CXLV.—*The Action of Nitric Acid on Bromophenolic Compounds.*

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IN the course of the work on 2:6-dibromo-4-nitrosophenol (Forster and Robertson, *Trans.*, 1901, **79**, 686), attention was drawn to the simultaneous replacement of bromine by nitroxyl and oxidation of the nitroso-derivative to bromodinitrophenol by means of nitric acid. It seemed desirable to determine, if possible, the conditions under which the bromine was liberated from benzenoid substances, as, although observations had been made, no extensive study of this subject had been undertaken. It is known that when tribromophenol is gently heated with nitric acid, the bromine atom in the para-position is first replaced and subsequently that in the ortho-position. If, however, 2:6-dibromo-4-acetylaminophenol be treated with nitric acid, the operation must be carried out in an acetic acid solution and close to its freezing point, 2-bromo-6-nitro-4-acetylaminophenol being obtained. The presence of the acetyl-amino-group in the para-position relatively to the hydroxyl causes the bromine to be very easily replaced. Armstrong and Lewis have shown (*Proc.*, 1900, **16**, 157) that benzoyl exerts a very remarkable inhibiting effect on certain reactions with phenols. The corresponding benzoylamino-compound was therefore prepared and nitrated, but the action of the nitric acid was found to be only very slightly slower than with the dibromoacetylaminophenol, 2-bromo-6-nitro-4-benzoylamino-phenol being the resulting product.

Auwers has pointed out (*Ber.*, 1902, **35**, 457) that 2:6-dibromo-4-methylnitro-1-ketodihydrobenzene in contact with water passes into 3-bromo-5-nitro-*p*-cresol, that is, the nitro-group appears to wander

into the *meta*-position, replacing the bromine atom. Now in the case of dibromoacetylaminophenol, the replaceable bromine occupies the *meta*-position relatively to the acetyl-amino-group, and it might be supposed, arguing from Auwers' work, that the first substance formed would be a nitroketone which would immediately change into the benzenoid compound thus :

Orton (this vol., 490, 806), in nitrating *s*-trihalogen anilines, found that bromine in the *para*-position, but never in the *ortho*-position, was replaced by a nitro-group, and that the nitroamine which could be isolated as an intermediate compound yields the same product on standing in an acetic acid solution containing a drop of sulphuric acid as was obtained in the direct nitration. As Orton points out, it is not necessarily correct to assume that the nitroamines occur as intermediate products, and, as in the case of phenols, there is no experimental evidence in favour of the view that nitrates are formed, the nitric acid would appear to act directly on the quinonoid tautomeric form.

If the hydrogen of the hydroxyl were replaced by other groupings, it might be supposed therefore that no liberation of bromine would occur, or at all events that the action would be much slower. Accordingly, the acetyl derivatives of tribromophenol and 2:6-dibromo-4-nitrophenol, 2:4:6-tribromoanisole, 2:6-dibromo-4-nitroanisole, and 2:6-dibromo-4-anisidine, and its acetyl and benzoyl derivatives were prepared, and it is of interest that in no case when the experiments were carried out on these substances under similar conditions was replacement of bromine by nitroxyl observed.

Inasmuch as 2:3:4:6-tetrabromo-5-nitrobenzoic acid can be prepared by the nitration of the bromo-acid (Meyer and Sudborough, *Ber.*, 1894, 27, 1584), the conclusion that a quinonoid form is essential for the liberation of bromine is strengthened. The investigation was accordingly extended to the hydroxybenzoic acids. When the dibromo-derivatives of salicylic and *p*-hydroxybenzoic acids are treated with nitric acid, the carboxyl group as well as a bromine atom is displaced, and in both cases 2-bromo-4:6-dinitrophenol results. When, however, tribromo-*m*-hydroxybenzoic acid is treated in the same way, two bromine atoms are replaced by the nitro-group, but the carboxyl group is not affected, and the resulting product in all probability is 2-bromo-

4 : 6-dinitro-3-hydroxybenzoic acid. The acetyl and methoxy-derivatives of the *o*- and *p*-hydroxy-acids behaved in the same way as the simple bromophenols.

EXPERIMENTAL.

p-Nitrosophenol, prepared according to the directions of Bridge (*Annalen*, 1893, 277, 85), was oxidised by nitric acid in the hope that the yield would be a much better one than is the case by the direct nitration of phenol. Baeyer and Caro used well cooled concentrated nitric acid to obtain the nitrophenol, but when the experiment was conducted at 0° with nitric acid of sp. gr. 1.42, I found 2 : 4-dinitrophenol to be the product. The method finally employed was as follows : 400 c.c. of dilute nitric acid (50 c.c. of acid of sp. gr. 1.42 to 150 c.c. of water) were heated to 40° and 50 grams of nitrosophenol gradually added in small portions. The reaction proceeded smoothly, and after all the nitrosophenol had been added, a dark red solution was formed which suddenly became a pasty mass of light brown needles. After one recrystallisation from water (with the aid of animal charcoal), the needles melted at 114° and were almost white. The yield of recrystallised product was 60 per cent. of the phenol taken, the yield by direct nitration of phenol amounting to 15 per cent at most.

Derivatives of 2 : 6-Dibromo-4-aminophenol.

2 : 6-Dibromo-4-acetylaminophenol.—Fifty grams of *p*-nitrophenol were dissolved in glacial acetic acid and two molecular proportions of bromine added to the cold solution. There is considerable development of heat, the temperature rising to 45–60°. The whole was allowed to stand for 12 hours, poured into water, filtered, and washed. In this way, a theoretical yield of 2 : 6-dibromo-4-nitrophenol (m. p. 142°) was obtained. The reduction of this compound to the corresponding amino-derivative was effected by tin and hydrochloric acid. The best yield is obtained by using only a very small quantity of hydrochloric acid, as in excess of that reagent the stannochloride of the base is insoluble. The mass became warm on covering the amine (m. p. 190°) with acetic anhydride, solution occurred accompanied with a violet coloration (compare Meldola, Woolcott, and Wray, *Trans.*, 1896, 69, 1324), and finally the whole solidified to a white paste. It may here be remarked that the violet colour, although noticeable in the large majority of cases, was not always observed. Meldola and his pupils ascribed the colour to an oxidising effect of acetyl peroxide ; here, at all events, it would seem to be due to some impurity in the base. The product is sparingly soluble in hot water, but dissolves easily in alcohol, acetic acid, or alkali, and the needles melt at 185–186°.

The crystals from acetic acid contain acetic acid of crystallisation and melt at 178—179°. On exposure to the air, they effloresce and then melt at 185°. Hölz (*J. pr. Chem.*, 1886, [ii], 32, 68) states that the substance forms small, glistening plates melting at 173—174°, whereas Friedländer and Stange (*Ber.*, 1893, 26, 2262) describe it as crystallising in needles soluble in alkali and melting at 185°:

0.1751 gave 0.2140 AgBr. Br = 52.01.

$C_8H_7O_2NBr_2$ requires Br = 51.78 per cent.

Action of Nitric Acid.—The acetyl compound suspended in glacial acetic acid and cooled to near the freezing point of the solution was treated with $1\frac{1}{2}$ mols. of nitric acid. Bromine was immediately liberated. The yellow product obtained on pouring the solution into ice water, after being washed and dried, was crystallised twice from methyl alcohol. The melting point of 6-bromo-2-nitro-4-acetylaminophenol is 230°:

0.1532 gave 12.8 c.c. nitrogen at 14° and 766 mm. N = 9.91.

0.1316 „ 0.0902 AgBr. Br = 29.23.

$C_8H_7O_4N_2Br$ requires N = 10.18. Br = 29.09 per cent.

The substance is very soluble in the usual organic solvents. All attempts to hydrolyse the compound proved futile.

2:6-Dibromo-4-benzoylaminophenol.—This compound was prepared from the corresponding aminophenol (Forster and Robertson, *loc. cit.*) in order to compare the influence of the benzoyl and acetyl radicles:

0.1211 gave 0.1227 AgBr. Br = 43.12.

$C_{13}H_9O_2NBr_2$ requires Br = 43.13 per cent.

It gives the nitro-derivative with nitric acid in precisely the same way as the acetyl-amino-compound, but the temperature required for the nitration is 18—20°. The product, *2-bromo-6-nitro-4-benzoylaminophenol*, easily dissolves in organic solvents and crystallises in small, yellow needles from methyl alcohol. After several crystallisations, it melts at 247°:

0.1341 gave 0.0729 AgBr. Br = 23.14.

$C_{13}H_9O_4N_2Br$ requires Br = 23.74 per cent.

2:3:6-Tribromo-4-acetylaminophenol.—Eighty grams of dibromo-acetylaminophenol were dissolved in glacial acetic acid, and while the solution was still warm one molecular proportion of bromine was added. After standing for twelve hours, the red prisms which had deposited were filtered off on the pump, washed, and dried. When dried, the crystals gradually became of a light brown colour and the mass weighed 77 grams. From the mother liquor, by addition of water, a yellow precipitate was obtained weighing 3 grams, which

consisted chiefly of bromoanil (m. p. 299—300°). The tribromoacetylaminophenol, after three recrystallisations from alcohol, formed white needles which melted at 224° with decomposition :

0.1141 gave 0.1653 AgBr. Br = 61.66.

$C_8H_6O_2NBr_3$ requires Br = 61.85 per cent.

When nitric acid was poured into an acetic acid solution of tribromoacetylaminophenol at the ordinary temperature, only a tar, small in amount, was obtained. On heating, the only recognisable products were oxalic acid, dibromodinitromethane, and probably bromoanil.

Action of Nitric Acid on the Acetyl Derivatives of 2:6-Dibromo-4-nitrophenol and Tribromophenol.—When nitric acid of sp. gr. 1.5 is poured on either of these acetyl compounds, bromine and nitrous fumes are liberated, but on dilution with water the original substance only is obtained, the action of the acid being apparently destructive. The melting point of tribromophenylacetate is 84°, Schunck and Marchlewski (*Annalen*, 1894, 278, 347) give 82°.

Anisole Derivatives.

2:6-Dibromo-4-nitroanisole.—An attempt to prepare this compound from the corresponding silver phenate and methyl iodide giving only a meagre yield, it was thought that the yield might be improved by the employment of Lander's method of etherification (*Trans.*, 1900, 77, 729). The dibromonitrophenol was dissolved in absolute alcohol and the silver oxide and methyl iodide added in Lander's proportions. After heating for three hours, the filtered solution was poured into dilute alkali, filtered, and dried. In this way, a 60—65 per cent. yield was obtained, and the unaltered phenol was recovered from the alkaline filtrate. Heating for four hours did not materially increase the yield. The white needles from alcohol melted at 123°; Körner (*Gazzetta*, 1874, 4, 390) gives 122.6°.

2:6-Dibromo-4-anisidine.—The reduction of the nitroanisole by tin and hydrochloric acid is slow owing to the insolubility of the compound in the acid. The amine is very easily soluble in the usual organic solvents, and crystallises best from light petroleum in small, white, glistening leaflets melting at 66°. Städel (*Annalen*, 1883, 217, 70) obtained this compound, but does not give its melting point :

0.1537 gave 0.2054 AgBr. Br = 56.87.

$C_7H_7ONBr_2$ requires Br = 56.94 per cent.

The *acetyl* derivative, prepared in the same way as the dibromoacetylaminophenol, forms long, slender needles from methylated spirit, and melts at 206°. It is sparingly soluble in boiling water or petroleum,

moderately so in benzene, and easily so in alcohol, methyl alcohol, ethyl acetate, acetic acid, or chloroform :

0.1860 gave 0.2178 AgBr. Br = 49.83.

$C_9H_9O_2NBr_2$ requires Br = 49.53 per cent.

The *benzoyl* derivative, prepared by means of the Schotten-Baumann reaction, crystallises from alcohol in needles which soften at 174° and melt at 180° . It is easily soluble in methyl alcohol, acetic acid, or alcohol, and moderately so in benzene, but almost insoluble in hot water :

0.1553 gave 0.1524 AgBr. Br = 41.76.

$C_{14}H_{11}O_2NBr_2$ requires Br = 41.99 per cent.

It is noteworthy that tribromoanisole and the above anisole derivatives do not liberate bromine when treated with nitric acid in the cold or at $30-40^\circ$

3 : 5-Dibromosalicylic Acid.

According to Lellmann and Grothmann (*Ber.*, 1884, 17, 2728), this acid can be most easily prepared by dissolving salicylic acid in glacial acetic acid in the cold and adding five atomic proportions of bromine. The liquid, after being allowed to stand for one hour, is poured into water and afterwards digested for some time with water to get rid of a volatile impurity. The product is finally converted into the barium salt, from which the pure acid is liberated. These directions were carried out up to the prolonged digestion with water, and as the acid melted at 216° (compared with 221° for the pure acid) it was regarded as comparatively pure. This, however, is by no means the case, as on attempting to prepare the acetyl derivative from the product melting at 216° , the substance obtained in a state of purity was the *acetyl* derivative of *tribromophenol*: it melted at 84° , and a mixture of it with a specimen of tribromophenyl acetate also melted at 84° ; further, it contained Br = 64.51 per cent. (calc. Br = 61.34 per cent.), was insoluble in caustic soda, and when hydrolysed gave a product melting at 94° , tribromophenol melting at $92-95^\circ$.

In order to ascertain the relative proportion of dibromosalicylic acid to tribromophenol, the crude brominated product (m. p. 202°) was submitted to steam distillation; tribromophenol passed over slowly (m. p. 92°), and the liquid remaining in the flask after filtration and cooling deposited white needles melting at $220-221^\circ$. In this experiment, 28 grams of tribromophenol and 14 grams of the dibromoacid were obtained.

Bromination in chloroform leads to the formation of 5-bromosalicylic

acid (m. p. 164°), and as, in a subsequent experiment conducted according to Lellmann and Grothmann's directions, it was observed that gas was evolved *after* pouring the acetic acid solution into water, the excess of bromine was destroyed by the addition of sodium bisulphite, 5-bromosalicylic acid being again obtained, but no tribromophenol. Finally, the bromination was found to proceed easily in the presence of iodine. Ten grams of salicylic acid were dissolved in glacial acetic acid and 9.7 c.c. of bromine (2.5 mols.) and one gram of iodine were added while the solution was hot. After being allowed to stand for one hour, the solution was heated for a short time, and when cold poured into a concentrated solution of sodium bisulphite, when the acid separated out as a white, crystalline precipitate. This proved to be a mixture of the dibromo- with the mono-salicylic acid, the dibromo-compound largely predominating. The two compounds can, however, be easily separated by fractional crystallisation from glacial acetic acid in which the dibromo-acid is the less soluble. From 25 grams of salicylic acid, 40 grams of pure 3:5-dibromosalicylic acid were obtained, together with 5 grams of an acid melting at 163° , and therefore probably 5-bromosalicylic acid. This is a 75 per cent. yield compared with 30—35 per cent. which can be obtained by Lellmann and Grothmann's method. The melting point of the acid is 221° ; Lellmann and Grothmann found 223° (*loc. cit.*):

0.2284 gave 0.2919 AgBr. Br = 54.39.

$C_7H_4O_3Br_2$ requires Br = 54.05 per cent.

A noteworthy point about this acid is that it decomposes carbonates with difficulty.

Action of Nitric Acid.—On addition of dibromosalicylic acid to nitric acid of sp. gr. 1.42, there is no liberation of bromine in the cold, but on very gently warming, the mass goes into solution with evolution of gas and bromine. After heating for two minutes on a water-bath, the liquid was poured on to ice and the yellow solid, after being collected and washed, crystallised from water. The resulting yellow needles melted at 117° and a mixture of this substance with bromodinitrophenol also melted at 117° , thus identifying the product. The needles were recrystallised from alcohol and analysed:

0.2530 gave 0.1827 AgBr. Br = 30.73.

$C_6H_3O_5N_2Br$ requires Br = 30.41 per cent.

In this experiment, therefore, the carboxyl group in addition to a bromine atom has been replaced by the nitro-group. From 10 grams of dibromosalicylic acid, 7.5 grams of 6-bromo-2:4-dinitrophenol were obtained.

Acetyl-3:5-dibromosalicylic acid, prepared in the usual way, melts

at 156° and crystallises from dilute alcohol in needles or leaflets. It is sparingly soluble in water or light petroleum but easily so in the other solvents:

0.1820 gave 0.2025 AgBr. Br = 47.35.

$C_9H_6O_4Br_2$ requires Br = 47.34 per cent.

Nitric acid of sp. gr. 1.42 to which a few drops of concentrated acid of sp. gr. 1.5 had been added liberated only a trace of bromine at 60°.

Methyl dibromo-*o*-methoxybenzoate was prepared from dibromosalicylic acid by Lander's method, alcohol again being used as solvent. It crystallises from petroleum in beautiful, long prisms which melt at 52° (compare Peratoner, *Gazzetta*, 1886, 16, 417). Dibromo-*o*-methoxybenzoic acid, prepared from the ester, melts at 194° (*loc. cit.*). Neither of these compounds liberates bromine when treated with nitric acid of sp. gr. 1.42 at 60°.

The *acetyl* derivative of 5-bromosalicylic acid does not seem to have been prepared hitherto; it melts at 168° when crystallised from alcohol:

0.2274 gave 0.1658 AgBr. Br = 31.03.

$C_8H_7O_4Br$ requires Br = 30.89 per cent.

3 : 5-Dibromo-4-hydroxybenzoic Acid.

Hlasiwetz and Barth (*Annalen*, 1865, 134, 276) found that by the action of bromine water on *p*-hydroxybenzoic acid they obtained tribromophenol. Beilstein makes the statement, evidently founded on this observation, that bromo-*p*-hydroxybenzoic acid cannot be obtained by direct bromination. Hähle (D.R.-P. 60637) obtained the monobromo-acid, but on attempting further bromination tribromophenol was the sole product. After the experience gained in the bromination of salicylic acid, it seemed advisable to re-examine the behaviour of *p*-hydroxybenzoic acid towards bromine. It was found that dibromo-*p*-hydroxybenzoic acid can be easily and readily obtained by carrying out the bromination in acetic acid in the presence of iodine and pouring the product into sodium bisulphite solution in the same way as with salicylic acid. The yield is 80 per cent. of the theoretical, and the melting point 267—268°. Methyl dibromo-*p*-methoxybenzoic acid was found to melt at 90—91°; Balbiano (*Gazzetta*, 1883, 13, 66) records 91.5—92° (corr.) as the melting point. On analysis:

0.2285 gave 0.2897 AgBr. Br = 53.95.

$C_7H_4O_5Br_2$ requires Br = 54.05 per cent.

On nitration, this acid yielded 2-bromo-4 : 6-dinitrophenol, just as in the case of dibromosalicylic acid.

The *acetyl* derivative crystallises from alcohol in needles melting at 207°. Nitric acid of sp. gr. 1.42 did not liberate bromine from it at 60° :

0.2527 gave 0.2810 AgBr. Br = 47.32.

$C_9H_6O_4Br_2$ requires Br = 47.34 per cent.

Balbiano (*Gazzetta*, 1884, 14, 10) records that 2 : 6-dibromo-4-nitro-anisole results from the action of fuming nitric acid on dibromoanisic acid. In this case, therefore, the carboxyl group but not the bromine atom has been replaced by the nitro-group.

The *ethyl ester* was prepared by Fischer and Speier's method (*Ber.*, 1895, 28, 3252). It melts at 99° and crystallises in needles from alcohol :

0.2556 gave 0.2969 AgBr. Br = 49.43.

$C_9H_8O_3Br_2$ requires Br = 49.38 per cent.

3-Bromo-4-hydroxybenzoic acid has been prepared by Hähle (*loc. cit.*), who does not give its melting point, and by Paal (*Ber.*, 1895, 28, 2411), who obtained it as white needles melting at 148°, by the oxidation of the corresponding aldehyde. It may be obtained by brominating *p*-hydroxybenzoic acid in acetic acid solution in the absence of iodine, and purified by the method recommended by Paal, namely, crystallisation from ethyl acetate and petroleum :

0.1575 gave 0.1377 AgBr. Br = 37.21.

$C_7H_5O_3Br$ requires Br = 36.87 per cent.

The *acetyl* derivative, melting at 155°, crystallises from alcohol in needles :

0.1839 gave 0.1347 AgBr. Br = 31.17.

$C_8H_7O_4Br$ requires Br = 30.89 per cent.

Bromination of m-Hydroxybenzoic Acid.

Ten grams of *m*-hydroxybenzoic acid were dissolved in glacial acetic acid, gently warmed, and three molecular proportions of bromine added. After the expiration of one hour, the crystals "A" which had deposited were filtered off, and the mother liquor was evaporated, when an oil "B," which quickly solidified, was obtained.

Product "A".—It was soon found that this was a mixture. By repeated fractional crystallisation from hot water, a product consisting of small tufts of glistening needles, which melted at 201—202°, was ultimately obtained. This proved on analysis to be a dibromo-*m*-hydroxybenzoic acid crystallising with one mol. of water :

0.1282 lost 0.0076 H_2O . $\text{H}_2\text{O} = 5.93$.

0.1983, dried for 4 hours at 110° , gave 0.2504 AgBr . $\text{Br} = 53.74$.

$\text{C}_7\text{H}_4\text{O}_3\text{Br}_2 \cdot \text{H}_2\text{O}$ requires $\text{H}_2\text{O} = 5.75$ per cent.

$\text{C}_7\text{H}_4\text{O}_3\text{Br}_2$ requires $\text{Br} = 54.05$ per cent.

As the determination of the constitution of this acid lay outside the scope of this inquiry, and the amount of *m*-hydroxybenzoic acid at my disposal was small, the further investigation of the substance was not attempted. It is probably 4 : 6-dibromo-3-hydroxybenzoic acid.

A substance melting at 212° and consisting of hair-like needles was also obtained, but was too small in amount for examination. Product "B" consisted mainly of tribromo-*m*-hydroxybenzoic acid and melted at 144° .

Tribromo-m-hydroxybenzoic Acid.—Werner (*Bull. Soc. Chim.*, 1886, [ii], 46, 276) obtained this acid from *m*-hydroxybenzoic acid by using bromine water, but it was thought better to adopt the following method of preparation. Five grams of *m*-hydroxybenzoic acid were made into a paste with glacial acetic acid and three mols. of bromine were added. Heat was developed, and after allowing the mixture to stand for two hours water was added and the mass filtered off, washed, and dried on porous earthenware. On recrystallisation from water, the needles melted at 146 — 147° , which is the melting point recorded by Werner.

Action of Nitric Acid.—The experiment on tribromo-*m*-hydroxybenzoic acid was carried out precisely in the same way as with dibromosalicylic acid. On pouring the product into water and filtering, a yellow solution was obtained which deposited a yellowish powder on concentration. It was recrystallised twice from water, in which it is freely soluble, and melted at 217 — 218° with decomposition. The calcium salt is somewhat explosive. Determination of bromine in the substance shows that two atoms of that element have been replaced by nitroxy, the resulting acid being a bromodinitro-*m*-hydroxybenzoic acid, and probably the 2-bromo-4 : 6-dinitro-acid :

0.1928 gave 0.1192 AgBr . $\text{Br} = 26.31$.

$\text{C}_7\text{H}_3\text{O}_7\text{N}_2\text{Br}$ requires $\text{Br} = 26.06$ per cent.

The acetyl and methoxy-derivatives of this acid were not prepared owing to lack of material.

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