

CXCIIL.—*The Bromination of Phenol. 2:4- and 2:6-Dibromophenol.*

By FRANK GEORGE POPE and ARTHUR SAMUEL WOOD.

CONSIDERABLE quantities of 2:4- and 2:6-dibromophenol being required for an investigation now in progress, it was found that the preparation of these compounds was, as a rule, attended by considerable difficulty, and that the yields obtained were in most cases rather small, more especially in the case of 2:6-dibromophenol.

Körner (*Annalen*, 1866, **137**, 205) prepared 2:4-dibromophenol by the direct bromination of phenol in the cold, whilst Peratoner

(*Gazzetta*, 1886, **16**, 402) obtained it by the heating of 3:5-dibromosalicylic acid with dilute sulphuric acid at 220—230°. Somewhat later, Schryver (*Trans.*, 1899, **75**, 618) showed that it could be obtained by direct bromination of phenol in carbon disulphide solution in the presence of some aluminium chloride, and Hewitt (*Trans.*, 1904, **85**, 1225), by suspending phenol in 75 per cent. sulphuric acid and adding bromine, succeeded in obtaining a 93 per cent. yield of the 2:4-dibromo-compound.

After trying the several methods above mentioned, we found that 2:4-dibromophenol could be most rapidly prepared if the bromination of phenol were carried out in the presence of hydrobromic acid. In one experiment 23.5 grams of phenol were suspended in 70 grams of hydrobromic acid (D 1.49), and the mixture was slightly warmed until the phenol melted. The solution was then cooled in a freezing mixture to -10° , and 80 grams of bromine dissolved in 40 grams of hydrobromic acid were run in very slowly, the temperature being kept below 0° . Bromine was absorbed very slowly, and when about half had been added, all the phenol had liquefied. The temperature of the mixture was now allowed to rise to 0° , the remainder of the bromine solution added more rapidly, and the mixture allowed to remain for one hour. At the end of this time the reaction mixture was heated slightly (to about 30°) until the colour of the bromine just disappeared; and then put aside for three hours. The supernatant hydrobromic acid was run off from the 2:4-dibromophenol, diluted somewhat with water, and recovered by distillation. The dibromophenol was melted under water, washed several times with small quantities of warm water by decantation, and finally dried in a vacuum desiccator. The yield of the crude product was 55 grams (87—88 per cent.), and it melted at 37.6° . After recrystallisation from light petroleum, 2:4-dibromophenol melts at 40° (corr.).

2:4-Dibromophenol crystallises in long, colourless needles. The melting point as given in the earlier preparations by different investigators is $34-35^{\circ}$ (Hewitt); $35-36^{\circ}$ (Peratoner); 40° (Körner). The lower values are probably due to the fact that 2:4-dibromophenol apparently retains traces of water which are difficult to remove, for on distillation of a specimen which had been kept over sulphuric acid in a vacuum for two weeks a small quantity of water was obtained as a first distillate. For further purification we recommend distillation of the bromo-compound under diminished pressure, and then recrystallisation from light petroleum. Working in this way, a product is obtained which melts sharply at 40° (corr.), and boils at $177^{\circ}/17$ mm.

The 2:4-dibromophenol thus obtained was characterised by the

preparation of various derivatives. The benzoate prepared by the Schotten-Baumann reaction crystallises from alcoholic solution in long, colourless needles, which melt at 97.5° (corr.), and is identical with the compound prepared by Autenrieth and Mühlinghaus (*Ber.*, 1907, **40**, 747) by the action of phosphorus pentabromide on phenyl benzoate. (Found, Br=44.40. Calc., Br=44.94 per cent.)

The *p*-nitrobenzoate was prepared in a similar manner from 2:4-dibromophenol and *p*-nitrobenzoyl chloride. It crystallises from glacial acetic acid in almost colourless groups of needles, and is readily soluble in benzene or glacial acetic acid, but is almost insoluble in light petroleum. It melts at 183.5° (corr.):

0.2061 gave 0.1911 AgBr. Br=39.45.

$C_{13}H_7O_4NBr_2$ requires Br=39.9 per cent.

The methyl ether was obtained by warming the dibromophenol in alkaline solution with an equivalent amount of methyl sulphate. It gradually separates from the reaction mixture as an oil. The oil was separated and well washed with water, and cooled in a freezing mixture. The crystalline mass was finally dried over sulphuric acid in a vacuum, and then crystallised from light petroleum. It separates from the solvent in colourless, transparent prisms, which melt at 61.3° (corr.). Körner, by methylating with methyl iodide in the presence of alkali, obtained the methyl ether, which melted at 59° .

The *ethyl ether* was prepared by dissolving 5 grams of the dibromophenol in alcohol, adding to the solution 0.5 gram of sodium dissolved in 15 grams of alcohol, and running in 3.5 grams of ethyl iodide. The whole was heated under reflux for three hours, and the excess of alcohol then distilled off. The residue was washed with water and cooled to 0° to induce solidification. It was finally dried under diminished pressure, and crystallised from light petroleum, from which it separates in transparent, colourless, rhombic plates, melting at 53.3° :

0.2041 gave 0.2766 AgBr. Br=57.66.

$C_8H_8OBr_2$ requires Br=57.14 per cent.

The *acetyl* derivative was prepared by heating 5 grams of the dibromophenol with 30 grams of acetic anhydride and 5 grams anhydrous sodium acetate for three hours. The excess of acetic anhydride was destroyed by keeping for some time with dilute alcohol, and the product gradually became solid. No convenient solvent could be obtained for crystallisation purposes, and the acetate was finally purified by distillation in a current of steam. It separates from the distillate in small, colourless needles, which melt at 36° (corr.):

0.3993 gave 0.515 AgBr. Br=54.86.

$C_8H_6O_2Br_2$ requires Br=54.42 per cent.

The nitro-derivative was prepared by dissolving 5 grams of the dibromophenol in 40 grams of glacial acetic acid, cooling the solution to 0° , and then running in 1 c.c. of fuming nitric acid dissolved in 5 grams of glacial acetic acid slowly and with vigorous stirring. The mixture was kept in ice for half an hour, and then poured into water. The precipitate was collected, washed, and recrystallised from glacial acetic acid, from which it separates in small, yellow prisms, melting at 117.5° (corr.). It is thus identical with the product obtained by Körner (*Zeitsch. Chem.*, 1868, 323) by the bromination of *o*-nitrophenol, and is 2:4-dibromo-6-nitrophenol.

2:6-Dibromophenol has been obtained in small yield by the distillation of tetrabromophenolphthalein with concentrated sulphuric acid (Baeyer, *Annalen*, 1880, **202**, 138); by the action of ethyl nitrite on 2:6-dibromo-*p*-aminophenol (Möhlau, *Ber.*, 1882, **15**, 2494; Schryver, *Trans.*, 1899, **75**, 618), or by the action of nitrous acid on 2:6-dibromoaniline (Heinichen, *Annalen*, 1889, **253**, 281). After trying the several methods, we drew the conclusion that it could be best obtained by the elimination of carbon dioxide from 3:5-dibromo-4-hydroxybenzoic acid. This acid has been previously prepared by Balbiano (*Gazzetta*, 1883, **13**, 69) by the distillation of the sodium salt of dibromoanisic acid with lime; by Alessi (*ibid.*, 1885, **15**, 243) by the decomposition of dibromoanisic acid with hydriodic acid; by Paal and Kromschroder (*Ber.*, 1895, **28**, 3236) by the oxidation of the corresponding aldehyde with dilute potassium permanganate in alkaline solution; and by Robertson (*Trans.*, 1902, **81**, 1482) by brominating the acid in acetic acid solution in the presence of iodine, and pouring the product of reaction into sodium hydrogen sulphite solution. Robertson obtains an 80 per cent. yield of the dibromo-acid in this manner, but we find that if the method of preparation is modified in the following manner a yield of 90 per cent. is possible, even after allowing for the tribromophenol formed in small quantity by replacement of the carboxyl group in a portion of the acid by bromine.

55.2 Grams of *p*-hydroxybenzoic acid were stirred into 1600 grams of 75 per cent. sulphuric acid, and the mixture was cooled to 0° , so as to avoid the formation of much tribromophenol during the course of the reaction. 128 Grams of bromine dissolved in 128 grams of glacial acetic acid were also cooled to 0° , and the solution run into the suspension of the hydroxybenzoic acid with vigorous stirring, the temperature being kept below 5° . The reaction proceeds slowly, and when about half the bromine is added

the mass sets to a stiff paste. The remainder of the bromine solution is now run in more rapidly, and the mixture stirred thoroughly in order that the bromine may be well diffused throughout the mass. During this operation a copious evolution of hydrogen bromide takes place. The reaction mixture is allowed to remain for one week, with occasional stirring, during which time the colour of the bromine gradually disappears. It is then poured into 4 litres of water, allowed to remain for about half an hour, collected, washed, and dried at about 80—100°. The crude acid obtained in this way, on drying under a glass funnel, was found to yield a small quantity of a crystalline sublimate, which melted at 89°, and was therefore most probably a little tribromophenol. To remove this, the crude acid was heated under reflux for half an hour with light petroleum, collected, and dried. The acid is readily soluble in alcohol, glacial acetic acid, ethyl acetate, or epichlorohydrin, crystallising from the latter solvent in fine, colourless needles, which melt at 268°. (Found, Br=54·36. Calc., Br=54·05 per cent.)

Consequently, taken in conjunction with the melting-point determination, these figures show that the acid is 3:5-dibromo-4-hydroxybenzoic acid. The crystals obtained on evaporation of the light petroleum extract, on recrystallisation melted at 95—96°, and hence consisted of 2:4:6-tribromophenol. The acid was characterised by conversion into its methyl ester, which melted at 126°, and into its ethyl ester, which melted at 108° (Robertson gives m. p. 99°).

Various methods were used for the elimination of carbon dioxide from the acid, the earlier experiments being conducted by heating 5 grams of the acid with 25 grams of a 5 per cent. solution of sulphuric acid to 150—160° for four hours in a sealed tube. The tube was then opened in order to relieve the pressure, sealed again, and heated for a further four hours.

The reaction mixture was then distilled in a current of steam, and the crude 2:6-dibromophenol obtained melted at 51—52°. A greater concentration of sulphuric acid in the tube slowed the reaction very greatly.

The effect of piperidine was then tried, 5 grams of the acid being heated with 25 grams of water and 15 drops of piperidine for two hours at 150°. The dark-coloured solid obtained was acidified and distilled in a current of steam, when 2:6-dibromophenol was obtained in almost theoretical yield, the crude product melting at 52—53°. Finally, it was found that exceedingly good yields were obtained by heating the acid with water alone to about 160° for several hours, but in consequence of the high pressures produced the tubes burst in the majority of the preparations. To obviate the loss of material it was found that the presence of sodium hydroxide

prevented the bursting of the tubes, but that then the yield of material decreased. Thirty grams of the acid were heated with 200 c.c. *N*-sodium hydroxide solution for $1\frac{1}{2}$ hours at 165° , the product acidified, and distilled in a current of steam, when 13 grams of 2:6-dibromophenol, crystallising in long, slender needles, melting at $56-57^{\circ}$ and boiling at $162^{\circ}/21$ mm., were obtained. (Found: Br=64.0. Calc., Br=63.5 per cent.)

The dibromophenol was characterised by conversion into its nitro-derivative, the nitration being carried out in glacial acetic acid solution at 0° , using fuming nitric acid in slight excess. The nitro-compound crystallises from dilute alcohol in small, yellow prisms, which melt at $144-145^{\circ}$, and is thus 2:6-dibromo-4-nitrophenol. The earlier literature dealing with this compound state that it decomposes at temperatures slightly above its melting point, but we find that it can be heated to a much higher temperature without decomposing, thus confirming an observation of van Erp (*Rec. trav. chim.*, 1910, [ii], 14, 187) that it does not decompose at 180° . The decomposition at the melting-point temperature seems to be more apparent when the substance is prepared by brominating *p*-nitrophenol in acetic acid solution.

The *methyl ether* of 2:6-dibromophenol was obtained by dissolving 5 grams of the phenol in 20 c.c. of methyl alcohol, and adding to the solution 1 gram of sodium dissolved in 15 c.c. of methyl alcohol, and then 5.6 grams of methyl iodide. The reaction mixture was heated under reflux for eight hours, and the excess of alcohol distilled off. The residue was then warmed with sodium hydroxide solution to remove the unchanged phenol, washed with water, and distilled under diminished pressure. The ether distils as a colourless oil, which boils at $143-145^{\circ}/34$ mm., and when cooled in a freezing mixture solidifies to a mass of colourless needles which melt at about 13° . It possesses an odour resembling that of anisole, but much more penetrating, and is readily soluble in all the more common organic solvents:

0.2482 gave 0.3484 AgBr. Br=59.74.

$C_7H_6OBr_2$ requires Br=60.15 per cent.

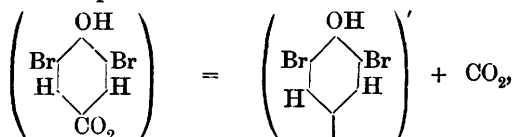
The *ethyl ether* was prepared in a similar manner, and after being well washed, solidified directly when placed in a freezing mixture to a mass of colourless crystals, which melt sharply at 40.6° . Its odour is very penetrating and persistent, and it is readily soluble in all the ordinary organic solvents:

0.2043 gave 0.2762 AgBr. Br=57.53.

$C_8H_8OBr_2$ requires Br=57.14 per cent.

We are inclined to the opinion that the elimination of carbon

dioxide from 3:5-dibromo-4-hydroxybenzoic acid is an ionic reaction for the rate of elimination is slower the greater the concentration of the mineral acid present. If water alone is used, the reaction is more rapid, whilst in the presence of bases or alkali hydroxides it is still more rapid, probably due to the increasing concentration of the acyl ions of the organic acid. It is thus probable that the reaction is to be represented as



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