217. *Synthesis of Diamino Sulphones.*

By Alan A. Goldberg.

p-Aminophenyl *β*-aminoethyl sulphone and *p*-aminophenyl *γ*-diethylaminopropyl sulphone have been prepared for examination as bacterial inhibitors. Two attempted methods of preparing such compounds have yielded anomalous results—*viz.*, (i) sodium *p*-acetamidobenzenesulphinate and diethylaminoethyl chloride gave bis-(*p*-acetamidophenylsulphonyl)ethane, and (ii) potassium *p*-acetamidobenzenesulphinate and potassium ethanolamine sulphate yielded dithioacetanilide.

In consequence of the high antibacterial activity of 4 : 4′-diaminodiphenylsulphone it was of interest to prepare analogues in which one of the phenyl nuclei was replaced by a short alkylene chain. It was thought that these *p*-aminophenyl ω-aminoalkyl sulphones might possess the activity of the diaminodiphenylsulphone but have a lower toxicity.

Several synthetic routes to these compounds and their derivatives were investigated. (1) The addition of *p*-acetamidobenzenesulphinic acid to ethyleneimine did not give the required *p*-acetamidophenyl β-aminoethyl sulphone although the addition of sulphurous acid to ethyleneimine readily yields taurine (Gabriel, *Ber.*, 1888, **21**, 2667). (2) Treatment of *p*-acetamidophenylsulphonyl acetic acid * with hydrazoic acid by the method of Oesterlin and Schmidt failed to effect replacement of the carboxyl group. In view of the formation of taurine from β-sulphopropionic acid (Rumpf, *Bull. Soc. chim.*, 1938, **5**, 877) the failure of the α-sulphonyl carboxylic acid to react with hydrazoic acid would indicate that the propinquity of the negative sulphonyl group inhibits the reaction; this would be in accordance with the observations of Rumpf that in converting the aliphatic dicarboxylic acids to the corresponding diamines the yields become progressively lower as the number of methylene groups decreases. (3) Although sodium ethanolamine sulphate reacts with sodium hydrogen sulphite with production of taurine (Goldberg, *J.*, 1943, 4) the interaction of sodium ethanolamine sulphate with sodium *p*-acetamidobenzenesulphinate in aqueous solution at 140° does not yield the desired *p*-acetamidophenyl ω-aminoethyl sulphone; reduction of the sulphinate takes place with formation of dithioacetanilide.

It was found, however, that the condensation of sodium *p*-acetamidobenzenesulphinate with β-bromoethylphthalimide gave p-*acetamidophenyl* β-*phthalimidoethyl sulphone* in good yield. Hydrolysis of this with dilute alkali effected deacetylation without interference with the phthaloyl residue while hydrolysis with concentrated hydrochloric acid gave the required p-*aminophenyl* β-*aminoethyl sulphone*, conveniently isolated as its *dihydrochloride.* This compound, although it possesses a toxicity of a lower order than 4 : 4′-diaminodiphenylsulphone possesses little activity against *Streptococcus aronson* infections in mice. Similarly sodium *p*-acetamidobenzenesulphinate and β-bromoethylbenzamide readily yielded p-*acetamidophenyl* β-*benzamidoethyl sulphone* which on acid hydrolysis gave the same diamino sulphone.

Interaction of sodium *p*-acetamidobenzenesulphinate with β-diethylaminoethyl chloride did not give the expected *p*-acetamidophenyl β-diethylaminoethyl sulphone. Condensation readily takes place in dry *iso*propyl

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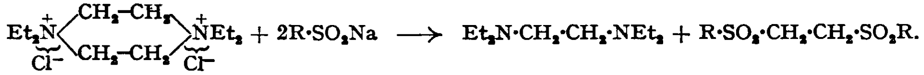
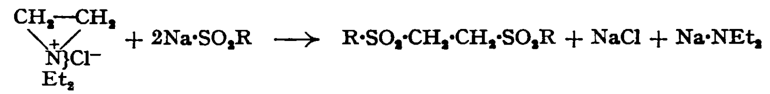
* This compound has been previously designated p-*acetamidobenzenesulphonylacetic acid.* The name now used is preferable since it indicates that the compound is a derivative of a phenyl sulphone and not of a sulphonic acid. (Temporary Editor).

alcohol or xylene solution with production of αβ-*bis*-(p-*acetamidophenylsulphonyl*)*ethane* in excellent yield together with elimination of diethylamine. The identity of the product was confirmed by its preparation by two synthetic routes which leave no doubt as to its constitution : (*a*) the interaction of sodium *p*-acetamidobenzenesulphinate with ethylene dibromide and (*b*) the condensation of sodium *p*-acetamidobenzenesulphinate with sodium αβ-dibromosuccinate with simultaneous decarboxylation by the method of Goldberg and Besly (this vol., p. 566). It is remarkable that the anomalous reaction between sodium *p*-acetamidobenzene sulphinate and diethylaminoethyl chloride gives the αβ-bis-(*p*-acetamidophenylsulphonyl)ethane in far higher yield than either of the two " rational " reactions for its synthesis. After this work had been completed, attention was drawn to F.P. 800,535 and B.P. 453,443, in which it is stated that the interaction of sodium *p*-acetamidobenzenesulphinate and diethylaminoethyl chloride in the presence of excess of sodium ethoxide or a base such as diethylamine yields *p*-acetamidophenyl β-diethylaminoethyl sulphone, m. p. 72°, while the condensation of the reactants in the absence of the sodium ethoxide or organic base gives " a compound m. p. 284° analysing for bis-(*p*-acetamidobenzene sulphonyl) ethane." Later G.P. 702,064, of which the abstract only is available (*Chem. Abs.*, 1942, **36**, 98), states that the interaction of sodium *p*-acetamidobenzenesulphinate with diethylaminoethyl chloride gives a compound, m. p. 284°, assumed by the patentees to be *p*-acetamidophenyl β-diethylaminoethyl sulphone, but which would appear actually to be identical with the disulphone described above.

A satisfactory explanation of the abnormality of this reaction is difficult to advance. On account of the ease with which diethylaminoethyl chloride quaternises to tetraethylpiperazinium dichloride there was the possibility that the reaction might take place, thus :



This was discounted by diethylamine and not tetraethylethylenediamine being produced in almost theoretical amount and by the sodium sulphinate failing to condense with preformed *NN*-tetraethylpiperazinium chloride. A rational explanation of the reaction may be that in certain circumstances diethylaminoethyl chloride undergoes monomeric quaternisation with formation of diethylethyleneimine chloride and the latter effects alkylation of the sulphur, thus :



This is in accordance with the experimental evidence that *ca.* 1 mol. of diethylamine is obtained from the reaction involving 2 mols. of the sulphinate. The alkylation of carbon, sulphur, and nitrogen with quaternary ammonium salts recorded by Snyder, Smith, and Stewart (*J. Amer. Chem. Soc.*, 1944, **66**, 202), Snyder and Speck (*ibid.*, 1939, **61**, 668, 2895), Hla Baw (*Quart. J. Ind. Chem. Soc.*, 1926, **3**, 101), Tarbell and Vaughan (*J. Amer. Chem. Soc.*, 1943, **65**, 231), and Rodionov (*Bull. Soc. chim.*, 1926, **39**, 305 ; 1929, **45**, 109) would appear to support this hypothesis. It is, however, noteworthy that anomalous formation of bis(phenylsulphonyl)ethane derivatives in substantial yield has been reported by the interaction of sodium benzenesulphinate (*a*) with 1 : 1 : 1-trichloroethane (Otto, *Ber.*, 1899, **31**, 1693); (*b*) with 1 : 1 : 2-trichloroethane (Otto, *Ber.*, 1894, **27**, 3055) and (*c*) with sodium αα-dichloropropionate (Otto, *Ber.*, 1886, **19**, 1835 ; *J. pr. Chem.*, 1889, **40**, 530) and it would accordingly appear that the $-SO_2\cdot CH_2\cdot CH_2\cdot SO_2-$ complex is a highly stable grouping readily and preferentially formed by intermolecular rearrangement.

Hydrolysis of αβ-bis-(*p*-acetamidophenylsulphonyl)ethane with dilute acid yielded αβ-bis-(*p*-aminophenylsulphonyl)ethane; this compound has a low toxicity but possesses no activity against streptococcal infections in mice.

p-Aminophenyl γ-diethylaminopropyl sulphone was prepared by a synthetic route suggested by Goldberg and Besly (*loc. cit.*). Alkylation of *p*-acetamidophenyl phenacyl sulphone with diethylaminoethyl chloride yielded the *C*-diethylaminoethyl derivative which on heating with dilute alkali is converted into benzoic acid amd *p*-aminophenyl γ-diethylaminopropyl sulphone. This compound has very little activity against *Streptococcus aronson* infections in mice.

EXPERIMENTAL.

p-*Acetamidophenyl β-Phthalimidoethyl Sulphone.*—Anhydrous potassium *p*-acetamidobenzenesulphinate (23·7 g., 0·1 mol.) and β-bromoethylphthalimide (25·5 g., 0·1 mol.) (*Org. Synth.*, Coll. Vol. 1, 119) were refluxed together in amyl alcohol (250 c.c.) containing a trace of copper powder for 8 hours. The amyl alcohol was removed by steam distillation and the residual insoluble material (24 g.) recrystallised from acetic acid when p-*acetamidophenyl β-phthalimidoethyl sulphone* (18 g.) was obtained in colourless prismatic needles, m. p. 228—230° (Found : N, 7·5; S, 8·4. $C_{18}H_{16}O_5N_2S$ requires N, 7·5; S, 8·6%).

p-*Aminophenyl β-Phthalimidoethyl Sulphone.*—The above acetyl compound (10 g.) was refluxed with 5N hydrochloric acid (100 c.c.) and ethanol (25 c.c.) for 45 minutes. The solution was filtered and, on cooling, p-*aminophenyl β-phthalimidoethyl sulphone* separated in nacreous flakes (6·6 g.), m. p. 200—202°. It was recrystallised from ethanol (Found : N, 8·6; S, 9·6. $C_{16}H_{14}O_4N_2S$ requires N, 8·5; S, 9·7%).

p-*Aminophenyl β-Aminoethyl Sulphone.*—*p*-Acetamidophenyl β-phthalimidoethyl sulphone (20 g.) was refluxed with 10N hydrochloric acid (400 c.c.) for 12 hours. Phthalic acid was removed from the cooled solution and the filtrate evaporated under reduced pressure to small volume. Sufficient warm water was added to effect solution, the pH value adjusted to 8·0 with 2N sodium hydroxide and the solution evaporated to dryness. The residue was extracted with a boiling mixture of alcohol and acetone (*ca.* 800 c.c.), the insoluble material removed and the solution evaporated to dryness on the water-bath under reduced pressure. The colourless residue was dissolved in boiling absolute alcohol (120 c.c.), filtered and hydrogen chloride passed in, a thick white precipitate appearing. A few drops of water were added to effect complete solution at the boiling point; on cooling, p-*aminophenyl β-aminoethyl sulphone dihydrochloride* separated in colourless small plates (8·8 g.), m. p. 234—236°. A sample, recrystallised from 98% ethanol containing a few drops of alcoholic hydrogen chloride, had m. p. 238—240° (Found in material dried at 100°/1 mm.: Cl, 26·2; N, 10·4; S, 11·4. $C_8H_{14}O_2N_2Cl_2S$ requires Cl, 26·0; N, 10·2; S, 11·7%). An aqueous solution of this dihydrochloride was treated with 5N sodium hydroxide and extracted several times with ether and the ethereal extract dried with sodium sulphate. On evaporation to small volume p-*aminophenyl β-aminoethyl sulphone* was obtained in almost theoretical amount in colourless long needles, m. p. 120—122° (Found: N, 14·3. $C_8H_{12}O_2N_2S$ requires N, 14·0%).

p-*Acetamidophenyl β-Benzamidoethyl Sulphone.*—β-Bromoethylbenzamide was obtained by the simultaneous addition of benzoyl chloride (76 g.) and 5N sodium hydroxide (220 c.c.) to a stirred ice-cold solution of β-bromoethylamine hydrobromide (102 g.; Cortese, *J. Amer. Chem. Soc.*, 1936, **58**, 191) in water (200 c.c.). After stirring for 1 hour the solid was collected, washed with water, dried in vacuo and recrystallised from benzene–ligroin (250 c.c.); yield 94 g. The colourless needles had m. p. 100—102° (Found: N, 6·4; Br, 34·8. Calc. for $C_9H_{10}ONBr$: N, 6·2; Br, 35·0%). β-Bromoethylbenzamide (22 g.) and anhydrous sodium *p*-acetamidobenzenesulphinate (22 g.) were refluxed with xylene (150 c.c.) containing a trace of copper powder for 5 hours. After removal of the xylene in steam the residual oil solidified (22 g.) and was recrystallised twice from dilute alcohol. p-*Acetamidophenyl β-benzamidoethyl sulphone* (11 g.) was obtained in colourless long needles, m. p. 218—220° (Found: N, 8·3; S, 9·2. $C_{17}H_{18}O_4N_2S$ requires N, 8·1; S, 9·3%).

This sulphone (5 g.) was refluxed with alcohol (30 c.c.) and 5N sodium hydroxide (15 c.c.) for 1½ hours. The alcohol was distilled off on the water bath under reduced pressure and the residue cooled with ice. The separated p-*aminophenyl β-benzamidoethyl sulphone* (4 g.) was recrystallised from 80% alcohol and obtained in clusters of colourless needles, m. p. 172—174° (Found: N, 9·4; S, 10·3. $C_{15}H_{16}O_3N_2S$ requires N, 9·2; S, 10·5%).

Hydrolysis of the *p*-acetamidophenyl β-benzamidoethyl sulphone with boiling 10N hydrochloric acid in the same manner as the above phthalimido-compound gave *p*-aminophenyl β-aminoethyl sulphone dihydrochloride.

αβ-Bis-(p-*acetamidophenylsulphonyl*)*ethane.*—Method 1. β-Diethylaminoethyl chloride hydrochloride (43 g., 0·25 mol.) was added to ice-cold 10N sodium hydroxide (250 c.c.) and the resulting liquid extracted three times with ether (500 c.c. in all). After drying with anhydrous potassium carbonate the ether was removed taking care that the temperature never exceeded 45—50°. When the residual trace of ether was removed under reduced pressure the yield of β-diethylaminoethyl chloride found to be 95—98% of theory. The base was dissolved in anhydrous *iso*propyl alcohol (350 c.c.) and the solution refluxed with anhydrous sodium *p*-acetamidobenzenesulphinate (44·1 g., 0·2 mol.) and a trace of copper powder for 4 hours. The suspension gradually changed in appearance and at the end of this period the liquid was filled with a voluminous crystalline solid. The alcohol was removed by steam distillation, the residual insoluble *αβ-bis-*(p-*acetamidophenylsulphonyl*)*ethane* (34 g.) collected, washed with water and dried. A sample recrystallised from a large volume of boiling 95% acetic acid or from aqueous pyridine gave the pure compound in the form of colourless felted needles, m. p. 282—284° (Found: C, 51·2; H, 4·9; N, 6·4, 6·6; S, 15·0, 15·1. $C_{18}H_{20}O_6N_2S_2$ requires C, 51·0; H, 4·7; N, 6·6; S, 15·1%). Four different preparations gave the compound in substantially the same yield, having the same m. p. and yielding the same analytical results. The disulphone was also obtained in approximately the same yield when anhydrous amyl alcohol was used in place of *iso*propyl alcohol and in rather less yield when a mixture of toluene and benzene (7 : 1) was used as diluent.

Method 2. Anhydrous sodium *p*-acetamidobenzenesulphinate (44·2 g.) was refluxed with a solution of ethylene dibromide (37·6 g.) in dry xylene (300 c.c.) in the presence of a trace of copper powder for 4½ hours. The xylene and excess ethylene dibromide were removed in steam and the residual insoluble solid (7·2 g.) collected. On recrystallisation from a large volume of boiling 95% acetic acid, the αβ-bis-(*p*-acetamidophenylsulphonyl)ethane was obtained in clusters of colourless needles, m. p. 284—286°, identical (mixed m. p.) with the product obtained by the first method (Found: N, 6·5; S, 15·2%).

Method 3. *p*-Acetamidobenzenesulphinic acid (20 g.; 0·1 mol.) and αβ-dibromosuccinic acid (13·8 g., 0·05 mol.) were suspended in water (40 c.c.) and 5N potassium hydroxide (40 c.c., 0·2 mol.) added; the pH value was adjusted to 7·0—7·5 by the addition of traces of sulphinic acid or N/100 potassium hydroxide and the clear solution refluxed for 18 hours. The heavy insoluble precipitate (4·8 g.) was recrystallised from 90% acetic acid or 90% dioxan and the αβ-bis-(*p*-acetamidophenylsulphonyl)ethane obtained in colourless needles (3·4 g.), m. p. 284—286°, identical (mixed m. p.) with the compound obtained by the two previous methods (Found: N, 6·5; S, 14·9%).

Identification of the other product of the reaction between sodium p-*acetamidobenzenesulphinate and β-diethylaminoethyl chloride.* (i) The reaction was carried out as in method 1, using the same quantities, care being taken to avoid loss of vola material, and the contents of the flask then slowly distilled in steam. The distillate (1800 c.c.) required 9·5 c.c. of 10N hydrochloric acid (0·095 mol. for neutralisation to phenolphthalein). This solution was made strongly acid with 10N hydrochloric acid and evaporated to small volume to remove the *iso*propyl alcohol (A). The cooled solution was then made strongly alkaline with 5N sodium hydroxide, and a strong odour of diethylamine was noticed. An acetone solution of *p*-toluenesulphonyl chloride, together with sufficient 5N sodium hydroxide to maintain an alkaline reaction, was added with shaking. After ½ hour, the liquid was neutralised with dilute hydrochloric acid, the acetone removed on the water-bath, and, after chilling, the solid (4·1 g.) collected. It was recrystallised from dilute alcohol and obtained in colourless short prisms, m. p. 60—62° and identified as *p*-toluene-*NN*-diethylsulphonamide (Found: N, 6·0; S, 14·1. Calc. for $C_{11}H_{17}O_2NS$: N, 6·2; S, 14·1%), proving the volatile amine to be diethylamine.

(ii) The procedure was the same as the foregoing except that the liquid (A) was chilled, basified with 10N sodium hydroxide and extracted several times with ether. The ethereal extract was dried with potassium carbonate and the ether slowly distilled into an ice-cooled receiver. The residual oil (2·5 g.) had b. p. 160—162° and was identified as β-diethylaminoethanol by conversion into diethylaminoethyl chloride hydrochloride, m. p. and mixed m. p. 204—206°, by refluxing with thionyl chloride. The clear ethereal distillate was saturated with hydrogen chloride, the white precipitate collected and recrystallised from a mixture of alcohol, acetone, and methyl ethyl ketone. Diethylamine hydrochloride (4·5 g.) was obtained in the characteristic nacreous flakes, m. p. 220—222° alone and in admixture with authentic material (Found: Cl, 32·6; Cl′, 32·5. Calc. for $C_4H_{12}NCl$: Cl, 32·5%). Two further experiments gave 4·6 g. and 4·5 g. respectively of recrystallised diethylamine hydrochloride, m. p. 220—222°, each yielding the same analytical results.

αβ-Bis-(p-*aminophenylsulphonyl*)*ethane.*—The above diacetyl compound (7 g.) was heated with acetic acid (200 c.c.) and 10N hydrochloric acid (100 c.c.). The compound rapidly dissolved and, in a short time, a precipitate began to appear. The liquid was vigorously refluxed for 4 hours, cooled, and the solid collected on sintered glass. This was suspended in boiling water (*ca.* 800 c.c.) and hydrochloric acid added until the material dissolved; the solution was then filtered (charcoal) and allowed to cool slowly. *αβ-Bis-*(p-*aminophenylsulphonyl*)*ethane dihydrochloride* was deposited in long colourless needles which were collected, washed with ether and dried under reduced pressure (4·9 g.); m. p. 330° (Found: N, 6·9; Cl, 17·1; S, 15·3; *M* by titration, 415. $C_{14}H_{18}O_4N_2Cl_2S_2$ requires N, 6·8; Cl, 17·2; S, 15·5%; *M*, 413). The dihydrochloride (4 g.) was ground to a fine powder, boiled with excess of aqueous ammonia, the base collected and recrystallised from 90% dioxan (*ca.* 350 c.c.) when *aβ-bis-*(p-*aminophenylsulphonyl*)*ethane* was obtained (2·6 g.) in small colourless prisms, m. p. 316—320° (Found: N, 8·3; S, 18·7, 19·0. $C_{14}H_{16}O_4N_2S_2$ requires N, 8·2; S, 18·8%).

The hydrolysis was also effected by refluxing the diacetyl compound (5 g.) with 95% acetic acid (200 c.c.) and sulphuric acid (25 c.c.) for 1½ hours. The initially clear solution soon began to deposit crystals. The mixture was cooled, the separated precipitate boiled with 50% aqueous ammonia and the free base collected. It was recrystallised from a large volume of 90% dioxan and gave the diamino disulphone in colourless small needles, m. p. 312—316°, identical with the above di-amino sulphone (Found: S, 18·6%).

Tetraethylethylenediamine.—This compound was prepared in the course of identifying the by-product in the above reaction and, since no satisfactory method of preparation appears to be described in the general literature, the methods used in the present investigation are recorded. (i) β-Diethylaminoethyl chloride hydrochloride (34·4 g., 0·2 mol.) was converted to the free base as described above and the ether completely removed under reduced pressure at a temperature not exceeding 45°. The residual oil (26 g.) was dissolved in dry benzene (40 c.c.) and diethylamine (22 g., 0·3 mol.) and the solution heated in a pressure bottle at 100° for 30 hours. The cooled reaction product was added to an excess of cold 10N sodium hydroxide, the mixture extracted four times with ether and the ethereal solution dried with potassium carbonate. The ether was removed and the residual oil distilled, tetraethylethylenediamine being obtained (22 g., 60%) as a mobile oil, b. p. 78°/11 mm., 83°/14 mm., and 60—62°/6 mm. A sample was dissolved in anhydrous ethyl alcohol and hydrogen chloride passed into the solution. Dry acetone was then added and, from the ice-cold solution, tetraethylethylenediamine dihydrochloride separated in colourless hard cubes. These, after washing with dry ether and drying at 80°/2 mm., had m. p. 184—186° (Found: Cl, 28·9. Calc. for $C_8H_{24}N_2$,2HCl: Cl, 29·0%). (ii) A solution of ethylene dibromide (37·6 g.; 20 c.c.) and diethylamine (37 g.; 54 c.c.) in benzene (75 c.c.) was heated in a closed bottle in the presence of a trace of copper powder for 30 hours. The product, isolated as described above, was tetraethylethylenediamine (24 g.), b. p. 83—85°/15 mm. and 188—190°/760 mm.

Condensation of Potassium p-*Acetamidobenzenesulphinate with Potassium Ethanolamine Sulphate.—Dithioacetanilide.* *p*-Acetamidobenzenesulphinic acid (100 g., 0·5 mol.) and ethanolamine sulphate (70·5 g., 0·5 mol.) (Goldberg, *J.*, 1942, 716) were dissolved in 1·66N potassium hydroxide (600 c.c., 1·0 mol.) and the strongly alkaline solution heated in an iron autoclave at 140° for 26 hours; the pressure developed was 50 lbs./sq. in. The resulting product was filtered and the deep chocolate-coloured insoluble material well washed into the filtrate; the filtrate and washings (1200 c.c.) had a pH value of 6·6. The insoluble material (94 g.) was refluxed with 90% alcohol (1 litre) containing aqueous ammonia (20 c.c.) and the boiling mixture filtered. The alcoholic filtrate on cooling precipitated long colourless needles (19 g.) and re-extraction of the residue with 90% alcohol gave a further quantity (total, 26 g.). The insoluble black residue (52 g.) was not further investigated. The colourless crystals were recrystallised from dilute alcohol and identified as dithioacetanilide (18 g.). The colourless long needles had m. p. 182—184° when lightly packed in the melting point tube and 216—218° when ground previously to insertion in the tube or placed in the tube and ground with a fine glass rod (Found: N, 8·2; S, 19·1. Calc. for $C_{16}H_{16}O_2N_2S_2$: N, 8·4; S, 19·3%). The lower and higher melting forms correspond with the α- and β-dimorphic forms described by Hinsberg (*Ber.*, 1906, **39**, 2427) and Zincke and Jörg (*ibid.*, 1909, **42**, 3374).

Dithioaniline. The foregoing dithioacetanilide (15 g.) in alcohol (50 c.c.) and 10N hydrochloric acid (50 c.c.) was refluxed on the water-bath for 1 hour by which time the liquid was filled with a heavy white crystalline precipitate. After cooling, the crystals (14 g.) were collected and recrystallised from methanol–ethanol containing a little hydrochloric acid. Dithioaniline dihydrochloride was obtained in colourless prismatic needles, m. p. 240—242° (softening at 234°) [Found: Cl, 21·8; S, 19·7%; *M* (titration) 325. Calc. for $C_{12}H_{12}N_2S_2$,2HCl: Cl, 22·1; S, 19·9%; *M*, 321]. When this dihydrochloride was dissolved in water and the solution made alkaline with cold 10N sodium hydroxide an oil separated and rapidly solidified. This was recrystallised from dilute methanol–ethanol and the dithioaniline obtained in good yield in long lemon-yellow needles, m. p. 78—80°, which were very soluble in ether (Found: N, 11·0; S, 25·6. Calc. for $C_{12}H_{12}N_2S_2$: N, 11·3; S, 25·8%).

p-*Aminophenyl γ-Diethylamino*-n-*propyl Sulphone.*—*p*-Acetamidophenyl phenacyl sulphone (15·85 g., Goldberg and Besly, *loc. cit.*) was added to a solution of sodium (1·15 g.) in anhydrous ethanol (120 c.c.) and the clear solution refluxed for 30 minutes. Diethylaminoethyl chloride (21 g., b. p. 55°/25 mm.) was added to the clear warm solution, the mixture allowed to stand for 2 hours at 40° with frequent shaking and then refluxed for 6 hours. When the filtered solution was evaporated to small volume and water added the alkylated product separated as a thick oil which could not be induced to crystallise. This oil was soluble in dilute acid and dilute alkali and also had an appreciable solubility in water. The oil was refluxed with alcohol (100 c.c.) and 5N sodium hydroxide (100 c.c.) for 2 hours, the solution adjusted to pH 7·2 with hydrochloric acid and the alcohol distilled away. The cooled solution was made strongly alkaline with 10N sodium hydroxide, the precipitated oil separated and extracted exhaustively with ether. The yellow ethereal solution was dried with potassium carbonate and the ether removed. Crude p-aminophenyl γ-diethylaminopropyl sulphone (6·1 g.) remained as thick oil which would not solidify. It was dissolved in alcohol (60 c.c.), the solution saturated with hydrogen chloride and filtered (charcoal) while boiling. On cooling, p-*aminophenyl γ-diethylaminopropyl sulphone dihydrochloride* separated in microcrystalline aggregates, m. p. 180—186° (decomp.). These were hygroscopic and could not be obtained analytically pure; for analysis they were dried over phosphorus pentoxide at 80°/1 mm. when there was slight loss of hydrogen chloride (Found: N, 7·8; Cl, 19·1; S, 10·0. $C_{13}H_{24}O_2N_2Cl_2S$ requires N, 8·1; Cl, 20·7; S, 9·3%).

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