the nitration. After the whole of the nitric acid had been added, stirring was continued for 10 minutes, and then a further quantity of the acid (0·5 mol.) was introduced under the same conditions. The temperature was finally allowed to rise to 0° and maintained at this value for 10 minutes while stirring was continued. Ice-water (200 c.c.) was added, and the mixture extracted thrice with light petroleum (b. p. 40—60°; altogether 120 c.c.). A small quantity of yellow needle-shaped crystals, having a greenish tinge when observed under the microscope, separated during the extraction. These were filtered off, washed once with light petroleum, dried, and weighed (0·067 g.). After one crystallisation from light petroleum (b. p. 80—100°) they had m. p. 100—101°, and were identified as 2 : 6-dinitro-4-methoxyphenol (Found: C, 39·6; H, 2·8; N, 13·3. Calc. for $C_7H_6O_6N_2$: C, 39·3; H, 2·8; N, 13·1%). Weselsky and Benedikt (*Monatsh.*, 1881, **2**, 370) give m. p. 102°.

The light petroleum extract in the filtrate was separated and washed successively with 1% potassium hydroxide and water until the potash extracts were colourless. A further quantity (0·241 g.) of slightly impure 2 : 6-dinitro-4-methoxyphenol (m. p. 100° after one crystallisation from light petroleum) was obtained by acidification of the potash extracts. The light petroleum was removed by drawing through the solution a slow stream of dry filtered air at 50—60° and finally by heating in a vacuum at 100° to constant weight (5·973 g.). Yield 89·6% (Found: N, 6·3. $C_{11}H_{15}O_4N$ requires N, 6·2%).

Hydrolysis of the mixture of isomeric nitro-4-tert.-*butoxyanisoles*. Preliminary experiments had indicated that, under the conditions about to be described, hydrolysis is complete in about 1 hour, and further, that 2-nitro-4-methoxyphenol (constituting about 70% of the mixture) is readily volatile in steam and sparingly soluble in water, whereas the 3-nitro-compound is practically non-volatile in steam and about 25 times as soluble in water as its isomeride. Accordingly, the mixture of nitrobutoxyanisoles (5·667 g.) was shaken at 16° with 34 c.c. each of concentrated hydrochloric acid and glacial acetic acid; orange-red crystals of 2-nitro-4-methoxyphenol separated almost immediately, but the mixture was left for 3 hours, and was then diluted with water to 500 c.c. and stirred mechanically for 2 hours. The crystals of 2-nitro-4-methoxyphenol were filtered off, washed with small quantities of water, and dried to constant weight (2·911 g.); they were quite pure and had m. p. 79—80°, unchanged by admixture

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* Dr. J. C. Smith, who suggested the use of a mixture of these acids for low-temperature nitrations, has informed the author that the proportion of nitro-isomerides formed in the low-temperature nitration of 4-ethoxyanisole is not affected by the addition of propionic acid to the acetic acid.

with an authentic specimen. The filtrate, containing the 3-nitro-4-methoxyphenol and a little of the 2-nitro-isomeride, was neutralised with potassium carbonate, and extracted with ether until the extracts were practically colourless. The ether was removed, the residue steam-distilled, and the 2-nitro-4-methoxyphenol in the distillate taken up with ether. The ethereal solution yielded 0·232 g. of impure crystals, from which 0·069 g. of the pure substance was obtained on crystallisation from light petroleum. A further small quantity (0·035 g.) of less pure material (m. p. 70—74°) separated on concentrating the mother-liquor. The residue in the steam-distillation flask on extraction with ether gave crystals of the yellow 3-nitro-4-methoxyphenol; these were triturated with a few c.c. of light petroleum, filtered off, dried to constant weight (1·083 g.) in a vacuum, and then had m. p. 97—98°, unchanged by admixture with an authentic specimen.

Calculation of the value of the directive power of the tert.*-butoxy-group relative to the methoxy-group* (100). 5·667 G. of mixed nitro-4-*tert.*-butoxyanisoles yielded: 2-Nitro-4-methoxyphenol, $> 2·911 + 0·069 < 2·911 + 0·232$ g.; mean 3·061 g. = 4·075 g. 3-nitro-4-*tert.*-butoxyanisole. 3-Nitro-4-methoxyphenol, 1·083 g. = 1·442 g. 2-nitro-4-*tert.*-butoxyanisole. The total weight of nitro-4-*tert.*-butoxyanisoles thus accounted for is 5·517 g., *i.e.*, 97·3%.

The following calculation of the value of the directive power is based on the very probable assumption that under the conditions of the nitration the yield of nitro-4-*tert.*-butoxyanisoles would have been 100% if there had been no hydrolysis.

Since 2 : 6-dinitro-4-methoxyphenol was the only isolable by-product, it would appear that the *tert.*-butoxy-group in the *o*-position to the nitro-group alone suffered hydrolysis. This necessitates the addition in the calculation of $5·667 \times (100 - 89·6)/100 = 0·658$ g. to the weight of 3-nitro-4-*tert.*-butoxyanisole, the directive power x then being given by the equation $x/100 = (4·075 + 0·658)/1·442$, whence $x = 328$. Even if the calculation is based on the amounts of the two nitro-4-methoxyphenols actually isolated, the value of x is as high as 283.

4-iso*Propoxyanisole*.—This *compound* was prepared by refluxing a mixture of pure quinol monomethyl ether (15·6 g.), potash (6·8 g.), *iso*propyl iodide (20·4 g.), and methyl alcohol (100 c.c.) for 6 hours, a further quantity of *iso*propyl iodide (10 g.) being added after 3 hours. The reaction mixture gave, by the usual procedure, 11·6 g. of a colourless oil, b. p. 103°/12 mm., 223°/751·5 mm. (Found: C, 72·6; H, 8·5. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·4%), representing a yield of 54% calculated on the quinol monomethyl ether employed.

Nitration of 4-iso*Propoxyanisole*.—The anisole (7·081 g.) was dissolved in a mixture of glacial acetic acid (15 c.c.) and propionic acid (2·5 c.c.) and the solution cooled to 5°. Nitric acid (3·85 g.; 1 mol.) in acetic acid (7·5 c.c.) was added as before, and soon after nitration began, the mixture could be cooled to 0° without causing crystallisation of the solvent. The colour of the solution remained yellow throughout. After the whole of the nitric acid had been added, stirring was continued for 10 minutes, and then a further quantity of the acid (0·5 mol.) was added under the same conditions. The rest of the procedure was precisely similar to that employed in the nitration of 4-*tert.*-butoxyanisole. Yield of nitro-4-*iso*propoxyanisoles: 8·909 g., *i.e.*, 99·0% (Found: N, 6·6. $C_{10}H_{13}O_4N$ requires N, 6·6%).

Hydrolysis of the mixture of isomeric nitro-4-iso*propoxyanisoles*. The mixture (8·730 g.) was heated on the water-bath with concentrated hydrochloric acid (53 c.c.) and glacial acetic acid (80 c.c.) for 10 hours, preliminary experiments having indicated that hydrolysis under these conditions is practically completed in less than 6 hours. Crystals of 2-nitro-4-methoxyphenol separated on allowing the solution to cool and stand over-night. This isomeride, separated as before but with dilution to 700 c.c., weighed 4·523 g. and was quite pure, m. p. and mixed m. p. 78—79°. A further quantity (0·435 g.) of impure 2-nitro-4-methoxyphenol, extracted from the distillate in the steam-distillation, gave 0·252 g. of pure substance on crystallisation from light petroleum. 3-Nitro-4-methoxyphenol could not be separated as quantitatively as in the preceding experiment, probably owing to slight contamination with products resulting from the partial hydrolysis of the methoxy-group ortho to the nitro-group.

Calculation of the value of the directive power of the iso*propoxy-group relative to the methoxy-group* (100). 8·730 G. of mixed nitro-4-*iso*propoxyanisoles afforded $> 4·523 + 0·252$ and $< 4·523 + 0·435$ g. of 2-nitro-4-methoxyphenol; mean 4·866 g. = 6·074 g. of 3-nitro-4-*iso*propoxyanisole, whence $x/100 = 6·074/(8·730 - 6·074)$ or $x = 229$.

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