# **108.** *The Significance of the Bromine Cation in Aromatic Substitution. Part II. Preparative Applicability.*

By D. H. DERBYSHIRE and WILLIAM A. WATERS.

Acid solutions of hypobromous acid contain a very much higher concentration of bromine cations than do acid solutions of free bromine. Highly reactive solutions containing bromine cations can be made by adding mercuric or silver salts gradually to solutions of bromine in water or acetic acid in the presence of either nitric or sulphuric acid. Benzene, chlorobenzene, bromobenzene, and *p*-dibromobenzene can be brominated with such mixtures in 2N-nitric acid; benzoic acid and methyl benzoate require a stronger nitric acid solution, whilst nitrobenzene, 2 : 4-dinitrotoluene, and *m*-dinitrobenzene need 90% sulphuric acid. The expected aromatic bromination products have been isolated from these substances in 60—80% yield.

Bromine cations can also be formed by adding potassium bromate to acid solutions of bromine, and these mixtures too constitute active brominating agents.

Acetic and propionic acids, methyl alcohol, and dioxan all resist attack by bromine cations in 2N-mineral acid.

The experimental evidence substantiates the polar-activation theory of aromatic substitution.

THE kinetic evidence given in Part I (preceding paper) shows that hypobromous acid becomes a powerful brominating agent in the presence of mineral acid owing to the production of bromine cations (1),

$$H^+ + HOBr \overset{K}{\rightleftharpoons} (H_2OBr)^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and the present paper indicates the importance of this equilibrium in preparative chemistry and gives examples of its applications.

The preparation of free hypobromous acid requires such care that the reagent as such cannot conveniently be used in quantity, and, as the following calculations show, only exceedingly minute concentrations of bromine cations can be present in aqueous solutions of free bromine.

The equilibrium constant for bromine hydrolysis (2) has the low value of $4{\cdot}7 \times 10^{-9}$ at room temperature (Liebhafsky, *J. Amer. Chem. Soc.*, 1934, **56**, 1500), and consequently the

$$H_2O + Br_2 \underset{K_{hyd.}}{\rightleftharpoons} HOBr + H^+ + Br^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

degree of hydrolysis $\alpha$ of a bromine solution of concentration $C$ in a medium of acidity $[H^+]$ is given by the relation

$$\alpha^2C^2[H^+]/C(1 - \alpha) = 4{\cdot}7 \times 10^{-9}$$

whence, writing $[H_2OBr^+] = K[H^+][HOBr]$ and remembering that $\alpha$ is small in acid solutions, we can deduce that

$$[H_2OBr^+] = \frac{\alpha C[H^+]}{K} = \text{approx.}\ \frac{7 \times 10^{-5}}{K}\sqrt{C[H^+]}$$

whilst for equivalent solutions of hypobromous acid

$$[H_2OBr^+] = C[H^+]/K$$

For M/10-solutions these two concentrations of bromine cations differ by an order of $10^4$ in N-acid, and become comparable only under conditions approaching neutrality (pH *ca.* 6) in which $\alpha$ increases. However, in these neutral solutions $[H_2OBr^+]$ is so minute that reactions due to bromine cations can no longer be clearly detected (compare the bromination of sodium toluene-ω-sulphonate and of sodium *p*-anisate studied in Part I).

However in acid media one can easily carry out brominations by means of bromine cations by adopting the simple procedure of adding to a bromine solution a further reagent which is capable of removing bromide anions from the system. For example, if silver nitrate is added to an aqueous bromine solution then, since the solubility product of silver bromide is $7{\cdot}7 \times 10^{-13}$ at 25°, the conversion of bromine into hypobromous acid, *via* the hydrolysis (2), is so complete that we may write

$$[H_2OBr^+] = [H^+][HOBr]/K = [H^+]([Ag^+]\ \text{added})/K$$

Mercuric salts can be used in the same way, and since mercuric bromide, though un-ionised in acid media, is soluble in water the following simple experiments may be conducted to demonstrate the production and reactivity of bromine cations.

A little bromine water is added to an aqueous solution of benzene in each of two vessels. (i) To one sample dilute nitric acid is added; the solution remains of a clear orange colour. (ii) To a second sample dilute mercuric nitrate solution is added; the colour almost vanishes owing to the conversion of bromine into inactive hypobromous acid. (iii) Sample (ii) is then treated dropwise with dilute nitric acid; the bromine colour begins to reappear and the mixture soon becomes turbid owing to the separation of droplets of bromobenzene. As the reaction proceeds the colour becomes fainter again. (iv) When the acidified sample (i) is treated with mercuric nitrate solution, the bromine colour fades and droplets of bromobenzene separate.

On the preparative scale we have found that benzene can be converted into bromobenzene in 80% yield by adding silver nitrate solution dropwise to a stirred emulsion of benzene in 2N-nitric acid containing bromine. The 20% loss in yield is due to the formation of dibromobenzene. Mercuric nitrate gave a 70% yield, but the separation of the product was rather more difficult, since mercuric bromide is both slightly soluble in ether and slightly volatile. Lead nitrate was useful only for rather more reactive substances such as toluene: lead bromide is decidedly more soluble than silver bromide.

Aromatic substances which are very insoluble in water can be brominated in a similar way by using aqueous acetic acid containing either nitric or sulphuric acid. In this way we have successfully brominated chlorobenzene, bromobenzene, *p*-dibromobenzene, benzoic acid, and methyl benzoate, and have isolated in high yield the expected products of their cationoid aromatic substitution. Inactive *meta*-substituting substances, such as nitrobenzene, *m*-dinitrobenzene, and 2 : 4-dinitrotoluene do not react appreciably with the low concentrations of bromine cations that are present in 1—2N-acid, but they can all be brominated very effectively in 90% sulphuric acid by the use of silver sulphate.

Silver sulphate is soluble in concentrated sulphuric acid, and when bromine is added to such a solution the mixture merely becomes opalescent, presumably because the acidity of the solution has diminished the hydrolysis of bromine so much that the solubility product of silver bromide is not greatly exceeded. When, however, the aromatic compound is added to this mixture, silver bromide is steadily deposited as the bromination proceeds. Evidently the removal of hypobromous acid, *via* $(H_2OBr)^+$, increases the bromide anion concentration so that silver bromide can be precipitated, and this simultaneous removal of both $(H_2OBr)^+$ and $(Br^-)$ allows the complete reaction with bromine to be effected. With *m*-dinitrobenzene however heating to 100° was necessary. In the absence of silver sulphate these inactive nitro-compounds do not react, even at 100°, with bromine in 90% sulphuric acid, but when it is added the expected bromo-derivative can easily be prepared in 60—80% yield.

Since no other method of bromination of these deactivated aromatic compounds, such as heating to a high temperature with an iron catalyst, gives comparable yields of clean material it is evident that free bromine cations must have an extremely high degree of reactivity. Nevertheless pyridine sulphate withstood attack under our conditions at 100°. It is possible that the free ion $Br^+$ rather than the solvated ion $(H_2OBr)^+$ may be present in these concentrated acid solutions, but we have not attempted as yet to discriminate between them. This direct experimental proof that the bromine cation will attack substances such as benzoic acid and nitrobenzene which are not attacked by molecular bromine substantiates the theory that the catalysts normally used to effect aromatic bromination do so by polar activation, *e.g.*, $Br_2 + FeBr_3 \rightleftharpoons (Br^+)(FeBr_4^-)$; their lower efficacy may perhaps indicate that ion-pairs rather than *free* bromine cations are often formed. Hence the major advantage of our new procedure may lie in the fact that the bromine cations are formed in solution and not on the surface of a solid catalyst.

The physical principle of effecting cationoid bromination by removing bromide anions from an acid solution of bromine can be applied practically in other ways than those described above. For instance in 1875 Krafft (*Ber.*, 1875, **8**, 1045) noted that a mixture of bromine with potassium bromate in 33% sulphuric acid constituted a brominating agent which would readily brominate both benzene and bromobenzene at room temperature, and we have confirmed that bromine–bromate mixtures are very effective in 50% sulphuric acid. The rôle of the bromate is clearly the removal of bromide anions

$$5H^+ + 5Br^- + HBrO_3 \rightleftharpoons 3H_2O + 3Br_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

and from the equilibria (1), (2), and (3) can be derived the relation

$$[H_2OBr]^+ = \text{Const.}\ [H^+][Br_2]^{\frac{2}{5}}[HBrO_3]^{\frac{1}{5}}$$

which indicates that even small concentrations of bromates should be exceedingly effective as catalysts.

It is interesting to note that the direct iodination of nitrobenzene has been effected by Masson and Hanby (*J.*, 1938, 1699) by the use of a very similar system in which they considered that iodine cations were present. Many other similar reaction mixtures for the preparation and study of the reactive cations of the halogens can now be envisaged.

It may be noted that we have, as yet, effected only the cationoid bromination of aromatic nuclei; alkyl side-chains, as in 2 : 4-dinitrotoluene, do appear not to be attacked. Though we have not attempted to carry out the cationoid bromination of saturated aliphatic molecules in concentrated sulphuric acid we have found that carefully purified specimens of acetic acid, propionic acid, methyl alcohol, and dioxan were all quite unaffected by hypobromous acid in 2N-sulphuric acid solution. In each case the drop in titre of the hypobromous acid was not detectable after an hour at 22·4°. This would appear to be a significant indication that the reaction (4) does not normally occur in aqueous solution, although it conflicts with the recent

$$H_2OBr^+ + R_3C{-}H \longrightarrow Br{-}CR_3 + H_3O^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

demonstration by Arcus, Campbell, and Kenyon (*J.*, 1949, 1510) that a Walden inversion can be brought about by an analogous exchange of ions in carbon tetrachloride solution. The discrepancy may perhaps be due to the solvation of the bromine cation and the stabilising effect of the ionising solvent on the substitution reaction as a whole.

## EXPERIMENTAL.

*Bromination of Benzene.*—Benzene (22 ml., 0·25 mol.) and bromine (6·5 ml., 0·125 mol.) were stirred together in 1 l. of 2N-nitric acid, and 22 g. (0·125 mol.) of silver nitrate in water (100 ml.) were added gradually during 1½ hours. Light was excluded from the reaction mixture. After removal of residual bromine by sodium sulphite the product was extracted with ether, dried, and fractionated. It gave 15 g. (80% calc. on the bromine) of pure bromobenzene. Rapid addition of the silver nitrate diminished the yield and produced more dibromobenzene. In the absence of silver nitrate there was no reaction.

*Brominations of Chlorobenzene, Bromobenzene, and* p-*Dibromobenzene.*—Chlorobenzene (12 ml., 0·1 mol.) and bromine (5·2 ml., 0·1 mol.) were dissolved in a mixture of glacial acetic acid (300 ml.) and diluted nitric acid [50 ml. (*d* 1·4) in 100 ml. of water]. To the stirred cold mixture, silver nitrate solution (17 g. in 50 ml. of water) was added dropwise during ½ hour. The resulting solution was diluted with water (2 l.), freed from residual bromine, partly neutralised and extracted with ether. The dried extract was fractionated and the resulting *p*-chlorobromobenzene crystallised from alcohol; yield, 11 g.; m. p. 65—67°.

Bromobenzene (17 g.) was treated similarly and gave 13 g. of *p*-dibromobenzene, of m. p. and mixed m. p. 85—86°. *p*-Dibromobenzene (12 g.) was brominated similarly in a mixture of 700 ml. of acetic acid, 65 ml. of nitric acid (*d* 1·4), and 50 ml. of water at 40°. The reaction product contained an involatile residue which was separated by fractional crystallisation from ethyl alcohol into 1 : 2 : 4-tribromobenzene, m. p. 42—44°, and 1 : 2 : 4 : 5-tetrabromobenzene, m. p. 177—178°.

*Bromination of Benzoic Acid and Methyl Benzoate.*—Benzoic acid (13 g., 0·1 mol.) and bromine (5·2 ml., 0·1 mol.) were dissolved in a mixture of glacial acetic acid (300 ml.), concentrated nitric acid (65 ml.), and water (50 ml.), and treated dropwise, with vigorous mechanical stirring, with aqueous silver nitrate (17 g. in 100 ml. of water). The resulting solution yielded 14 g. of *m*-bromobenzoic acid, m. p. 152—154°. Methyl benzoate (16 g.) was treated similarly and the product was distilled under reduced pressure; it gave 7 g. of methyl *m*-bromobenzoate, b. p. 117—130°/20 mm., m. p. 28—30°.

*Bromination of Nitrobenzene and 2 : 4-Dinitrotoluene.*—Nitrobenzene (10 ml., 0·1 mol.) and bromine (5·2 ml., 0·1 mol.) were dissolved in a mixture of 90 ml. of concentrated sulphuric acid and 10 ml. of water, and silver sulphate (17 g., 0·1 mol.) was then added. The mixture was shaken mechanically for 16 hours, after which time the colour of the bromine had almost disappeared and silver bromide had been precipitated. The resulting solution was diluted with water, freed from remaining bromine, and extracted with ether. The dried extract solidified on cooling and gave 14·8 g. (70%) of *m*-bromonitrobenzene, m. p. and mixed m. p. 55—56°.

2 : 4-Dinitrotoluene (18·5 g., 0·1 mol.) was brominated in a similar manner during 36 hours and gave 16 g. (80%) of 6-*bromo*-2 : 4-*dinitrotoluene* which crystallised from alcohol in long pale yellow needles, m. p. 57·5—58° (Found: N, 10·6. $C_7H_5O_4N_2Br$ requires N, 10·7%). These became deep yellow on prolonged exposure to sunlight and gave a very intense reddish-purple colour when treated with acetone and aqueous potassium hydroxide. The compound was not hydrolysed when refluxed with alcoholic potassium hydroxide, and hence the bromine is neither adjacent to a nitro-group nor in the side-chain.

*Bromination of* m-*Dinitrobenzene.*—*m*-Dinitrobenzene (8·5 g., 0·05 mol.), bromine (3 ml.), and silver sulphate (8 g.) were dissolved in concentrated sulphuric acid (100 ml.). The mixture was left overnight without the onset of reaction; it was then heated under a reflux at 100° for 11 hours, during which silver bromide was steadily deposited. The resulting solution, after dilution with water, yielded 6·5 g. of a solid organic product which, after repeated crystallisation from alcohol, gave 5·5 g. of 1-bromo-3 : 5-dinitrobenzene of m. p. 77—78° (Found: Br, 32·0. Calc. for $C_6H_3O_4N_2Br$: Br, 32·3%). Elion (*Rec. Trav. chim.*, 1923, **42**, 145) gives m. p. 77°.

Pyridine was heated at 100° in a similar mixture for 2 days but gave no recognisable quantity of bromination product.

*Bromination of Benzoic Acid with Bromine and Bromic Acid.*—Benzoic acid (13 g., 0·1 mol.) and bromine (2·1 ml.) were dissolved in a mixture of glacial acetic acid (250 ml.) and concentrated sulphuric acid (150 ml.). A solution of potassium bromate (4 g. in 50 ml. of warm water) was added slowly during ½ hour, with vigorous stirring, and the temperature maintained at 25° by external cooling. Precipitation of *m*-bromobenzoic acid was noted after about 20 minutes' reaction. After the mixture had been stirred continuously for a further hour, a second, similar portion of potassium bromate solution was added slowly during ½ hour. Finally the precipitated *m*-bromobenzoic acid, m. p. 150—154° (11 g.), was collected on a sintered-glass filter, washed with a little water, and dried.

*Brominations effected with Mercuric Nitrate.*—(i) Benzene (15 ml.), bromine (5·2 ml.), acetic acid (400 ml.), and nitric acid [33 ml. (*d* 1·4) in 100 ml. of water] were stirred together at room temperature, and mercuric nitrate solution (17 g. in 75 ml. of water) was dropped in during ½ hour. The bromine had then disappeared. The product was diluted, partly neutralised (sodium carbonate), and repeatedly extracted with ether. The extract, when washed with alkali, dried, and fractionated, gave 10 g. (70%) of bromobenzene.

(ii) Benzoic acid (13 g., 0·1 mol.), bromine (5·2 ml.), glacial acetic acid, and nitric acid [65 ml. (*d* 1·4) and 50 ml. of water] were stirred together at about 23°, and an aqueous solution of mercuric nitrate (17 g. as above) was added during ½ hour; mercuric bromide was deposited. After a further ½ hour the solution was poured into water (2 l.), freed from bromine (sodium sulphite), and extracted with ether. The extract was freed from mercuric salts by means of hydrogen sulphide and then concentrated. From the residue 12 g. (60%) of pure *m*-bromobenzoic acid, m. p. and mixed m. p. 154—155°, were obtained by recrystallisation from alcohol–water.

*The Stabilities of Some Aliphatic Compounds.*—(i) *Acetic acid.* A product purified by fractional distillation from chromium trioxide, and stable both to free bromine and to potassium permanganate, was used. 20 Ml. were mixed with 20 ml. of 10N-sulphuric acid and 10 ml. of approx. 0·02N-hypobromous acid and kept in a thermostat at 17° for 20 minutes. There was no change in the potassium iodide–thiosulphate titre of the mixture.

(ii) *Propionic acid.* The acid was purified by heating 50 ml. with 2 g. of chromium trioxide on a steam-bath for 2 hours, and was finally fractionated under reduced pressure from fresh chromium trioxide. It had b. p. 55°/23 mm. and wa sstable to permanganate. A mixture of 5 ml. in 15 ml. of water, 20 ml. of 5N-sulphuric acid and 10 ml. of *ca.* 0·02N-hypobromous acid exhibited no titre change during 50 minutes' storage at room temperature.

(iii) *Methyl alcohol.* A sample, purified by refluxing with sodium hypoiodite, was distilled from silver nitrate and finally dried over quicklime and fractionated; it then had b. p. 66°/675 mm. A mixture similar to that of (ii) above showed no change in titre during 40 minutes.

(iv) *Dioxan.* 150 Ml. of dioxan, 8 ml. of bromine, and 60 ml. of 50% sulphuric acid were heated at 100° for ½ hour. Excess of bromine was removed with sulphur dioxide, and the solution was then made alkaline with aqueous potassium hydroxide. The lower aqueous layer was removed and the remaining dioxan was dried (KOH) and fractionated carefully. The pure product, b. p. 100·5°/767 mm., was stable both to cold neutral potassium permanganate solution and to an acid hypobromous acid solution similar to that used for (ii) above.

One of us thanks the Department of Scientific and Industrial Research for a Maintenance Grant.

THE DYSON PERRINS LABORATORY, OXFORD.

[*Received, October* 31*st*, 1949.]