

CCLXXXV.—*The Nitrosation of Phenols. Part XII.*
Resorcinol Mono-n-propyl Ether.

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THE attack of the kationoid reagent in the nitrosation of resorcinol monomethyl ether was found by the authors (J., 1929, 2775) to be almost entirely at the 6-position, whereas with the monoethyl ether (J., 1930, 963) 10—15% of nitrosation occurred in the 4-position; it has now been found that the *n*-propyl ether is nitrosated in the latter position to the extent of 20·5%, a result which supports our views (*loc. cit.*), according to which the order of ionisation repression of the *op*-directing phenolic group is Me < Et < *n*-Pr.

Alternatively, should the *n*-propoxy-group exert an inductive electron-attraction, the 4-carbon atom (*loc. cit.*, formula III, with *n*-Pr in place of Me), being less deactivated in the *n*-propoxy- than in the ethoxy- and the methoxy-homologue, would be relatively more reactive.

The former assumptions also receive support in that the *n*-propyl ether is much less readily nitrosated than its ethyl analogue, which, in turn, is less reactive than the methyl ether. Steric effects may also influence the rate of nitrosation, but these should not disturb the order derived from electronic considerations.

The solubility (5.78%) of 6-nitroso-3-*n*-propoxyphenol in benzene is appreciably greater than that of the ethoxy- (1.32%) or the methoxy- (2.26%) homologue, and indicates that co-ordination (*loc. cit.*, formula V) of the *o*-nitroso- and the hydroxyl group is greatly intensified in the *n*-propyl compound, so that the increased activation of the chelating electrons of the nitroso-group has greatly exceeded the concurrent increased repression of ionisation. This is to be expected, since the *n*-propoxy-group, being para to the nitroso-group, would exert its positive alternating effect, and being meta to the hydroxyl-group, would have a weaker general effect.

Although the chlorine atoms in 1 : 3-dichloro-4-nitrobenzene are readily replaced by methoxyl, and the 3-chlorine atom by ethoxyl (*loc. cit.*), yet *n*-propyl-alcoholic sodium *n*-propoxide gave no definite results.

The constitution of 6-nitroso-3-*n*-propoxyphenol has been established by its oxidation to 6-nitro-3-*n*-propoxyphenol, a steam-volatile compound obtained by mono-nitration of resorcinol mono-*n*-propyl ether and also from 6-nitro-3-*n*-propoxyaniline (see below). The constitution of the latter substance was established by its preparation from 3-chloro-4-nitrophenyl *n*-propyl ether. Further, 6-nitro-3-*n*-propoxyphenol gave an ethyl ether identical with the *n*-propyl ether obtained from authentic 4-nitro-3-ethoxyphenol (*loc. cit.*).

The constitution of 4-nitroso-3-*n*-propoxyphenol was proved (i) by its oxidation to 4-nitro-3-*n*-propoxyphenol, which formed the non-steam-volatile portion in the mono-nitration of resorcinol mono-*n*-propyl ether, and (ii) by its formation from 4-nitroso-3-*n*-propoxydimethylaniline by means of caustic alkalis.

6-Nitro- and 4-nitro-3-*n*-propoxyphenols have also been obtained synthetically from *m*-nitrophenol via *m*-nitrophenyl *n*-propyl ether, 3-*n*-propoxyacetanilide, 6- and 4-nitro-3-*n*-propoxyacetanilides (by nitration), and the corresponding amines (by the standard procedure, Hodgson, E. P. 200,714).

It is noteworthy that in an attempted nitration of resorcinol di-*n*-propyl ether, depropylation occurred, a mixture of 6-nitro- with a little 4-nitro-3-*n*-propoxyphenol being obtained; this resembles the behaviour of the diethyl ether towards nitration (Weselsky and Benedikt, *Monatsh.*, 1880, **1**, 891; Nietzki and Mächler, *Ber.*, 1890, **23**, 719) and nitrosation (Hodgson and Clay, J., 1930, 1872).

EXPERIMENTAL.

1. *Preparation of the Resorcinol n-Propyl Ethers.*—Resorcinol (55 g.), dissolved in *n*-propyl alcohol (150 c.c.), is treated with freshly prepared sodium *n*-propoxide (11 g. of sodium in 175 c.c. of *n*-propyl alcohol) and *n*-propyl iodide (95 g.), the whole being heated under reflux for 6 hours, and excess *n*-propyl alcohol then removed by distillation. The oily reaction product is precipitated by addition of water, separated, and steam-distilled, the distillate (8 litres) saturated with sodium chloride, and extracted with ether. From the ethereal extract, by means of 10% sodium hydroxide solution, the resorcinol mono-*n*-propyl ether is worked up in the usual way and finally distilled; b. p. 256—257° (yield 16 g.) [Found (Zeisel): OPr, 38·5. Calc.: OPr, 38·8%].

The ethereal solution (remaining after the alkaline extraction) was distilled, and yielded 5—6 g. of the di-*n*-propyl ether as a highly refractive yellow oil, b. p. 250—260° (Kariof, *Ber.*, 1880, **13**, 1677, gives b. p. 251°). This gave a red colour with concentrated sulphuric acid but no colour with alcoholic ferric chloride; it still boiled over a range after being heated for 2 hours under reflux with 20% aqueous hydrochloric acid.

2. *Nitrosation of Resorcinol Mono-n-propyl Ether.*—The methods previously described for the mono-methyl and -ethyl ethers (*loc. cit.*, pp. 2777, 964) gave unsatisfactory results, much tarry material being obtained. Kietabl's procedure (*Monatsh.*, 1898, **19**, 536), suitably modified, eventually gave the best results. The ether (5 g.), dissolved in a mixture of alcohol (10 c.c.) and glacial acetic acid (10 c.c.), was treated gradually (with stirring and below 0°) with a solution of sodium nitrite (5 g.) in water (10 c.c.). The reaction mixture, which immediately turned red, was stirred for an hour (ice-cold), the sides of the vessel being repeatedly scratched. The reddish-brown crystalline precipitate (A) was filtered off, and dried in a vacuum over quicklime; yield, 3·6 g. The filtrate when diluted with water yielded 1·2 g. of crystals (B) which were darker than (A).

3. *Separation of the Isomerides by Benzene Extraction.*—The benzene used was previously dried over metallic sodium. (a) The crude product A (3·5 g.) was shaken for 30 minutes in the cold with benzene (100 c.c.) and the insoluble matter (0·62 g., 17·7%) filtered off and dried; it yielded nothing to a further 50 c.c. of benzene. Similar extraction of product B (1 g.) left 0·3 g. (30%) of insoluble matter. These insoluble residues crystallised from boiling alcohol (charcoal) in bright yellow leaflets, decomp. 170—175° (Found: N, 8·0. $C_9H_{11}O_3N$ requires N, 7·7%), of 4-nitroso-3-*n*-propoxyphenol (see p. 2105).

(b) From the two benzene solutions only a single product could be isolated, which was shown (see below) to be 6-nitroso-3-n-propoxyphenol; it crystallises from benzene-light petroleum in bronze-green leaflets, which turn brown between 70° and 80° and melt at 93° to a deep brown liquid (Found: N, 7.9. $C_9H_{11}O_3N$ requires N, 7.7%). The crystals from alcohol are brownish-yellow prisms, m. p. 93°.

4. *Oxidation of the Benzene-soluble Fraction with Dilute Nitric Acid.*—The nitrosation product (1 g.) was suspended in water (10 c.c.) and vigorously stirred during the gradual addition of 10 c.c. of a mixture of concentrated nitric acid (3 parts; *d* 1.4) and water (1 part); the temperature rose to about 30°, nitrous fumes were evolved, and a red oil separated. After 2 hours, the mixture was diluted with water and steam-distilled, the volatile 6-nitro-3-n-propoxyphenol being extracted with ether, the extract dried with anhydrous sodium sulphate, the ether removed by distillation, and the residual oil extracted with light petroleum; when cooled in ice, the last extract deposited yellow glistening leaflets of 6-nitro-3-n-propoxyphenol (see p. 2103), m. p. 34° (Found: N, 7.3. $C_9H_{11}O_4N$ requires N, 7.1%), which gave a sparingly soluble orange-yellow sodium salt.

5. *Oxidation of the Benzene-insoluble Fraction with Alkaline Potassium Ferricyanide.*—The crude product (0.5 g.), dissolved in 10% aqueous potassium hydroxide (30 c.c.), was mixed with a saturated aqueous solution of potassium ferricyanide (10 g.) and heated on the water-bath until the deep red solution changed to orange-yellow, whereupon it was filtered hot, cooled, and acidified with dilute sulphuric acid. The greenish-white precipitate of 4-nitro-3-n-propoxyphenol, crystallised from hot water in almost white leaflets (Found: N, 7.2. $C_9H_{11}O_4N$ requires N, 7.1%), m. p. 86° either alone or mixed with an authentic specimen; it is not volatile in steam.

6. *Oxidation of the Crude Nitrosation Mixture.*—(a) *With alkaline potassium ferricyanide.* The crude product (5 g.) was oxidised as above and steam-distilled, the volatile and the non-volatile product being worked up as above; yields: 1.2 g. of 6-nitro-, and 0.4 g. of 4-nitro-3-n-propoxyphenol.

(b) *With dilute nitric acid.* With procedure as above, 5 g. of crude product gave 2.5 g. of 6-nitro-isomeride together with a resin.

7. *Nitration of Resorcinol Mono-n-propyl Ether.*—(a) *In ether.* The product (1 g.), dissolved in dry ether (50 c.c.) and cooled to about -10° , was treated gradually with fuming nitric acid (0.4 c.c.; *d* 1.5) below -5° , and then boiled for 15 minutes. A little water (5 c.c.) was next added, the ether removed by distillation, and the

residual brown oil steam-distilled; the volatile 6-nitro-3-*n*-propoxyphenol was isolated as the sparingly soluble sodium salt (0.8 g.), which, after treatment with acid, ether, and light petroleum as above, crystallised from the latter solvent in yellow leaflets, m. p. 34° (Found: N, 7.3%). The hot filtrate from the non-volatile residue deposited a small amount of 4-nitro-3-*n*-propoxyphenol in almost white leaflets, m. p. 86° (Found: N, 7.3%).

(b) *In acetic anhydride.* The product (1 g.), dissolved in acetic anhydride (5 c.c.), was treated below 0° (with stirring) with fuming nitric acid (0.4 c.c.; *d* 1.5) in acetic anhydride (2 c.c.), and kept for 3 hours at room temperature. The solution was poured on ice and steam-distilled, the subsequent procedure being as under (a) above; 0.6 g. of the sodium salt of 6-nitro-3-*n*-propoxyphenol was obtained, but no 4-nitro-isomeride could be isolated.

8. *Nitration of Resorcinol Di-n-propyl Ether.*—The ether (1 g.), prepared according to Wilson and Adams (*J. Amer. Chem. Soc.*, 1923, 45, 534), was dissolved in dry ether (20 c.c.) and nitrated and worked up as for the monopropyl ether (above), except that it was kept over-night at room temperature instead of being boiled; 0.3 g. of 6-nitro-3-*n*-propoxyphenol was isolated, but only a trace of the 4-nitro-isomeride.

9. *Proof of the Constitutions of 4- and 6-Nitro-3-n-propoxyphenols.*—*m*-Nitrophenyl *n*-propyl ether. A freshly prepared solution of sodium ethoxide (5 g. of sodium in 125 c.c. of absolute alcohol) was added to a mixture of *m*-nitrophenol (30 g.), absolute alcohol (125 c.c.), and *n*-propyl iodide (45 g.), and the whole refluxed for 8 hours, after which the excess alcohol and *n*-propyl iodide were removed by distillation. The residual reddish-brown oil was steam-distilled, and the almost colourless volatile oil solidified over-night to a pale greenish-yellow crystalline aggregate, which separated from alcohol in small white prisms of the required ether (32 g.), m. p. 28° (Found: N, 8.0. C₉H₁₁O₃N requires N, 7.7%). Reduction of the above product (20 g.) was effected by gradual addition of iron powder (20 g.) to its warm solution in glacial acetic acid (60 c.c.) and water (60 c.c.). After the reaction had abated, the mixture was heated for 2 hours on the water-bath, then made alkaline with sodium hydroxide, and steam-distilled, the colourless volatile liquid, *m*-aminophenyl *n*-propyl ether, being extracted with ether and purified by distillation; b. p. 257—258°/752 mm. (Found: N, 9.6. C₉H₁₃ON requires N, 9.3%). The hydrochloride crystallises from water in colourless needles, m. p. 155° (Found: N, 7.8; Cl, 18.7. C₉H₁₄ONCl requires N, 7.5; Cl, 18.9%), the sulphate in white needles much less soluble in water than the hydrochloride, the picrate in fine golden-yellow needles, m. p. 147—148° (Found:

N, 15.0. $C_{15}H_{16}O_8N_4$ requires N, 14.7%), and the *monoacetyl* derivative from dilute alcohol in long white needles, m. p. 71° (Found : N, 7.5. $C_{11}H_{15}O_2N$ requires N, 7.3%).

10. *Nitration of m-Acetamidophenyl n-Propyl Ether*.—The ether (10 g.), dissolved in acetic anhydride (50 c.c.), was treated gradually (vigorous stirring) with fuming nitric acid (5 g.; *d* 1.5) in acetic anhydride (25 c.c.), the temperature being kept below 0° during the operation and for one hour afterwards; the violet-green liquid was poured on ice, kept over-night, and the pale yellow nitration product (8.7 g.) filtered off, washed, and dried.

Separation of the isomerides. The whole of the above mixture was exhaustively extracted with boiling light petroleum. The soluble portion, *4-nitro-3-acetamidophenyl n-propyl ether* (4.5 g.) crystallised from alcohol in canary-yellow needles, m. p. 97° (Found : N, 12.0. $C_{11}H_{14}O_4N_2$ requires N, 11.8%), which were readily hydrolysed when heated (1 g.) with dilute sulphuric acid (5 c.c.; 50% by vol.) on the water-bath until a clear solution was obtained (15 mins.). From this solution, *4-nitro-3-aminophenyl n-propyl ether* was precipitated by dilution with water, and then crystallised from dilute alcohol in golden-yellow prismatic needles, m. p. $98-99^\circ$ (Found : N, 14.6. $C_9H_{12}O_3N_2$ requires N, 14.3%); the product was slowly volatile in steam and readily soluble in the usual organic solvents. On diazotisation (1 g.) in dilute sulphuric acid and treatment by the standard procedure (Hodgson, *loc. cit.*), the steam-volatile *6-nitro-3-n-propoxyphenol* (0.3 g.) was obtained, m. p. 34° , identical with the volatile products described in Sections 4 and 7.

3-Chloro-4-nitrophenol was converted into its *n-propyl ether* via its silver salt, and the ether heated under reflux with alcoholic ammonia which was replenished periodically during 6 hours. The boiling mixture was then filtered, diluted with hot water, and allowed to cool; *4-nitro-3-aminophenyl n-propyl ether* separated, and was crystallised from dilute alcohol; m. p. and mixed m. p. with above product $98-99^\circ$.

The isomeric *6-nitro-3-acetamidophenyl n-propyl ether*, which was insoluble in light petroleum, was crystallised first from boiling water (charcoal) and then from chloroform-light petroleum; small white needles (1.2 g.), m. p. $120-121^\circ$ (Found : N, 12.1. $C_{11}H_{14}O_4N_2$ requires N, 11.8%). *6-Nitro-3-aminophenyl n-propyl ether* was obtained by hydrolysis as above; it crystallised from dilute alcohol in brownish-yellow needles, m. p. 117° (Found : N, 14.6. $C_9H_{12}O_3N_2$ requires N, 14.3%); it was insoluble in light petroleum, sparingly soluble in boiling water, non-volatile in steam, and readily soluble in alcohol, benzene, and acetic acid. This amine (0.5 g.), in a very fine suspension (obtained by rapid cooling

of its solution in hot dilute sulphuric acid), was diazotised by addition of sodium nitrite (0.25 g.) in water (1 c.c.) below 0°, and the clear yellow diazo-solution was boiled under reflux for $\frac{1}{2}$ hour with dilute sulphuric acid. The 4-nitro-3-*n*-propoxyphenol formed was removed by ether extraction and, after subsequent crystallisations from water and dilute alcohol, was obtained in almost white leaflets, m. p. 86°, identical (mixed m. p.) with the non-volatile product described in Sections 5 and 7.

11. 4-Nitroresorcinol Di-*n*-propyl Ether.—This was obtained by heating the silver salt of either nitration product of resorcinol mono-*n*-propyl ether with *n*-propyl iodide. It crystallised from water in very pale yellow needles, m. p. 50° (Found: N, 6.1. C₁₂H₁₇O₄N requires N, 5.9%).

12. 3-*n*-Propoxydimethylaniline.—3-*n*-Propoxyaniline (18 g.) was gradually added to methyl sulphate (30 c.c.), and after the reaction had moderated, the mixture was heated on the water-bath for 2 hours, and cooled; addition of 10% aqueous sodium hydroxide destroyed the excess methyl sulphate and liberated the bases, which were extracted with ether, worked up as usual, and kept in contact with acetic anhydride (20 c.c.) for one hour to combine with any primary or secondary bases. The mixture was then poured into water, heated for one hour on the water-bath, cooled, made alkaline with sodium carbonate, and steam-distilled, the volatile 3-*n*-propoxydimethylaniline being ether-extracted and purified by distillation; it is a colourless refractive oil, b. p. 262—263°/747 mm. (Found: N, 8.1. C₁₁H₁₇ON requires N, 7.8%), which rapidly becomes yellow on exposure to light. The *picrate* crystallises from alcohol in sulphur-yellow needles, m. p. 150—152° (decomp.) (Found: N, 14.0. C₁₇H₂₀O₈N₄ requires N, 13.7%).

13. Nitrosation of 3-*n*-Propoxydimethylaniline.—A solution of the foregoing compound (5 g.) in concentrated hydrochloric acid (9 c.c.) and water (20 c.c.) was nitrosated between 0° and 5° by gradual addition of sodium nitrite (2.5 g.) in water (4 c.c.). The deep red solution quickly deposited the *hydrochloride* of 4-nitroso-3-*n*-propoxydimethylaniline (5.5 g.), which crystallised from water in bright yellow needles, m. p. 151—152° (Found: N, 11.7; Cl, 14.2. C₁₁H₁₇O₂N₂Cl requires N, 11.5; Cl, 14.5%). The free *base* crystallised from benzene-light petroleum in small, bright green needles, m. p. 98° (Found: N, 13.8. C₁₁H₁₆O₂N₂ requires N, 13.5%).

14. 4-Nitroso-3-*n*-propoxyphenol.—A solution of the above hydrochloride (3 g.) in water (50 c.c.) was slowly added in 5 c.c. portions to 5% aqueous sodium hydroxide (100 c.c.) boiling under reflux, the free base which separated as a green oil being allowed to disappear before the next addition. The final clear red solution

was cooled, and ice (50 g.) was added, followed by cold hydrochloric acid. The greenish-yellow precipitate of 4-nitroso-3-*n*-propoxyphenol readily crystallised from alcohol in bright yellow scales, which darkened above 150° and decomposed at 170—175° (Found : N, 7.9. Calc. for $C_9H_{11}O_3N$: N, 7.7%); it is sparingly soluble in alcohol and glacial acetic acid but almost insoluble in ether and benzene, gives the nitrosoamine test (red, changing to blue with alkalis), and is oxidised by alkaline potassium ferricyanide to 4-nitro-3-*n*-propoxyphenol, m. p. 86° (Found : N, 7.3%), identical (mixed m. p.) with the non-volatile product described in Sections 5 and 7.

15. 6-Nitroresorcinol 1-Ethyl 3-*n*-Propyl Ether.—(a) The orange-yellow silver salt of 4-nitro-3-ethoxyphenol was heated for 15 mins. under reflux with a mixture of *n*-propyl iodide and ethyl alcohol, and the product steam-distilled. Alcohol and propyl iodide passed over readily, and the required ether much more slowly; the last crystallised from hot water in stout, pale yellow prisms, m. p. 39° (Found : N, 6.4. $C_{11}H_{15}O_4N$ requires N, 6.2%).

(b) By an analogous procedure from 6-nitro-3-propoxyphenol an identical product was obtained, m. p. and mixed m. p. 39° (Found : N, 6.3%).

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