

250. *The Direct Dibromination of m-Bromophenol and an Example of Group Migration.*

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KOHN and STRASSMANN (*Monatsh.*, 1925, **45**, 597) described but did not orientate the tribromophenol obtained by bromination of *m*-bromophenol, and Hodgson and Nixon (J., 1929, 2424) subsequently designated the product as 2 : 4 : 5 (or 3 : 4 : 6)-tribromophenol. The attention of the senior author having been drawn by the Editor of Beilstein to apparent anomalies in this field, he decided to re-examine the bromination problem. For this purpose the following substances have been prepared without ambiguity : 2 : 3 : 4- and 2 : 4 : 5 (or 3 : 4 : 6)-tribromo-phenol and -anisole, 2 : 3 : 4-tribromo-6-nitro-phenol and -anisole, and 2-nitro-3 : 4 : 6-tribromo-phenol and -anisole.

The attempted dibromination of *m*-bromophenol in glacial acetic acid solution (Kohn and Strassmann, *loc. cit.*) is found to give a mixture from which 2 : 3 : 4 : 6-tetrabromophenol and both the isomeric 2 : 3 : 4- and 2 : 4 : 5-tribromophenols have been isolated. When the reaction is carried out in carbon tetrachloride, however, 3 : 4-dibromophenol is formed immediately, indicating ready bromination in the 4-position, but prolonged keeping is required for further bromination, whereupon 2 : 4 : 5-tribromophenol predominates. From theoretical considerations it seems probable that the 2 : 3 : 4- should be less readily tetrabrominated than the 2 : 4 : 5-isomeride; hence the third bromine atom would enter the 6-position in 3 : 4-dibromophenol more rapidly than the 2-position, with subsequent

further bromination to 2 : 3 : 4 : 6-tetrabromophenol. This would account for the large amount of the latter product, and the predominance of 2 : 3 : 4- over 2 : 4 : 5-tribromophenol in the reaction product.

When 3-bromo-2-nitrophenol is treated with bromine in glacial acetic acid solution, group migration occurs, since 2 : 3 : 4-tribromo-6-nitrophenol results, although when the reaction is carried out by alkaline hypobromite, or in alcoholic solution, normal substitution ensues and 3 : 4 : 6-tribromo-2-nitrophenol is obtained.

The results of Kohn and his collaborators are therefore interpreted as follows: The product of m. p. 78° (Kohn and Strassmann, *loc. cit.*) is a mixture, and its methyl ether of m. p. 67° is similarly a mixture, since 2 : 3 : 4- and 2 : 4 : 5-tribromoanisoles have m. p.'s 106° and 105° respectively. The bromonitroanisole of m. p. 105° (109°) (Kohn and Sussmann, *Monatsh.*, 1926, **46**, 580) is 2 : 3 : 4-tribromo-6-nitroanisole. The product of m. p. 70° obtained by Kohn and Pfeiffer (*Monatsh.*, 1927, **48**, 222) is 3 : 4 : 6-tribromo-2-nitroanisole (m. p. 72°) which on demethylation by hydrobromic acid gives 3 : 4 : 6-tribromo-2-nitrophenol of m. p. 127° and not 122° as stated by them; the latter m. p. might have indicated a transformation into the 2 : 3 : 4-tribromo-6-nitrophenol (m. p. 123°), but this does not occur.

EXPERIMENTAL.

(Throughout, the designation 2 : 4 : 5- is used instead of 3 : 4 : 6-tribromophenol.)

Bromination of m-Bromophenol.—(1) *In glacial acetic acid solution.* The phenol (5.2 g.), dissolved in acetic acid (25 c.c.), was treated gradually (stirring) with bromine (9.6 g.) in the same solvent (20 c.c.), the mixture diluted with water, and the precipitated bromophenols filtered off. Three separate processes were used: (a) The solid was recrystallised 5 times from light petroleum, pure 2 : 3 : 4 : 6-tetrabromophenol being obtained, m. p. and mixed m. p. with authentic specimen 113° (Found: Br, 77.8. Calc.: Br, 78.0%). (b) The solid was steam-distilled, and the more volatile portion (about half the crude precipitate) twice crystallised from ethylene dichloride–light petroleum, affording colourless needles of 2 : 4 : 5-tribromophenol, m. p. and mixed m. p. with authentic specimen, 87° (Found: Br, 72.4. Calc.: Br, 72.5%); the substance remaining in the flask was 2 : 3 : 4 : 6-tetrabromophenol. (c) The mixed bromophenols were crystallised from 90% formic acid; the bulk of the tetrabromophenol first separated, after which water was added to the mother-liquor, and the resulting precipitate fractionally steam-distilled; the more volatile fraction was recrystallised 5 times from 90% formic acid and finally obtained in colourless prisms, m. p. and mixed m. p. with authentic 2 : 3 : 4-tribromophenol, 95° (Found: Br, 72.6. $C_6H_3OBr_3$ requires Br, 72.5%); on methylation with diazomethane, 2 : 3 : 4-tribromoanisole was obtained, m. p. and mixed m. p. with authentic specimen, 106° (Found: Br, 69.4. $C_7H_5OBr_3$ requires Br, 69.6%).

(2) *In carbon tetrachloride solution.* The phenol (2.6 g.), dissolved in carbon tetrachloride (25 c.c.), was treated with bromine (2.4 g.; 1 mol.); 3 : 4-dibromophenol soon crystallised out in colourless prisms, m. p. 80° (Found: Br, 63.4. Calc.: Br, 63.5%). With two mols. of bromine (4.8 g.), the further bromination was very slow; after 24 hours at room temperature, the mixture was extracted with sodium hydroxide solution, the alkaline extract acidified (hydrochloric acid), and the precipitate recrystallised 5 times from 90% formic acid; m. p. and mixed m. p. with authentic 2 : 4 : 5-tribromophenol, 86–87°; no tetrabrominated product was isolated under these conditions.

(3) *In nitrobenzene solution.* The second bromine atom entered more rapidly than in (2), but otherwise the results were identical. Methylation of the product of m. p. 86–87° by diazomethane gave 2 : 4 : 5-tribromoanisole, which crystallised from 90% formic acid in colourless needles, m. p. and mixed m. p. with authentic specimen, 105° (Found: Br, 69.5. $C_7H_5OBr_3$ requires Br, 69.6%).

Bromination of *m*-bromoanisole did not proceed without a catalyst, but in presence of iodine it gave a mixture of tetra- and penta-bromoanisoles.

Preparation of 2 : 4 : 5-Tribromophenol.—2 : 5-Dibromophenol (2.5 g.), dissolved in acetic acid (20 c.c.) was gradually treated with bromine (1.6 g.) in acetic acid (10 c.c.); after 30 mins. at room temperature, water was added, and the mixture steam distilled; 2 : 4 : 5-tribromophenol passed over, and crystallised from ethylene dichloride–light petroleum in colourless needles, m. p. 87° (Henley and Turner, *J.*, 1930, 928, give m. p. 85–86°) (Found: Br, 72.5. Calc.: Br, 72.5%). Methylation with diazomethane gave 2 : 4 : 5-tribromoanisole; colourless needles, m. p. 105°.

Nitration of 2:5-Dibromophenol.—Concentrated sulphuric acid (5 g.) was stirred into a solution of sodium nitrate (4 g.) in water (10 c.c.), and the mixture added gradually below 25° to a solution of 2:5-dibromophenol (4 g.) in ethylene dichloride (80 c.c.). A trace of sodium nitrite was necessary to initiate the nitration, and after 1 hour's stirring the lower layer was washed with water and steam-distilled. The volatile 3:6-dibromo-2-nitrophenol was dissolved in sodium hydroxide solution and treated with excess bromine; 3:4:6-tribromo-2-nitrophenol was precipitated on acidification, and crystallised from 90% formic acid; pale yellow plates, m. p. 127° (Found: N, 3.9; Br, 63.6. $C_6H_2O_3NBr_3$ requires N, 3.7; Br, 63.8%).

The non-steam-volatile 2:5-dibromo-4-nitrophenol crystallised from ethylene dichloride in pale yellow needles, m. p. 110° (Found: Br, 53.7. $C_6H_3O_3NBr_2$ requires Br, 53.9%), and was methylated by diazomethane in ethereal solution; the anisole was reduced by iron and hydrochloric acid, the amine being extracted with benzene, and the latter solution with aqueous hydrobromic acid; Sandmeyer treatment gave 2:4:5-tribromoanisole, which was removed by steam distillation, and crystallised from 90% formic acid; colourless needles, m. p. 105° (Kohn and Pfeiffer, *loc. cit.*, give m. p. 105°) (Found: Br, 69.5%).

Preparation of 2:3:4-Tribromo-6-nitrophenol.—(a) *From 5-bromo-2-nitrophenol.* The initial material (2 g.; Hodgson and Moore, J., 1926, 157) was dissolved in 10% sodium hydroxide solution (20 c.c.), treated with a solution of bromine (3.2 g.) in the same reagent (25 c.c.), and the mixture heated for ½ hour at 50°, and cooled. 2:3:4-Tribromo-6-nitrophenol was precipitated by hydrochloric acid and crystallised from methyl alcohol; yellow prisms, m. p. 123° (Found: Br, 63.7. Calc.: Br, 63.8%). The same product was obtained by direct bromination in ethyl alcohol.

(b) *From 2:3-dibromophenol.* The phenol (2 g.) was dissolved in acetic acid (14 c.c.), and nitrated at 0° by gradual addition of nitric acid (0.5 c.c.; *d* 1.5) in acetic acid (5 c.c.); the mixture was stirred for 2 hours, diluted and steam-distilled; the volatile 2:3-dibromo-6-nitrophenol [which crystallised from alcohol in yellow needles, m. p. 105° (Found: Br, 53.7. $C_6H_3O_3NBr_2$ requires Br, 53.9%)] was dissolved (0.6 g.) in alcohol (10 c.c.) and brominated by addition of bromine (0.1 c.c.) in alcohol (5 c.c.), 2:3:4-tribromo-6-nitrophenol being ultimately obtained; yellow prisms, m. p. and mixed m. p. with product from (a) 123° (Found: Br, 63.6%).

Preparation of 2:3:4-Tribromo-6-nitroanisole.—The above phenol, dissolved in ether, methyl alcohol, or benzene, was treated with excess of diazomethane in ether, the solution extracted with sodium hydroxide solution, to remove unchanged substance, and washed successively with water, hydrochloric acid, and water; evaporation of the ether afforded 2:3:4-tribromo-6-nitroanisole; colourless needles, m. p. 109°, from 90% formic acid (Kohn and Sussmann, *loc. cit.*, give m. p. 109°) (Found: Br, 61.3. Calc.: Br, 61.5%). Demethylation by hydrobromic acid as below gave the original 2:3:4-tribromo-6-nitrophenol (m. p. and mixed m. p. 123°).

Removal of the Nitro-Group from 2:3:4-Tribromo-6-nitroanisole.—Iron powder (1 g.) was heated under reflux with hydrochloric acid (*d* 1.19; 3 c.c.) and water (20 c.c.) until evolution of hydrogen had ceased; the anisole (1 g.) was added, together with more iron powder (1 g.), and the mixture refluxed for 4 hours, and then extracted with benzene. The hydrochloride of the amine, precipitated by saturation of the filtered extract with hydrogen chloride, was filtered off, dried, dissolved in alcohol (20 c.c.), concentrated sulphuric acid (2 c.c.) added, and the mixture cooled and stirred for ½ hour after addition of 5 times the theoretical weight of sodium nitrite. The clear liquor was boiled until the diazonium salt was decomposed (2 hours; tested by coupling with β -naphthol), and then steam-distilled; the 2:3:4-tribromoanisole which passed over crystallised from 90% formic acid in colourless plates, m. p. 106° (Found: Br, 69.5. $C_6H_3OBr_3$ requires Br, 69.6%). Demethylation by hydrobromic acid gave authentic 2:3:4-tribromophenol, which crystallised from 90% formic acid in colourless prisms, m. p. 95° (Found: Br, 72.5. $C_6H_3OBr_3$ requires Br, 72.5%).

Preparation of 3:4:6-Tribromo-2-nitrophenol.—3-Bromo-2-nitrophenol (2 g.) (Hodgson and Moore, *loc. cit.*) was brominated with alkaline hypobromite as for the 6-nitro-isomeride (above). The sparingly soluble sodium salt of the 3:4:6-tribromo-2-nitrophenol separated, and was filtered off, converted into the phenol by treatment with hydrochloric acid, and then crystallised from 90% formic acid; pale yellow plates, m. p. 127° (Found: N, 4.0; Br, 63.6. $C_6H_2O_3NBr_3$ requires N, 3.7; Br, 63.8%); its m. p. was depressed by 30° when it was admixed with the 6-nitro-isomeride (m. p. 123°). Bromination of 2-nitro-3-bromophenol in alcohol below 25° gave the above product of m. p. and mixed m. p. 127° (Found: Br, 63.7%).

Methylation by diazomethane (as above) gave 3:4:6-tribromo-2-nitroanisole, which

crystallised from 90% formic acid in colourless prisms, m. p. 72° (Found : N, 3·8; Br, 61·5. Calc. for $C_7H_4O_3NBr_3$: N, 3·6; Br, 61·5%).

Demethylation of 3 : 4 : 6-Tribromo-2-nitroanisole.—This substance (1 g.) was heated for 3 hours under reflux with hydrobromic acid (48%; b. p. 126°), the product being dissolved in sodium hydroxide solution, reprecipitated by hydrochloric acid, and crystallised from 90% formic acid; m. p. 127°, not depressed by admixture with the 3 : 4 : 6-tribromo-2-nitrophenol, but depressed by the 6-nitro-isomeride (Found : Br, 63·6%).

Removal of the Nitro-group from 3 : 4 : 6-Tribromo-2-nitroanisole.—By the same procedure as for the 6-nitro-isomeride, 2 : 4 : 5-tribromoanisole was obtained; colourless needles from 90% formic acid, m. p. 105° (Found : Br, 69·4%). Mixed m. p. with authentic and other specimens, 105°; depressed, however, to 85° by 2 : 3 : 4-tribromoanisole (m. p. 106°).

Action of Bromine on 3-Bromo-2-nitrophenol.—(a) *In glacial acetic acid solution.* The phenol (2 g.), dissolved in acetic acid (10 c.c.), was treated with a solution of bromine (3·2 g.) in acetic acid (10 c.c.), the mixture heated to 50°, and then kept over-night. On addition of water, 2 : 3 : 4-tribromo-6-nitrophenol was precipitated; it crystallised from methyl alcohol in yellow prisms, m. p. and mixed m. p. with authentic specimen, 123° (Found : Br, 63·7%). Methylation by diazomethane gave 2 : 3 : 4-tribromo-6-nitroanisole, which crystallised from 90% formic acid in colourless needles, m. p. 109° (Found : Br, 61·4%); demethylation by hydrobromic acid as above gave 2 : 3 : 4-tribromo-6-nitrophenol; m. p. 123°.

(b) *In ethyl alcohol.* The above quantities, with alcohol instead of acetic acid, reacted below 25° to give, after 30 mins., a precipitate of 3 : 4 : 6-tribromo-2-nitrophenol on addition of water. This product is much more soluble in methyl alcohol than the 6-nitro-isomeride but crystallises from 90% formic acid in pale yellow plates, m. p. 127° (Found : Br, 63·6%).

Action of Bromine on 3 : 4 : 6-Tribromo-2-nitrophenol.—The phenol (1 g.), dissolved in acetic acid (10 c.c.), was treated with bromine (0·3 c.c.), and the mixture heated to 50°; a yellow precipitate separated, which had m. p. 220—225° but was not investigated further; it is probably a bromoanil-like substance.

The authors thank Mr. R. J. H. Dyson for valuable preparative and analytical assistance, and the Imperial Chemical Industries, Ltd., for their various gifts.

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[Received, June 2nd, 1933.]