234. *The Preparation of 4-Aminophenyl Sulphones. Part II. The Reaction between 4-Acetamidobenzenesulphinic Acid and Aromatic Nitroso-compounds.*

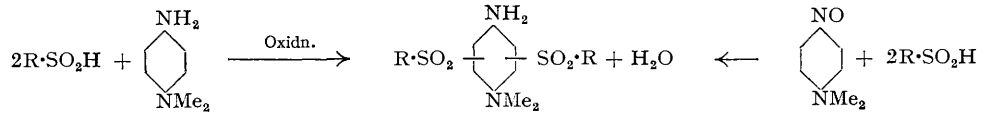
By S. Pickholz.

Hinsberg's explanation of the reaction between aromatic sulphinic acids and *p*-nitrosoalkylanilines is incorrect. Besides a very small amount of a disulphone, which is claimed by Hinsberg as the only product of the reaction, a disulphonamide and a sulphone-sulphonamide are formed as the main products. These three compounds are isomeric. A monosulphonamide, which can also be obtained by hydrolysis of the disulphonamide, is simultaneously formed to a lesser extent. The reaction between the sulphinic acid and *p*-nitrosophenol leads to the formation of the sulphonic acid salt of the same monosulphone as is formed by the oxidation of *p*-aminophenol in presence of the sulphinic acid (see Part I, this vol., p. 685).

In studies on the reaction between aromatic sulphinic acids and quinones, quinoneimines, or compounds which can produce these by intermediate oxidation, Hinsberg (*Ber.*, 1894, **27**, 3259; 1896, **29**, 2029) put forward the claim that the condensation product formed from two moles of benzenesulphinic acid and one mole of *p*-nitroso-

dimethylaniline was identical with the disulphone formed by the *in situ* oxidation of one mole of *p*-aminodimethylaniline in presence of at least two moles of benzenesulphinic acid.

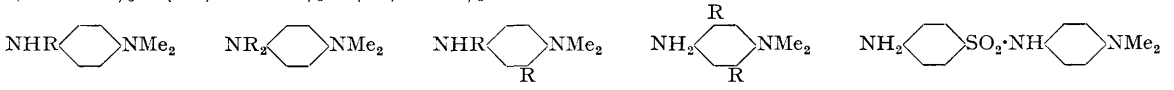
These reactions, which the same author formulated as follows :



were repeated in condensations with 4-acetamidobenzenesulphinic acid. By deacetylation of the condensation products it was hoped to prepare compounds with more than one 4-aminophenyl sulphone group in the molecule and so to extend the work, already described in Part I (*loc. cit.*) on unsymmetrical sulphones as potential chemotherapeutic agents, to disulphones containing the essential 4-aminophenyl sulphone structure.

The interaction of the sulphinic acid with the diamine goes probably *via* the mono- to the di-sulphone. An example of this kind is the preparation of 4-*amino*-2 : 5(?)-*bis*-(4′-*acetamidophenylsulphonyl*)-N-*dimethylaniline* (IV) which so far confirms part of Hinsberg's formulation, the orientation of the two sulphone groups being tentatively assumed in accordance with it. The same compound would be expected from the reaction between 4-acetamidobenzenesulphinic acid and *p*-nitrosodimethylaniline. This reaction, however, proved much more complex, and its investigation forms the main part of the present paper. Two publications by Bamberger and Rising (*Ber.*, 1901, **34**, 228, 232) describe the reaction between *p*-toluenesulphinic acid and nitrosobenzene or phenylhydroxylamine. From phenylhydroxylamine not fewer than seven different compounds were isolated, but remarkably enough none of these was related to the products described here. That may be due partly to different conditions for the condensations and partly, as the authors pointed out when comparing their results with Hinsberg's, to the possibility that nitrosobenzene and *p*-nitrosodimethylaniline behave differently.

From the interaction of 4-acetamidobenzenesulphinic acid (2 moles) and *p*-nitrosodimethylaniline (1 mole) in water–alcohol–hydrochloric acid, the following products were isolated in the yields stated : (I), 5—10% ; (II), 30—40% ; (III), 50—60% ; (IV), 1—2%.



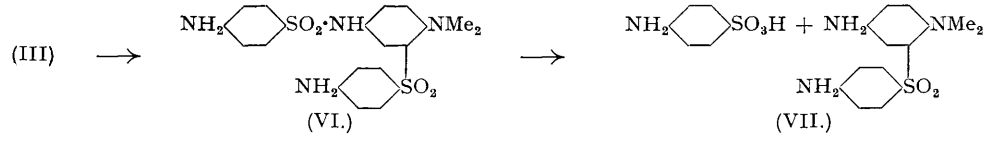
(I.) (II.) (III.) (IV.) (V.)

(R = *p*-NHAc·C_6H_4·SO_2.)

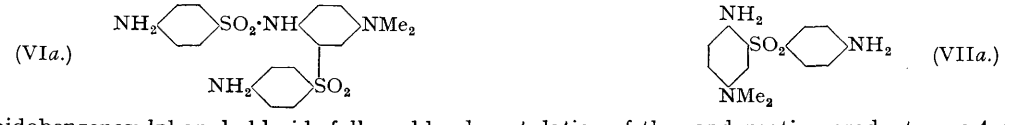
It will thus be seen that the disulphone (IV) (according to Hinsberg the only product) is formed in very small proportion, the main products being the isomeric 4-(*bis*-4′-*acetamidobenzenesulphonyl*)*amino*-N-*dimethylaniline* (II) and 2′-*dimethylamino*-4-*acetamido*-5′-(4″-*acetamidobenzenesulphonamido*)*diphenyl sulphone* (III). The presence of 4-(4′-acetamidobenzenesulphonamido)-*N*-dimethylaniline (I) may be due, at least in part, to secondary formation from (II). The deacetylated 4-(4′-aminobenzenesulphonamido)-*N*-dimethylaniline (V) was actually obtained by prolonged hydrolysis of (II) with simultaneous formation of sulphanilic acid.

The identities of (I), (II), and (V) were established by condensing *p*-aminodimethylaniline with 4-acetamidobenzenesulphonyl chloride to (I) and subsequently causing (I) to react with a second mole of the sulphonyl chloride ; (II) was then formed. Hydrolysis of (I) and (II) gave the same product (V) which had been made previously (Ganapati, *J. Ind. Chem. Soc.*, 1938, **15**, 525) by a method similar to the above sulphonyl chloride condensation.

The constitution of (III), the main product, was established as follows. Deacetylation with hydrochloric acid gave 4-*amino*-2′-*dimethylamino*-5′-(4″-*aminobenzenesulphonamido*)*diphenyl sulphone* (VI), which was split with 50% sulphuric acid at 140—150° to sulphanilic acid and 4 : 5′-*diamino*-2′-*dimethylaminodiphenyl sulphone*



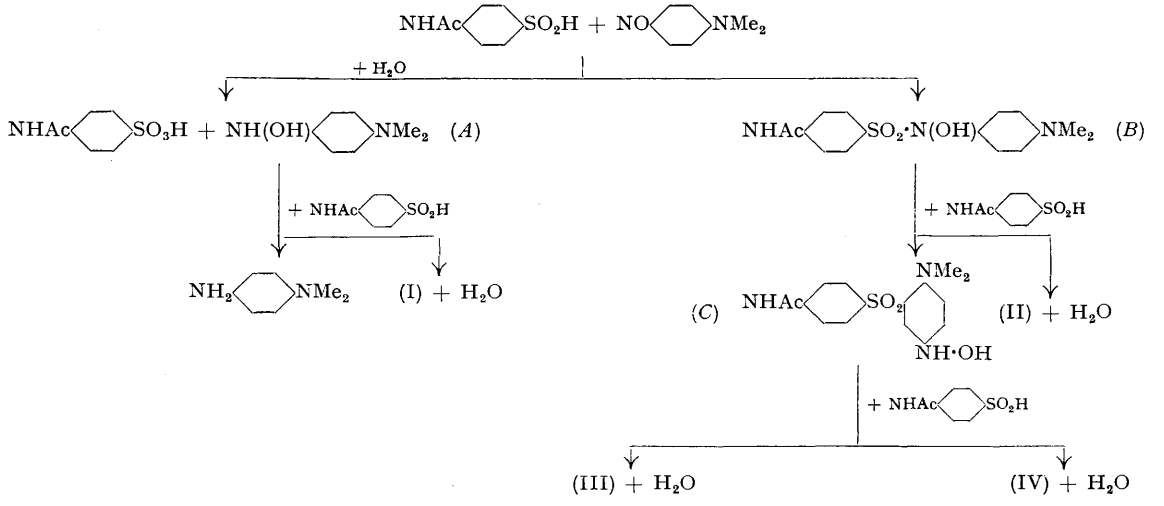
(VII). (VII) is isomeric with 4 : 2′-diamino-5′-dimethylaminodiphenyl sulphone (VII*a*), which had previously been obtained by the intermediate oxidation of *p*-aminodimethylaniline in the presence of 4-acetamidobenzenesulphinic acid and subsequent deacetylation (cf. Part I). Interaction of the acetyl derivative with



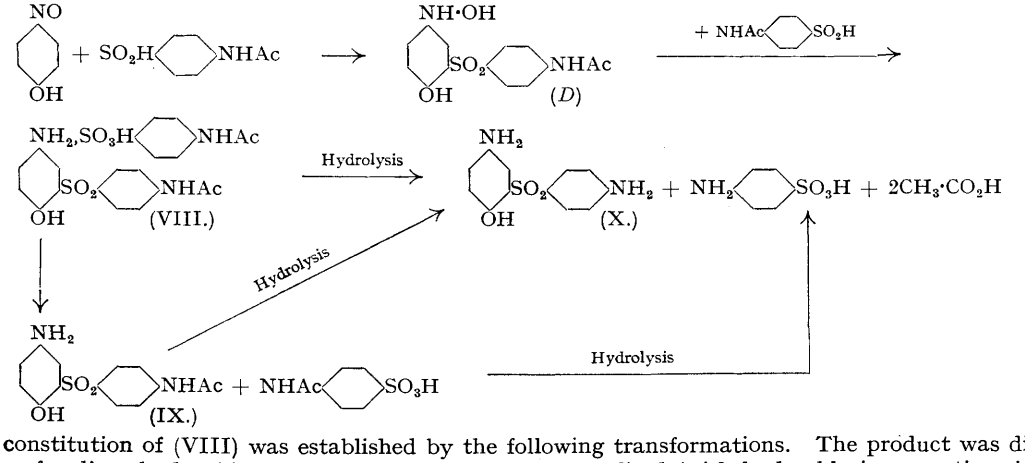
4-acetamidobenzenesulphonyl chloride followed by deacetylation of the condensation product gave 4-*amino*-5′-*dimethylamino*-2′-(4″-*aminobenzenesulphonamido*)*diphenyl sulphone* (VI*a*), isomeric with (VI), thus further demonstrating the related but different constitutions of the isomeric sulphones (VII) and (VII*a*). The structure of (VI) was conclusively established by an independant synthesis. Starting from (V) and oxidising this

substituted *p*-aminodimethylaniline in presence of 4-acetamidobenzenesulphinic acid and deacetylating the condensation product, a substance identical with (VI) was isolated. That the sulphone group had entered the *m*- and not the *o*-position to the amino group [as would have happened with *p*-aminodimethylaniline itself (see Part I)] is presumably due to the presence of the 4-aminophenylsulphonyl group as substituent, which appears to have weakened the normally *ortho* directing influence of the amino-group.

To explain the formation of compounds (I—IV), the hypothetical intermediate formation of *p*-hydroxylaminodimethylaniline (*A*) and its 4-acetamidobenzenesulphone derivative (*B*) may be postulated (see scheme). Interaction of *A* with a second molecule of sulphinic acid gives (I) with elimination of water, and *B* by a similar reaction would lead to (II). *B* may undergo a rearrangement to the sulphone *C*, in the manner proposed by Bamberger and Rising (*loc. cit.*) for the reaction with nitrosobenzene, and then may by subsequent addition of sulphinic acid form the sulphone-sulphonamide (III). A small amount of *C* may be directly reduced by a second molecule of sulphinic acid with simultaneous formation of (IV). The complete reduction of *p*-nitroso- to *p*-amino-dimethylaniline as a further, but in the present discussion unimportant, side reaction may be mentioned.



In contrast to the complex behaviour of *p*-nitrosodimethylaniline, that of *p*-nitrosophenol proved to be simple. When brought into reaction with 4-acetamidobenzenesulphinic acid (2 moles) under conditions similar to the foregoing, only one product (VIII) was formed which was identified as the *salt* (or double compound) of 4-acetamidobenzenesulphonic acid with 5′-amino-4-acetamido-2′-hydroxydiphenyl sulphone (IX). This last compound has been described as the product which can be obtained by the intermediate oxidation of *p*-aminophenol and 4-acetamidobenzenesulphinic acid (Part I).



The constitution of (VIII) was established by the following transformations. The product was dissolved in excess of sodium hydroxide solution and this solution neutralised (with hydrochloric or acetic acid). An almost quantitative precipitate of (IX) was obtained. The filtrate contained 4-acetamidobenzenesulphonic acid, which on hydrolysis broke up into acetic acid and sulphanilic acid. No precipitate was formed when the same filtrate was tested with ferric chloride solution, thus demonstrating the absence of 4-acetamidobenzenesulphinic acid (aromatic sulphinic acids in general give insoluble Fe^{+++} salts; cf. also Feigl, " Qualitative Analysis by Spot Tests," 2nd Ed., New York, 1939, 302). Hydrolysis of (VIII) gave sulphanilic acid and

4 : 5′-diamino-2′-hydroxydiphenyl sulphone (X) which was also obtained by deacetylation of (IX). The formation of (VIII) proceeds probably as follows. *p*-Nitrosophenol combines with one mole of the sulphinic acid to the intermediate (but not isolated) 5′-hydroxylamino-4-acetamido-2′-hydroxydiphenyl sulphone, *D*. This is reduced by a second mole of the sulphinic acid to (IX) which in turn forms with the simultaneously produced 4-acetamidobenzenesulphonic acid the salt (VIII) (see scheme).

Tests for antibacterial activity were carried out with (IV*a*), (V), and (VI) [obtained by deacetylation from (IV), (I), and (III)] as described previously (Part I). (V) was practically non-toxic, and its activity of the order of that of sulphanilamide. (VI), like (VI*a*), was practically devoid of any activity both *in vitro* and *in vivo*. (IV*a*) gave fluctuating but inferior results *in vivo* in comparison with sulphanilamide, while its *in vitro* activity was quite high.

Although it is not claimed at this stage that the reactions described here are general, preliminary experiments appear to show that similar condensations occur with *p*-nitrosodiethylaniline, *p*-nitroso-*o*- and *m*-cresol, and (repeating Hinsberg's experiments) with benzenesulphinic acid. These experiments have had to be temporarily interrupted, but it is hoped to carry them to conclusion later.

Experimental.

4-(4′-*Acetamidobenzenesulphonamido*)-N-*dimethylaniline* (I).—(*a*) The hydrochloride of *p*-nitrosodimethylaniline (Hodgson and Nicholson, *J.*, 1941, 472, 36 g.) was dissolved in dilute hydrochloric acid (10 c.c. in 500 c.c. water) and a suspension of 4-acetamidobenzenesulphinic acid (81 g.) in ethanol (300 c.c.) and water (200 c.c.) added with stirring, the dark brown solution being kept at 35—45°. During the reaction the colour changed, and after 15—20 minutes a clear greenish solution was obtained. After 1 hour, water (300 c.c.) was added; this precipitated a dark green resinous product. The mixture was then adjusted to pH 4—4·5 with dilute ammonia (1 : 5; 100 c.c.). More insoluble material was formed, which was filtered off [mixture of (II) and (III)]. The mother liquors were made alkaline with ammonia (pH 7·3—7·5) and a third precipitate was obtained, filtered off, dried (12·5 g.), and digested in the cold with ethanol (50 c.c.). The dark blue ethanol extract was removed, and the insoluble residue dried and boiled under reflux with 95% ethanol (30 c.c.); the crystals still undissolved (6 g.) were recrystallised twice from 90—95% ethanol, to yield cream coloured crystals (4 g.), m. p. 193—195° (Found: S, 9·5. Calc. for $C_{16}H_{19}O_3N_3S$: S, 9·6%).

(*b*) *p*-Aminodimethylaniline (5 g.) was dissolved in dry pyridine (10 c.c.), and 4-acetamidobenzenesulphonyl chloride (10 g.) dissolved in dry pyridine (25 c.c.) gradually added with stirring. The bluish mixture became warm and was heated for 30 minutes on the steam-bath to complete the reaction. After cooling, glacial acetic acid (25 c.c.) was added, and finally water (50 c.c.), and the mixture left for some hours; it was then almost solid. It was diluted with water (50 c.c.) and the crystals were filtered off. Two recrystallisations from 90% ethanol gave 7—8 g. of cream coloured coarse needles, m. p. 194—195°, giving no m. p. depression with the former product (Ganapati gives m. p. 196°).

4-(*Bis*-4′-*acetamidobenzenesulphonyl*)*amino*-N-*dimethylaniline* (II).—(*a*) 4-Acetamidobenzenesulphinic acid (80 g.) was suspended in water (2000 c.c.) and a solution of the hydrochloride of *p*-nitrosodimethylaniline (33 g.) in water (1000 c.c.) brought into reaction as before. After 4 hours 10% sodium acetate solution (1000 c.c.) was added, and stirring continued for 2 hours longer. The yellowish-green precipitate was collected, washed with water, and dried in a vacuum. This material was stirred for an hour at room temperature with 10% aqueous sodium hydroxide solution (800 c.c.) and the insoluble product filtered off, washed with more sodium hydroxide solution, then thoroughly with water, and dried. The crude material (31 g.) was boiled under reflux with 95% ethanol (150—200 c.c.). After cooling, the insoluble crystals were collected, washed with ethanol, and dried. A sample, recrystallised from ethanol–acetone (2 : 1) gave almost white needles, m. p. 214—216° (decomp.) The *compound* was insoluble in sodium hydroxide solution, not very soluble in dilute acids, cold acetone, or ethanol (Found: N, 10·8; S, 12·3. $C_{24}H_{26}O_6N_4S_2$ requires N, 10·6; S, 12·1%).

(*b*) 4-(4′-Acetamidobenzenesulphonamido)-*N*-dimethylaniline (6 g.) was dissolved in 5% sodium hydroxide solution (20 c.c.) and a solution of 4-acetamidobenzenesulphonyl chloride (5 g.) in acetone (30 c.c.) slowly added with stirring. The mixture was cooled externally and kept alkaline by adding more sodium hydroxide solution when necessary. After 1 hour the mixture was acidified with dilute hydrochloric acid and then diluted with water until a first flocculant precipitate was formed. This was removed and the filtrate diluted with water until no more separated. The substance was collected on the following day, washed with water, dried, and boiled with methanol (100 c.c.). The filtrate was concentrated to about 30—40 c.c. and cooled. On keeping, crystals formed which, after recrystallisation from ethanol–acetone, had m. p. 213—215°, identical with the compound above (4 g.).

Separation of (II) *and* (III).—The yellowish-green precipitate, which was formed by neutralising the above reaction mixture from 4-acetamidobenzenesulphinic acid and *p*-nitrosodimethylaniline, was boiled under reflux in 90% ethanol. After some minutes the dark green solution deposited crystals whilst still hot. The heating was stopped after 20 minutes and the mixture left overnight; the crystals were then collected and washed with ethanol until the washings were colourless. The substance was twice recrystallised from 90% ethanol, giving white needles, m. p. 212—214° (20 g.), identical with (II). Traces of (III) were present and were very difficult to remove by recrystallisation, but were easily separated by treatment with sodium hydroxide solution as described earlier. The alcoholic mother liquors from all crystallisations were combined, concentrated, and left for some days; crops of (II) and (III) were then obtained which were again recrystallised. The whole procedure was rather tedious and unsatisfactory, especially for the separation of (III).

4-(4′-*Aminobenzenesulphonamido*)-N-*dimethylaniline* (V).—(*a*) (I) (5 g.) was deacetylated by boiling it in 10% hydrochloric acid (50 c.c.) for 1 hour. The bluish solution was filtered (charcoal) and the filtrate neutralised with dilute ammonia. The slightly cream coloured precipitate was recrystallised from 90% ethanol; white needles (3 g.), m. p. 228—230° (Ganapati records m. p. 232°) (Found: S, 10·8; N, 14·6. Calc. for $C_{14}H_{17}O_2N_3S$: S, 11; N, 14·4%).

(*b*) The bis-compound (II) (28 g.) was boiled for 2 hours under reflux with 95% ethanol (40 c.c.) and 16% hydrochloric acid (80 c.c.). The solution was cooled overnight in a refrigerator and the crystals (sulphanilic acid 7·2 g.) collected. The mother liquors were decolorised with charcoal and filtered. The filtrate was neutralised with ammonia and a yellowish-green precipitate obtained. This was collected and stirred with 1·5% sodium hydroxide solution (200 c.c.). A small amount of an insoluble yellowish-green substance remained undissolved and was removed (IV*a*). The alkaline filtrate was decolourised with charcoal and after filtration neutralised with acetic acid. The grey precipitate, twice recrystallised from 90% ethanol, gave white needles (14 g.), m. p. 227—229°, identical with the above substance from (I).

2′-*Dimethylamino*-4-*acetamido*-5′-(4″-*acetamidobenzenesulphonamido*)*diphenyl Sulphone* (III).—The alkaline mother liquors from (II) were twice decolorised with charcoal. The yellow filtrate was acidified with dilute acetic acid and the cream coloured precipitate isolated, dried (50 g.), and dissolved in hot 93% ethanol (150—200 c.c.). The dark solution was twice filtered (charcoal) and left overnight. White needles formed which were collected, washed with ethanol and ether, and dried. The *product* had m. p. 245—247° (30—35 g.). It was slightly soluble in stronger acid, easily in sodium

hydroxide solution, not in acetone, ethanol or methanol, difficultly in benzene (Found: S, 12·2; N, 10·9. $C_{24}H_{26}O_6N_4S_2$ requires S, 12·1; N, 10·6%).

4-Amino-2'-dimethylamino-5'-(4''-aminobenzenesulphonamido)diphenyl Sulphone (VI).—(*a*) By deacetylation of (III). Isolation and purification of (VI) were carried out generally as described for (V). No sulphanilic acid was formed. The *product* formed white needles, m. p. 196—198°, soluble in acid and alkaline solutions (Found: S, 14·5. $C_{20}H_{22}O_4N_4S_2$ requires S, 14·3%).

(*b*) 4-(4'-Aminobenzenesulphonamido)-*N*-dimethylaniline (V; 7 g.) was dissolved in 2% hydrochloric acid (1200 c.c.). A suspension of 4-acetamidobenzenesulphinic acid (5 g.) in water (50 c.c.) was added with stirring, the temperature raised to 50—60°, and 10% aqueous ferric chloride (100 c.c.) run in during 15 minutes. A solution was obtained from which tarry material separated after 2 hours. This was removed, the filtrate diluted with an equal volume of water, and a second tarry precipitate collected with the aid of charcoal. The clear filtrate was neutralised with sodium acetate. A partly crystalline product separated, which was collected, washed with water, and dried in a vacuum (4 g.). It was hydrolysed, without further purification, with a mixture of ethanol (10 c.c.) and 10% hydrochloric acid (30 c.c.). After prolonged boiling a brown solution was obtained which was decolourised with charcoal. The filtrate was neutralised with sodium bicarbonate and the precipitate recrystallised 3 times from ethanol; white to cream needles, m. p. 195—198° (1·5 g.). No m. p. depression, when mixed with a sample from (*a*).

4 : 5'-Diamino-2'-dimethylaminodiphenyl Sulphone (VII).—A solution of (VI) (10 g.) in 50% sulphuric acid was heated at about 140—150° for 1 hour. The dark solution was cooled, diluted with water (500 c.c.), and almost neutralised with sodium hydroxide. The precipitate (4 g.) was collected, redissolved in dilute hydrochloric acid, the solution decolourised with charcoal, and the filtrate neutralised with sodium bicarbonate. The precipitate was recrystallised from 95% ethanol and white crystals obtained, m. p. 208—210°. The *compound*, isomeric with (VII*a*), was soluble in acid, but insoluble in sodium hydroxide solution (Found: S, 10·7; N, 14·6. $C_{14}H_{17}O_2N_3S$ requires S, 11; N, 14·4%).

4-Amino-5'-dimethylamino-2-(4''-aminobenzenesulphonamido)diphenyl Sulphone (VI*a*).—To a mixture of 2'-amino-5'-dimethylamino-4-acetamidodiphenyl sulphone (Part I) (6 g.) and dry pyridine (10 c.c.) was added a solution of 4-acetamidobenzenesulphonyl chloride (4·4 g.) in dry pyridine (15 c.c.). The dark solution was heated on the steam-bath for 1 hour. After cooling, it was treated with glacial acetic acid (25 c.c.) followed by water (25 c.c.). Crystallisation began and was completed by dilution with more water (100 c.c.) in portions. The precipitate was collected, washed with water, and recrystallised from 80% aqueous ethanol (150 c.c.) to yield slightly yellow needles, m. p. 234—235° (5·5 g.), of *5'-dimethylamino-4-acetamido-2'-(4''-acetamidobenzenesulphonamido)diphenyl sulphone* [isomeric with (III)] (Found: S, 12·3. $C_{24}H_{26}O_6N_4S_2$ requires S, 12·1%). The acetylated sulphone (3·5 g.) was hydrolysed as usual and the deacetylated product precipitated with dilute ammonia. For purification, it was dissolved in hot acetone, the solution decolourised with charcoal, and the warm filtrate triturated with water until crystallisation began; cream needles, m. p. 218—220° (2·2 g.). The *substance* was soluble in acid and alkaline solutions (Found: S, 14·5; N, 12·8. $C_{20}H_{22}O_4N_4S_2$ requires S, 14·3; N, 12·6%).

4-Amino-2 : 5(?)-bis-(4'-acetamidophenylsulphonyl)-N-dimethylaniline (IV).—To a solution of 2'-amino-5'-dimethylamino-4-acetamidodiphenyl sulphone (6 g.) in 10% hydrochloric acid (100 c.c.) was added a solution of 4-acetamidobenzenesulphinic acid (4 g.) in 50% aqueous ethanol (30 c.c.). 10% Ferric chloride solution (60 c.c.) was added drop by drop with stirring at 50—60°. The mixture at first became cloudy and later a tarry product separated. Stirring was stopped after 1 hour and the supernatant liquid decanted from the precipitate. This was boiled with ethanol (30 c.c.) and changed to yellowish-brown crystals (3·5 g.). A sample, recrystallised from 90% ethanol, formed yellowish needles, m. p. 276—278°, insoluble in acid and in sodium hydroxide solution (Found: S, 12·2; N, 10·8. $C_{24}H_{26}O_6N_4S_2$ requires S, 12·1; N, 10·6%). The same *compound* could be prepared in one step from *p*-aminodimethylaniline in a similar way, using the starting materials in the ratio amine : sulphinic acid : ferric chloride = 1 : 2 : 4, instead of sulphone : sulphinic acid : ferric chloride = 1 : 1 : 2. The first method is, however, preferable.

4-Amino-2 : 5(?)-bis-(4'-aminophenylsulphonyl)-N-dimethylaniline (IV*a*).—(*a*) The foregoing compound (1 g.) was hydrolysed with 10% hydrochloric acid (20 c.c.), the solution diluted with an equal volume of water, and dilute ammonia (1 : 4) added until a slight cloudiness persisted. The solution was clarified with charcoal and the filtrate brought to pH 2·5—3 with more ammonia. Bright yellowish-green crystals precipitated, which were collected and washed with water, methanol, and ether. No further purification was necessary. The *compound* was soluble in strong acids, and in warm acetone, ethanol, or methanol, insoluble in sodium hydroxide solution. Solutions in acetone or ethanol showed a very intense yellowish-green fluorescence, which was extinguished on acidifying the solutions with hydrochloric or sulphuric acid; m. p. 263—264° (0·5 g.) (Found: S, 14·5; N, 12·8. $C_{20}H_{22}O_4N_4S_2$ requires S, 14·4; N, 12·6%).

(*b*) The yellowish-green product which remained undissolved in sodium hydroxide solution [see preparation of (V) from (II)] was purified by dissolving in hot acetone, filtering (charcoal), and slowly concentrating the filtrate. Yellowish-green crystals separated, m. p. 263—265°, not depressed by the disulphone obtained from (*a*).

4-Acetamidobenzenesulphonic Acid Salt of 5'-Amino-4-acetamido-2'-hydroxydiphenyl Sulphone (VIII).—To a suspension of *p*-nitrosophenol (15 g.) in water (300 c.c.) was added 4-acetamidobenzenesulphinic acid (56 g.) partly dissolved in hot water (300 c.c.). The mixture was slowly heated to 85—90° with stirring for 1 hour and the dark solution filtered (charcoal). The filtrate was cooled to about 50—60° and a tarry precipitate removed. The liquors were left with cooling and cream crystals obtained (45—50 g.), which recrystallised from water to give white needles, m. p. 206—208° (decomp.) after having been dried for some hours at 110—120°. The *product* was soluble in hot water, acid, and caustic solutions, but only slightly in ethanol or acetone (Found: S, 12·1; N, 8·2. $C_{22}H_{23}O_8N_3S_2$ requires S, 12·3; N, 8·1%).

5'-Amino-4-acetamido-2'-hydroxydiphenyl Sulphone (IX).—(VIII) (5 g.) was dissolved in excess of cold dilute sodium hydroxide solution and neutralised with acetic acid. A cream precipitate was obtained and recrystallised from ethanol. It had m. p. 233—235° and was identical with the reaction product from *p*-nitrosophenol and 4-acetamidobenzenesulphinic acid (Part I).

4 : 5'-Diamino-2'-hydroxydiphenyl Sulphone (X).—(*a*) (VIII) (4 g.) was boiled with dilute hydrochloric acid (1 : 4; 30 c.c.) for 1 hour and the solution cooled. Sulphanilic acid crystallised out (1·1 g.) and was removed, the filtrate evaporated to dryness, and the residue extracted with hot ethanol; a second crop of sulphanilic acid (0·4 g.) was then collected. The alcoholic mother liquors were concentrated, diluted with water, and decolorised with charcoal. The filtrate was neutralised with ammonia and the precipitate (1·9 g.) further purified by recrystallisation from methanol. The product, m. p. 210—212°, was identical with that previously described (Part I).

(*b*) The same substance was obtained by alkaline hydrolysis of (VIII) and subsequent neutralisation of the solution with acetic acid.

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