

The replacement of Sulphonic Acid groups in Amino-sulphonic Acids by Halogen Atoms.

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In the preparation of 2:6-dibromo-sulphanilic acid from sulphanilic acid, tribromoaniline is always obtained as a bye-product and the amount of this becomes very appreciable unless certain precautions are taken. (Heinichen, *tynnalén*, 1889, 253, 268.) The formation of *s*-tribromoaniline is also observed during the formation of 2:6-dibromo-*p*-aminobenzoic acid. These observations indicate that a sulphonic or carboxylic group in the para position with respect to an amino group is readily replaced by bromine.

This has been confirmed by experiments on the action of bromine water on solutions of 2:6-dibromo-sulphanilic acid, the results prove that an almost quantitative yield of *s*-tribromoaniline can be obtained in the cold and that the other product is sulphuric acid.

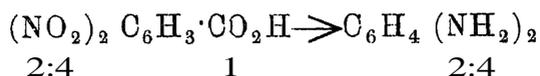
An examination of the literature shows that *s*-tribromoaniline is also formed during the bromination of *o*-aminobenzene-sulphonic acid but not during the bromination of the isomeric *meta* acid.

The replacement of halogen atoms by nitro groups is a well known phenomenon and has been studied by Zincke (*J. Pr. Chem.* 1900, (11), 61, 561); Dahmer (*Annalen* 1904, 333, 346); Robertson (*J. C. S. Trans.* 1908, 95, 793; 1912, 101, 1961); Gibbs and Robertson (*ibid* 1914, 105, 1885) and Robertson and Briscoe (*ibid* 1912, 101, 1964) in the case of brominated phenols. The replacement of carboxylic groups by halogen atoms has also been observed by Gibbs and Robertson (*loc. cit.*) and the replacement of $\cdot\text{CO}_2\text{H}$, $\cdot\text{CHO}$, $\cdot\text{CO}$, CH_3 groups by nitro groups in the case of aromatic hydroxy compounds has been investigated by Salway (*ibid* 1909, 95, 115); Harding and Weizmann (*ibid* 1910, 97, 1126); Harding (*ibid* 1911, 99, 1585; 1914, 105, 2790) and Thomes and Siebeling (*Ber.* 1911, 44, 2115.) The reactive positions are the 2, 4 and 6 positions with respect to the hydroxyl group and compounds in which the replaceable groups are in the 3 and 5 positions are not decomposed by nitric acid.

A reaction of somewhat analogous type is the splitting of certain amino-benzhydrols by the action of bromine (Clarke and Patch *J. Am. Chem. Soc.* 1912, 34, 912; Esselen and Clarke *ibid* 1914, 36, 308). For example with *p*- or *o*-amino-benzhydrol $C_6H_5 \cdot CH(OH) \cdot C_6H_4 \cdot NH_2 + Br_2 \rightarrow C_6H_5 \cdot CHO + C_6H_4 Br \cdot NH_2 + HBr$, the complex $C_6H_5 \cdot CH(OH)$ becomes replaced by bromine. Here also decomposition does not occur with *m*-amino or with unsubstituted benzhydrols, but does with all benzhydrols containing an amino or alkylated amino group in the ortho or para position to the $C_6H_5 \cdot CH(OH)$ group.

Blanksma (*Rec. Trav. Chim.* 1905, 24, 320) has observed that, during the reduction of certain aromatic nitro compounds by tin and hydrochloric acid, atoms or groups of atoms are eliminated from the benzene nucleus and replaced by hydrogen.

The groups thus replaced are bromine, iodine, carboxylic and sulphonic provided they are in the ortho or para position with respect to the original nitro group, for example:—



The halogen atoms in *o*- or *p*-substituted anilines can also be removed by a process of reduction, for example:—



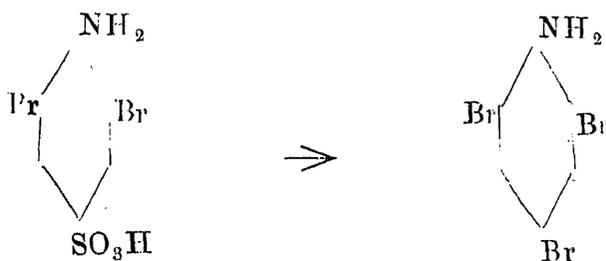
(Compare also Jackson *Am. Chem. J.* 1896, 18, 467; Jacobson *Ber.* 1888, 21, 2826). Kelbe (*Ber.* 1882, 15, 39; 1883, 16, 67) and Heller (*ibid* 1913, 46, 2703) have observed the removal of sulphonic acid groups from hydroxy-anthraquinone-sulphonic acids by means of halogens and Schmidt (*Ber.* 1904, 37, 63) has shown that the nitro-group in ∞ nitro-anthraquinone can be replaced by the sulphonic acid group by merely warming the nitro-compound with an aqueous solution of neutral alkali sulphite. He has also proved that a sulphonic acid group in the ∞ position in the anthraquinone molecule is readily replaced by ethoxy or methoxy groups.

Blanksma (*Rec. Trav. Chim.* 1910, 29, 377) has made use of the readiness with which sulphonic acid or carboxylic acid groups in the ortho or para position with respect to an amino group can be replaced by bromine for elucidating the constitution of certain amino-sulphobenzoic acids containing all three groups— NH_2 , CO_2H , SO_3H .

All these researches indicate the reactivity of certain substituents when in the positions 2, 4 or 6 with respect to an amino or hydroxy group in an aromatic compound.

The experiments described in this paper were undertaken with the object of studying the action of halogens on various amino-sulphonic and amino-carboxylic acids including some of the naphthalene series.

The results indicate that when bromine is employed, an almost quantitative yield of the compound formed by replacing the sulphonic acid group by bromine is obtained, for example :—



2 : 6-Dibromosulphanilic acid

s-Tribromaniline.

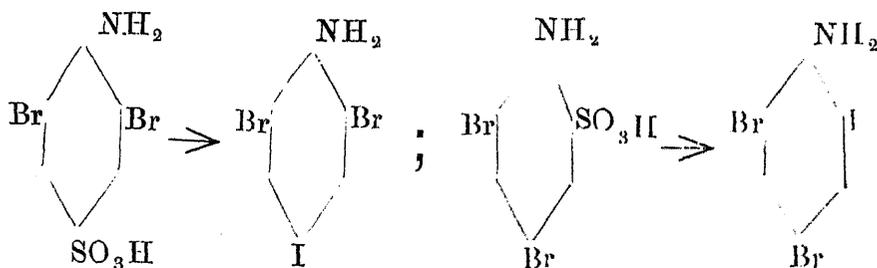
The replacement can be brought about by means of bromine water, fresh potassium hypobromite solution, or an acidified solution of bromide and bromate of potassium. The yield in all cases is over 90% of the theoretical and the other product is sulphuric acid. Similar results are obtained when 4 : 6-dibromoaniline-2-sulphonic acid is used.

Chlorine reacts with the two isomeric dibromo-aniline-sulphonic acids but the products are not pure 4-chloro-2 : 6-dibromo- and 2-chloro-4 : 6-dibromo-anilines, but mixtures containing tribromo-aniline. The formation of such mixtures can most easily be explained by assuming that bromine is displaced from one molecule of the dibromo acid and reacts with a second molecule yielding tribromo-aniline. The replacement of bromine by chlorine in bromoanilines has already been observed by several investigators. Wegscheider (*Monatshefte* 1897, 18, 329) was able to show that at 240° hydrochloric acid transforms s-tribromo-aniline into the corresponding trichloro compound. Chatterway and Orton (*J. C. S. Trans.* 1901, 79, 822), have shown that the chlorine atom in acetylchloroamino-2 : 4-dichlorobenzene is able to displace bromine in such compounds as s-tribromoaniline and 2-chloro-4 : 6-dibromoaniline and in the latter case they were able to isolate a certain amount of a dichloro-bromo-aniline.

Orton and Reed (*ibid*, 1907, 91, 1543) have shown that in the chlorination of 2:4-dibromoaniline and other bromo derivatives of aniline mixtures of dichlorobromoanilines and *s*-tribromoaniline are formed. From the products from 2:4-dibromoaniline they obtained, by fractional crystallisation, a well defined crystalline substance melting at 110° and the results of analysis proved that this consisted of 59.3% of tribromoaniline and 40.7% of dichlorobromoaniline assuming that these are the only two compounds present. In some of our experiments on the action of chlorine on 4:6-dibromoaniline-2-sulphonic acid a crystalline product was obtained from which well defined crystals softening at 107-109° and melting at 110° were isolated after four crystallisations from alcohol. A product with the same melting point was also obtained by the action of chlorine on 2:4-dibromoaniline.

The analysis of these crystals agreed closely with the results given by Orton and Reed (*loc. cit*). A melting point curve of mixtures of *s*-tribromoaniline and 2-chloro-4:6-dibromoaniline has been examined (see figure 1, page 142) and it is shown that this curve is practically a straight line and that a mixture melting at 110° has the composition given by Orton and Reed.

Solutions of iodine have no action on the dibromoanilinesulphonic acids even at 100°, but the replacement of the sulphonic acid group by iodine can be effected by means of iodine monochloride dissolved in glacial acetic acid. The products formed are respectively 2:6-dibromo-4-iodo-aniline and 2:4-dibromo-6-iodo-aniline, neither of which has been previously prepared.



Experiments were also made with the corresponding dibromo-aminocarboxylic acids, but it was found that the carboxylic group is more difficult to displace. With bromine good yields of *s*-tribromoaniline were obtained, but with chlorine and iodine monochloride replacement was not observed in the case of the *para*. and only to a very slight extent in the case of the *ortho* compound.

Comparative experiments were made with the object of determining whether the ortho or para sulphonic acid group is the more readily replaced by bromine. Although the experiments do not show close agreement among themselves, they indicate that the sulphonic acid group which is in the ortho position to an amino is more reactive than the same group when in the para position, as in most of the experiments made the yield of tribromoaniline was greater when aniline-*o*-sulphonic acid was used.

Experiments were made with 2-naphthylamine-6-sulphonic acid. The addition of bromine water to an aqueous solution of the ammonium salt of the acid produced no precipitate and the colour of the first few drops of the bromine water was not discharged. The addition of a bromate-bromide mixture also produced no precipitate. So far experiments with other amino-sulphonic acids of the naphthalene series have not been tried.

In order to show that a sulphonic acid group in the meta position, with respect to the amino group, is inactive and not readily displaced by halogens, the action of chlorine, bromine and iodine monochloride on 2:4:6-tribromo-3-aminobenzene-sulphonic acid and the corresponding carboxylic acid was studied, but in no case was the formation of a tetra halogenated aniline observed.

EXPERIMENTAL.

I. EXPERIMENTS WITH 2:6-DIBROMOSULPHANILIC ACID.

The acid was prepared by passing air, saturated with bromine vapour, through an aqueous solution of sulphanilic acid. After the requisite amount of bromine had been used, the precipitate of *s*-tribromoaniline was removed and the clear filtrate concentrated when nearly colourless crystals of the dibromosulphanilic acid were obtained.

A. Replacement of the Sulphonic Acid Group by Bromine.

Expt. 1. The theoretical amount of bromine water was added to a well stirred aqueous solution of 0.4008 gram of potassium 2:6-dibromosulphanilate, $\text{NH}_2 \cdot \text{C}_6\text{H}_2\text{Br}_2 \cdot \text{SO}_3\text{K}$, at the ordinary temperature (23-26°C). The precipitate of tribromoaniline was removed, washed with water and dried in the air until constant. Weight of the precipitate = 0.353 gram and the melting point 119°. This corresponds with a 98.6% yield of tribromoaniline, the melting point of which is 119.4°.

Expts. 2, 3, 4 and 5. were similar to 1 and the yields of tribromoaniline varied from 92.3 to 100%.

In some of these experiments the filtrate from the tribromoaniline was tested for sulphuric acid and the amount of sulphuric acid determined.

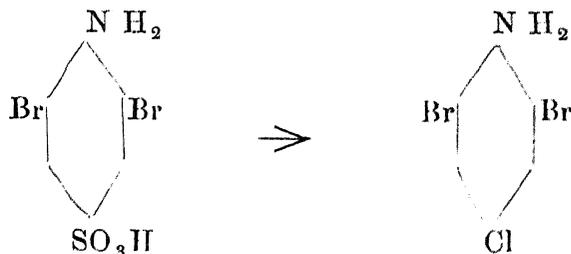
The amounts found varied from 90-106% of the theoretical value.

Expt. 6. The theoretical amount of freshly prepared potassium hypobromite solution (1 molecule) was gradually added to an aqueous solution of 0.512 gram of the dibromo acid and the precipitate treated as in Expt. 1. The weight of the precipitate was 0.426 gram and its melting point 118-119°. This corresponds with a 90% yield.

Expt. 7. Similar to 6. The yield of tribromoaniline was 95% and the melting point 117-119°.

Expt. 8. A solution of 0.5462 gram of the dibromo acid containing a slight excess of potassium bromate and potassium bromide was gradually acidified with sulphuric acid and the precipitated tribromoaniline removed. The weight was 0.49 gram, and the melting point 116-118°, corresponding with a 97% yield.

B. Replacement of the Sulphonic Acid Group by Chlorine.



Expt. 9. The addition of the theoretical amount of chlorine water to a well stirred aqueous solution of the potassium salt of the 2:6-dibromo acid gave a minute quantity of a brown precipitate containing potassium.

Expt. 10. A similar experiment was made using 0.606 gram of the free acid in place of the potassium salt. The addition of the chlorine water produced a brown colouration. A small amount of a brown precipitate melting at 97° was obtained, but the amount was too small for investigation.

Expt. 11. The theoretical amount of a freshly prepared solution of potassium hypochlorite was added to a well stirred

solution of 0.447 gram of the dibromo acid acidified with hydrochloric acid at the ordinary temperature. A small amount of a brown precipitate softening at 80° and melting at 97° was obtained.

Expts. 12, 13 and 14 Similar to 11 but with the addition of acetic acid in place of hydrochloric. Brown or black products were obtained from which a definite substance could not be isolated.

15. A stream of chlorine gas was passed through an aqueous solution of 0.435 gram of the dibromo acid and gave 0.1652 gram of a reddish coloured precipitate which softened at 93-94° but was not completely melted at 115°.

Expt. 16. The theoretical amount of a standard solution of chlorine in glacial acetic acid was added to a solution of 0.403 gram of the dibromo acid in 0.5 cc. of water and 4 cc. of glacial acetic acid. 0.256 gram of a colourless crystalline precipitate was obtained m. p. 97-99°, whereas the pure 4-chloro-2:0-dibromo-aniline melts at 95.5°.

% *Expt.* 17. Similar to 16. • 1.06 grama of the dibromo acid were used and 0.169 gram of crystalline precipitate melting at 98-99° was obtained. A further quantity of 0.458 gram melting at 91° was obtained by pouring the mother liquor from the crystalline precipitate into water.

18. Similar to 17. 4.312 grams of dibromo acid were used and a total yield of 2.86 grams of chlorinated product was obtained corresponding with an 83% yield.

The crystals melted at 98-99° but after one crystallisation from alcohol the melting point had risen to 103-104°. The product obtained by pouring into water melted at 87-88° but after two crystallisations from alcohol melted at 99-101°.

C. Replacement of the Sulphonic Acid Group by Iodine.

Expts. 19, 20 and 21. were made by heating the dibromo acid with solutions of iodine in potassium iodide at temperatures between 150 and 200°, for several days. At the lower temperature no change occurred and at the higher temperature a small amount of a black substance was formed.

Expt. 22. To a solution of 0.509 grain of dibromosulphanilic acid in 10 cc. of glacial acetic acid and 2.5 cc. of

water an excess of iodine monochloride was added and on standing 0.20 gram of colourless crystals melting at 146° was obtained.

Expt. 23. In a similar experiment from 0.5084 gram of dibromo acid 0.294 gram of crystalline 2:6-dibromo-4-iodo-aniline m. p. 146° was obtained.

Expt. 24. One and a half times the theoretical amount of a glacial acetic acid solution of iodine monochloride was added to 0.454 gram of the dibromo acid dissolved in 6 cc. of glacial acetic acid and a few drops of water. The mixture was warmed and allowed to crystallise. A further quantity of crystals was obtained by concentrating the mother liquor. A total yield of 83% of the 4-iodo derivative was obtained melting at $147-148^{\circ}$.

Expts. 25 and 26. Similar to 24. The yields were respectively 60% and 80%. •

Expt. 27 was similar to 24 and was carried out with 3.78 grams of dibromo acid. A 75% yield of colourless crystals melting at $147-148^{\circ}$ was obtained.

Expt. 28. Similar to 27 and using 4.2 grams of dibromo acid. Yield 89%. M. P. $147-148^{\circ}$.

The 2:6-dibromo-4-iodo-aniline, $C_6H_4NBr_2I$, crystallises from glacial acetic acid, light petroleum (b. p. $60-80^{\circ}$) or alcohol in glistening white needles m. p. $147-148^{\circ}$.

Analysis:—0.2782 gave 0.4506 of mixed silver bromide and iodide and after treatment with chlorine 0.3176 of silver chloride I = 33.42 and Br. = 42.61%. The theoretical values are I = 33.68 and Br. =

2:6-dibromo-4-iodo-acetanilide, $C_8H_6ONBr_2I$. A 90% yield of the mono acetyl derivative can be obtained by using Smith and Orton's method of acetylation (*J. O. S. Trans.* 1908, 93, 1242). It crystallises from alcohol in colourless needles melting at $240-247^{\circ}$.

Analysis:—0.2240 gave 0.3264 of mixed silver bromide and iodide theoretical value = 0.3264.

2:6-dibromo-4-iodo-diacetanilide, $C_{10}H_8O_2NBr_2I$, prepared by Smith and Orton's method (*loc. cit.*) crystallises from alcohol in small needles melting at $166-167^{\circ}$.

II. EXPERIMENTS WITH 4:6-DIBROMOANILINE-2-SULPHONIC
ACID.

Bromoaniline-*ortho*-sulphonic acid was prepared by the method of Kreis (Annalen, 1895 286, 380) and was further brominated in the same manner as sulphanilic acid (page 137) The dibromo acid crystallises anhydrous in small rhombic crystals or with 1 H₂O in prismatic crystals.

A. Displacement of the sulphonic acid group by Bromine.

29.—*tt*?J were similar to experiments 1 — 8 with the exception that the dibromo-*ortho*-sulphonic acid was used in place of the isomeric *para*-acid. The yield of tribromoaniline in these experiments varied from 92-98%, and the melting point of the uncrystallised product from 115-117° to 117-119°.

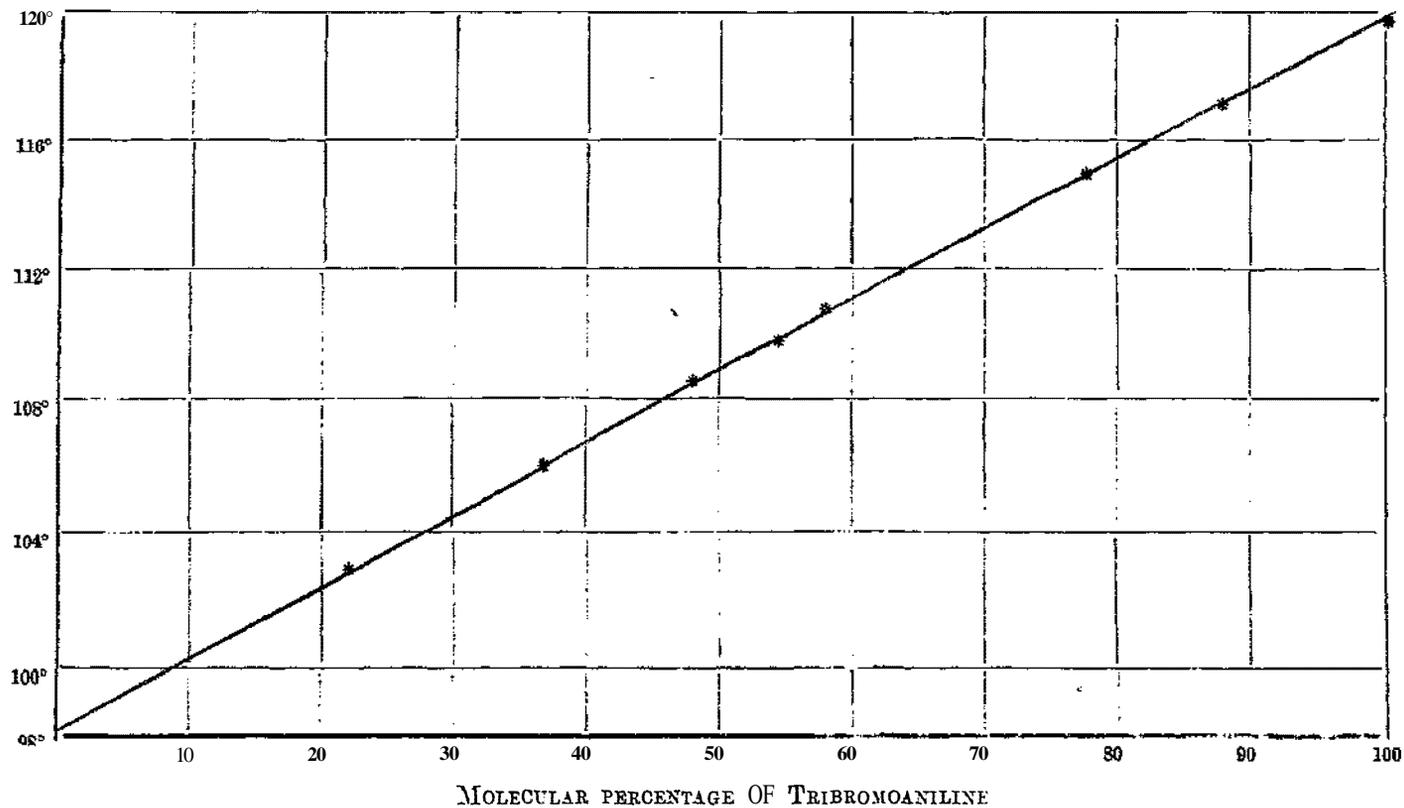
B. Displacement of the Sulphonic acid Group by Chlorine.

Expt. 34. The calculated amount of a glacial acetic acid solution of chlorine was added to a warm solution of 0.348 gram of the dibromo-*ortho*-sulphonic acid dissolved in a mixture of 2 cc. of water and 4 cc. of glacial acetic acid. On cooling colourless crystals melting at 100-104° were obtained and on pouring into water a pink precipitate m. p. 95-96° was obtained. The total weight was 0.190 gram. The melting point of pure 2-chloro-4:6-dibromoaniline is 99°.

Expts 35 and 36. Similar to No. 34 but a slight excess of chlorine solution was added. The yields were respectively 78 and 75%, and the crystalline product after crystallisation from alcohol melted at 105-106°.

Attempts to prepare pure 2-chloro-4:6-dibromoaniline by the chlorination of 2:4-dibromo-aniline were also fruitless, crystalline products melting at 105-106°, or after three crystallisations from alcohol at 110-111° were obtained.

Figure 1.



Melting point curve of mixtures of 2-Chloro-4:6-dibromoaniline and S. Tribromoaniline.

C. Replacement of the Sulphonic Acid Group by Iodine.

37. One and half times the theoretical amount of a glacial acetic acid solution of iodine monochloride was added to a warm solution of 0.325 gram of the dibromo acid in 2.5 cc. of water and 5 cc. of glacial acetic acid. On cooling a 41.6% yield of a crystalline product melting at 123-124° was obtained.

Expt. 38. Similar to No. 37 but twice the theoretical amount of iodine monochloride was taken and the dibromo acid was dissolved in 1.5 cc. of water and 5 cc. of glacial acetic acid. The mother liquor from the crystals when poured into water gave a reddish coloured precipitate melting at 112-115°. Total yield 88.5%.

Expt. 39. Similar to No. 38 but using 3 grams of dibromo acid. Yield (5

4 : 6-Dibromo-2-iodo-aniline $C_6H_4NBr_2I$, crystallises from alcohol or glacial acetic acid in glistening needles melting at 124-125°.

Analysis :—0.2090 gave 0.3402 of mixed silver bromide and iodide and after treatment with chlorine 0.2387 of silver chloride. $I=32.04$ and $Br=43.98\%$. The calculated percentages are 33.68 and 42.42 respectively.

4 : 6-Dibromo-2-iodo-acetanil $C_8H_6ONBr_2I$, crystallises from alcohol in slender feathery needles melting at 237°.

:—0.2180 gave 0.3180 of mixed silver bromide and iodide corresponding with the theoretical value of 0.3178.

III. EXPERIMENTS WITH 2 : 4 : 6-TRIBROMO-AMINOBE ACID.

Expt. 40. The theoretical amount of bromine water was added to an aqueous solution of the tribromo acid, but no precipitate of a brominated aniline was obtained and even after standing for some time the amount of free bromine present in the solution corresponded with the amount originally added.

Expts. 41-45. Similar to 40 but using acidified hypobromite solution and acidified bromate-bromide mixture. Even on warming in closed bottles a precipitate of a brominated was not obtained.

Expt. 46. A solution of chlorine in glacial acetic acid was added to a concentrated sulphuric acid solution of the tribromo acid but on pouring into water a precipitate was not obtained.

Expt. 47 A similar experiment to No. 46 but using a glacial acetic acid solution of iodine monochloride. A substituted aniline was not formed.

IV. COMPARATIVE EXPERIMENTS ON THE REPLACEMENT OF THE SULPHONIC ACID GROUP BY BROMINE IN THE ISOMERIC ORTHO-AND PARA-AMINO-BENZENE-SULPHONIC ACIDS.

The experiments were made by using dilute (namely 1 per cent) aqueous solutions of the respective acids and running in the theoretical amount (2 molecules) of carefully standardised bromine water from a burette, the point of which dipped under the surface of the sulphonic acid solution in order to avoid loss of bromine vapour. If the reaction proceeds normally then the only product should be the corresponding dibromoaminosulphonic acid, but if the sulphonic acid group is removed a precipitate of tribromoaniline is obtained. In all cases the formation of precipitate was observed, but only towards the end of the addition of the bromine water. In each experiment the precipitate was removed, washed, dried and weighed. In all cases the solutions during the addition of bromine water were kept well agitated by means of a mechanical stirrer. The result of a large number of experiments is to show that in the case of sulphanilic acid the following factors affect the yield of tribromoaniline to a very slight extent only. (a) Temperature:—the range examined was from 0 to 44°. (b) Rate of addition of bromine solution. (c) Rate of stirring. (d) Exposure to light.

Expts. 48 and 55. The following results were obtained with a solution of bromine containing 0.01433 grain of bromine per c. c. and using 50 c. c. of the 1 per cent solution of the sulphonic acids:—

Ortho acid		Para acid
Weight of Tribromoaniline.		Weight of Tribromoaniline.
0.1688 gram	...	0.0914 g ram
0.1824 „	...	0.0710 „
0.1916 „	...	0.0202 „
0.1918 „	...	0.0214 „

Expts. 66-61. The following results were obtained by running in the theoretical quantity of standard hypobromite to solutions of the sulphonic acids acidified with hydrochloric acid :—

Ortho acid	Para acid
0.1336	0.0214
0.0774	0.0298
0.0612	0.0068

The results appear to justify the conclusion that the ortho-sulphonic acid group is relatively more reactive than the para.

V. EXPERIMENTS WITH DIBROMO-ORTHO AND DIBROMO-PARA-AMINOBENZENECARBOXYLIC ACIDS.

Expt. 62. As the carboxylic acids are extremely sparingly soluble in water, solutions of their ammonium salts were used. 0.445 gram of 4:6-dibromo-2-aminobenzene-1-carboxylic acid was dissolved in excess of ammonia solution and bromine water added gradually, care being taken that the solution was always alkaline. Considerably more than the theoretical amount of bromine was required as part was used up in oxidising the ammonia to nitrogen. An 84% yield of *s*-tribromoaniline, somewhat discoloured and with the low melting point 111-113°, was obtained.

Expt. 63. 0.261 gram of the same acid was dissolved in excess of ammonia and the solution mixed with an excess of potassium bromide and bromate. Dilute sulphuric acid was added and then dilute ammonia and these additions were alternated until the addition of sulphuric acid produced no further precipitate. The repeated addition of ammonia was to dissolve up the dibromoamino acid precipitated together with tribromoaniline on the addition of sulphuric acid. A 91% yield of practically pure tribromoaniline melting at 118-119° was obtained.

Expt. 64. 0.36 gram of the dibromo-ortho-amino was dissolved in 5 cc, of glacial acetic acid and the theoretical amount of an acetic acid solution of chlorine added. As crystals did not separate even after some time, the solution was poured into excess of water and the resulting precipitate treated with dilute ammonia in order to remove any undecomposed acid. The portion insoluble in ammonia had m. p. 95-97° and after crystallisation from light petroleum gave a fraction melting at 103-105° indicating the formation of mixtures similar to those obtained from the dibromoamino-ortho-sulphonic acid and chlorine (*Expts.* 34

Expt. 65. This experiment was similar to No. 62 but the corresponding 2:6-dibromo-4-aminobenzene-1-carboxylic acid was used. From 0.407 gram of the acid 0.313 gram of tribromoaniline m. p. 110-116° was obtained corresponding with a 70% yield.

Expt. 66. Similar to No. 63 but using 0.362 gram of the dibromo-*p*-amino acid. A 90% yield of practically pure tribromoaniline melting at 117-119° was obtained.

Definite substances could not be isolated from the products of the action of chlorine on the dibromo-*p*-amino acid. In most cases the original acid was recovered.

Experiments on the replacement of the carboxylic acid group by iodine in the case of both the ortho and the para acids were unsuccessful.

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