214. *Bromination of Resorcinol Monobenzoate and Nitration of* 4 : 6-*Dibromoresorcinol* 3-*Benzoate. An Example of Group Migration.*

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In dry chloroform solution, resorcinol 3-benzoate is brominated in three stages, the initial reaction being mainly in the 6-position and subsequent attack taking place at the 4- and finally at the 2-position. It would appear, therefore, that the activated condition of the

monobenzoate is represented by the formula $BzO\cdot C\begin{matrix}CH\cdot C(OH)\\CH{=}{=}CH\end{matrix}CH$. The almost quantitative character of the 6-bromination was established by methylation of the product to 6-*bromoanisyl* 3-*benzoate*, hydrolysis to 6-*bromo*-3-*hydroxyanisole*, and nitration to 6-*bromo*-4-*nitro*-3-*hydroxyanisole*, which was obtained in over 90% yield. The isomeric 4-*bromoanisyl* 3-*benzoate* has been synthesised for constitutional reasons.

The constitution of 4 : 6-*dibromoresorcinol* 3-*benzoate* follows from its hydrolysis to 4 : 6-dibromoresorcinol and the failure of this product to give eosin when condensed with phthalic anhydride, as well as from the identity of 4 : 6-*dibromoresorcinol dibenzoate* prepared from it and from authentic 4 : 6-dibromoresorcinol.

When 4 : 6-dibromoresorcinol 3-benzoate is mononitrated by nitric acid in glacial acetic acid solution, 2 : 4-*dibromo*-6-*nitroresorcinol* 3-*benzoate* results, indicating migration of bromine from the 6- to the 2-position (compare Hodgson and Smith, J., 1931, 2268), but when acetylorthonitric acid is used in acetic anhydride medium a certain amount of 2-nitration appears to occur.

Although resorcinol is readily monobenzoylated by benzoyl chloride in aqueous sodium carbonate, the di-*p*-toluenesulphonyl derivative is always formed with *p*-toluenesulphonyl chloride; 2-nitroresorcinol also affords only di-derivatives with methyl sulphate, benzoyl chloride, and *p*-toluenesulphonyl chloride.

A useful method for the preparation of 2-nitroresorcinol afforded 6-nitroresorcinol 3-methyl ether when applied to resorcinol monomethyl ether.

Experimental.

(a) *Monobromination.*—A solution of resorcinol 3-benzoate (2·14 g., m. p. 133°) in chloroform (20 c.c., dried over calcium chloride) was treated gradually with one of bromine (1·6 g.) in a little dry chloroform; colourless needles of 6-*bromoresorcinol* 3-*benzoate* (2·5 g.) separated, m. p. 169° after recrystallisation from alcohol (Found : Br, 27·0. $C_{13}H_9O_3Br$ requires Br, 27·3%). When ordinary (*i.e.*, moist) chloroform was used, dibromination occurred. 6-*Bromoanisyl* 3-*benzoate*, prepared by the action of methyl sulphate on an aqueous sodium carbonate suspension of the above product, crystallised from alcohol in colourless needles, m. p. 140° (Found : Br, 25·9. $C_{14}H_{11}O_3Br$ requires Br, 26·0%).

4-*Bromo*-6-*nitroresorcinol* 3-*methyl ether* was prepared from 6-bromoresorcinol 3-benzoate (3 g.) by methylation as above, followed by hydrolysis with boiling aqueous sodium hydroxide to 6-bromo-3-hydroxyanisole, acidification of the alkaline solution with dilute sulphuric acid, and addition in the cold of an excess of sodium nitrite. When the mixture was steam-distilled after 12 hours, 4-bromo-6-nitroresorcinol 3-methyl ether (2·2 g.) passed over; it crystallised from water or aqueous alcohol in pale yellow, elongated parallelepipeds, m. p. 114° (Found : Br, 32·1. $C_7H_6O_4NBr$ requires Br, 32·2%). It was synthesised from 6-nitroresorcinol 3-methyl ether (7 g.) by treatment of its dry chloroform solution at room temperature with bromine (7 g.) in dry chloroform, separating after 1 hour. 2 : 4-*Dibromo*-6-*nitroresorcinol* 3-*methyl ether* was prepared by the action of alkaline sodium hypobromite on 6-nitroresorcinol 3-methyl ether and on the two monobromo-products previously described; it crystallised from aqueous 50% alcohol in bright yellow needles, m. p. 128° (Found : Br, 48·7. $C_7H_5O_4NBr_2$ requires Br, 48·9%).

Synthesis of 4-*Bromoanisyl* 3-*Benzoate.*—4-*Bromo*-3-*nitroanisole* was prepared by diazotising 3-nitro-*p*-anisidine (14 g.) at 0° in a solution of concentrated sulphuric acid (16 c.c.) and water (60 c.c.), adding the mixture to a hot aqueous solution of sodium bromide (10 g.) and copper sulphate (28 g.), and removing the product by steam-distillation; it crystallised from alcohol in yellow needles, m. p. 32° (Found : Br, 34·4. $C_7H_6O_3NBr$ requires Br, 34·5%). Reduction by the usual iron process gave 4-bromo-*m*-anisidine, which was removed by steam-distillation and isolated as the *hydrochloride*; this crystallised from water in colourless needles, m. p. 186° (Found : Cl + Br, 48·1. C_7H_8ONBr,HCl requires Cl + Br, 48·4%). Conversion into 4-bromo-3-hydroxyanisole was carried out by the standard steam distillation-decomposition process (Hodgson, E.P. 200,714), and benzoylation by the Schotten–Baumann reaction gave 4-*bromoanisyl* 3-*benzoate*, which crystallised from alcohol in colourless needles, m. p. 65° (Found : Br, 25·8. $C_{14}H_{11}O_3Br$ requires Br, 26·0%).

(b) *Dibromination.*—The details were as under (a) but 3·2 g. of bromine were used. 4 : 6-*Dibromoresorcinol* 3-*benzoate* was produced, which crystallised from alcohol in colourless needles,

m. p. 155° (Found : Br, 42·9. $C_{13}H_8O_3Br_2$ requires Br, 43·0%). Hydrolysis with boiling aqueous 10% sodium hydroxide (slight excess) and treatment of the cooled solution with carbon dioxide gave 4 : 6-dibromoresorcinol, which was removed in ether and crystallised on slow evaporation in long colourless parallelepipeds (m. p. 110°); recrystallised from hot water, long colourless needles were obtained, m. p. and mixed m. p. with an authentic specimen, 112° (Found : Br, 59·5. Calc. : Br, 59·7%). On chlorination, 2-chloro-4 : 6-dibromoresorcinol was formed; it crystallised from hot water in colourless needles, m. p. 86°, identical with an authentic specimen.

4 : 6-*Dibromoresorcinol dimethyl ether*, prepared by adding methyl sulphate to a moist mixture of 4 : 6-dibromoresorcinol and potassium carbonate, was volatile in steam and crystallised from dilute alcohol in colourless plates, m. p. 65° (Found : Br, 54·0. $C_8H_8O_2Br_2$ requires Br, 54·1%). 4 : 6-*Dibromoanisyl* 3-*benzoate* was formed by shaking a suspension of 4 : 6-dibromoresorcinol 3-benzoate in aqueous sodium carbonate with methyl sulphate; it crystallised from alcohol in colourless needles, m. p. 95° (Found : Br, 41·3. $C_{14}H_{10}O_3Br_2$ requires Br, 41·4%). 4 : 6-*Dibromoresorcinol dibenzoate* was prepared by adding benzoyl chloride to an aqueous sodium hydroxide solution of (a) 4 : 6-dibromoresorcinol and (b) 4 : 6-dibromoresorcinol 3-benzoate; in each case the precipitated dibenzoate crystallised from 50% aqueous alcohol in colourless needles, m. p. 164° (Found : Br, 33·4. $C_{20}H_{12}O_4Br_2$ requires Br, 33·6%).

Nitration of 4 : 6-*Dibromoresorcinol* 3-*Benzoate.*—(a) The benzoate (2 g.), dissolved in hot glacial acetic acid (20 c.c.), was well stirred to promote rapid crystallisation while cooling, and treated at 25° with nitric acid (0·5 c.c.; *d* 1·5) in glacial acetic acid (2 c.c.); the temperature rose to 35° and complete dissolution occurred. The solution was finally heated to 50° and allowed to cool gradually, and 2 : 4-*dibromo*-6-*nitroresorcinol* 3-*benzoate* precipitated by cautious addition of water; it crystallised from dilute acetic acid in bright yellow parallelepipeds, m. p. 141° (Found : Br, 38·2. $C_{13}H_7O_5NBr_2$ requires Br, 38·4%). It was not volatile in steam, and formed a scarlet sodium salt insoluble in excess of alkali. Hydrolysis by boiling 10% aqueous sodium hydroxide and cautious acidification of the deep red solution precipitated 2 : 4-dibromo-6-nitroresorcinol, which crystallised from aqueous alcohol in a lattice of golden-yellow parallelepipeds, m. p. 151° (Dahmer, *Annalen*, 1904, **333**, 360, gives m. p. 148—149°) (Found : Br, 51·0. Calc. : Br, 51·1%), identical with a specimen prepared by the dibromination of 6-nitroresorcinol. It was readily soluble in hot water, from which it crystallised in long needles, was slowly volatile in steam, and gave a scarlet sodium salt readily soluble in excess of alkali. (b) The benzoate (2 g.), dissolved in acetic anhydride (20 c.c.), was treated gradually at 10—20° with diacetylorthonitric acid (2 c.c.) with vigorous stirring. After 15 minutes, the solution was poured into water, and the precipitate crystallised from alcohol; m. p. 130° (Found : Br, 38·3. $C_{13}H_7O_5NBr_2$ requires Br, 38·4%). It appeared to be a mixture, for hydrolysis with aqueous sodium hydroxide and treatment as above gave a product consisting of red micro-prisms and yellow needles, m. p. 145° (Found : Br, 49·9. Calc. : Br, 51·1%), apparently of 4 : 6-dibromo-2-nitro- and 2 : 4-dibromo-6-nitro-resorcinol, the latter predominating.

(c) *Tribromination.*—Resorcinol 3-benzoate (5 g.) was treated in chloroform solution with bromine (5 c.c.). 2 : 4 : 6-*Tribromoresorcinol* 3-*benzoate* crystallised from chloroform–light petroleum in large prisms, m. p. 120° (Found : Br, 53·1. $C_{13}H_7O_3Br_3$ requires Br, 53·2%), very soluble in methyl and ethyl alcohol, glacial acetic acid, less soluble in light petroleum, and slightly soluble in hot water. Hydrolysis with boiling aqueous sodium hydroxide gave 2 : 4 : 6-tribromoresorcinol.

Preparation of 2-*Nitroresorcinol and of* 6-*Nitroresorcinol* 3-*Methyl Ether.*—Resorcinol (11 g.) or resorcinol monomethyl ether (12 g.) was dissolved in the minimum amount of glacial acetic acid and treated with oleum (60 g.; 26%); the pasty yellow mass of sulphonated product was nitrated at 0° by nitric acid (5 c.c.; *d* 1·5) in glacial acetic acid (10 c.c.), the solution kept for 1 hour and diluted with water, and the sulphonic acid groups eliminated by superheated steam; 2-nitroresorcinol (8 g.; m. p. 85°) or 6-nitroresorcinol 3-methyl ether (8 g.; m. p. 95°) passed over.

4 : 6-*Dibromo*-2-*nitroresorcinol.*—This was prepared by dissolving 2-nitroresorcinol (1 g.) in glacial acetic acid (10 c.c.), adding a solution of bromine (1 c.c.) in glacial acetic acid (5 c.c.), and heating the mixture gradually to 50°. On cooling, 4 : 6-dibromo-2-nitroresorcinol separated at 35° in scarlet micro-prisms, m. p. 124° (Weselsky and Benedikt, *Monatsh.*, 1880, **1**, 895, give m. p. 117°) (Found : Br, 50·0. Calc. : Br, 51·1%).

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