727. *Antituberculous Compounds. Part IX.* Some Dialkylaminoalkyl Sulphones and Related Compounds.*

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A number of alkyl 2-diethylaminoethyl sulphones have been prepared, together with related compounds in which the sulphonyl group was replaced by other atoms or groups. Of these the sulphides are outstandingly active *in vitro*. Some aminomethyl sulphones of the type *p*-Me·C_6H_4·SO_2·CH_2·NRR′ were also prepared. The corresponding alkyl aminomethyl sulphones appear to be too unstable to exist.

In the course of the preparation of amino-substituted Bunte salts, an interesting difference in the behaviour of 2-diethylamino- and 2-dioctylamino-ethyl chlorides was observed.

Many aliphatic amines, particularly those containing 16—20 carbon atoms, possess marked activity *in vitro* against *Mycobacterium tuberculosis* (Stanley, Coleman, Greer, Sacks, and Adams, *J. Pharmacol.*, 1932, **45**, 121; Borrows, Hargreaves, Page, Resuggan, and Robinson, *J.*, 1947, 197) but are inactive *in vivo*. Many aromatic amines also show a high degree of activity *in vitro* (*e.g.*, Bloch, Lehr and Erlenmeyer, *Helv. Chim. Acta*, 1945, **28**, 1406), but activity *in vivo* is shown only by compounds of the diaminodiphenyl sulphone type which contain a sulphone group in addition to the amino-groups. It therefore appeared of interest to examine the effect of the introduction of sulphonyl groups into aliphatic amines. The

$NEt_2·CH_2·CH_2·XR$ (I) $\quad$ $Me·N(CH_2·CH_2·SO_2·C_8H_{17})_2$ (II) $\quad$ $Pr·CH(S·CH_2·CH_2·NEt_2)_2$ (III)

alkyl 2-diethylaminoethyl sulphones (I; X = SO_2, R = Bu, C_8H_{17}, and $C_{16}H_{33}$) were prepared by the oxidation of the corresponding sulphides (I; X = S). Methylbis-2-octylsulphonylethylamine (II) was similarly prepared as an example of an amine with two β-sulphonyl groups. The activities *in vitro* of these sulphones, recorded in the experimental section, were of a low order. The intermediate sulphides (I; X = S), however, showed high activity. The single sulphoxide prepared, 2-diethylaminoethyl octyl sulphoxide (I; X = SO, R = C_8H_{17}), was intermediate in activity between the corresponding sulphide and sulphone.

* Part VIII, preceding paper.

Several isosteric analogues of the sulphides were accordingly prepared in which replacement of the sulphur atom by other atoms or groups would afford some measure of the specific effect of the sulphur atom on antituberculous activity. The following compounds were prepared by standard procedures: (1) butyl 2-diethylaminoethyl ether and 2-diethylaminoethyl octyl ether as oxygen analogues, (2) diethylheptylamine and diethylundecylamine as methylene analogues, and (3) 2-diethylaminoethyl nonyl ketone as a carbonyl analogue. All showed reduced activity. The specificity of the sulphur in the β-position to the diethylamino-group was further shown by the preparation of 3-diethylaminopropyl propyl sulphide (I; X = CH_2·S, R = Pr) which was much less active than the isomeric butyl 2-diethylaminoethyl sulphide (I; X = S, R = Bu). Butaldehyde bis-2-diethylaminoethyl mercaptal (III) was prepared by condensation of either butaldehyde and 2-diethylaminoethanethiol hydrochloride or 1 : 1-dichlorobutane and sodium 2-diethylaminoethyl sulphide but the second 2-diethylaminoethyl sulphide residue had an adverse effect on activity.

As further types of basic sulphones, bis-2-diethylaminoethyl sulphone and *p*-aminophenyl 2-diethylaminoethyl sulphone were prepared. Neither proved to be of interest. The sulphide and sulphoxide corresponding to the former were also ineffective. The disulphide showed slight activity.

p-Me·C_6H_4·SO_2·CH_2R (IV) RS·SO_2·ONa (V) RS·SO_3·OR (VI)

A few α-amino-sulphones were prepared by condensation of hydroxymethyl *p*-tolyl sulphone (IV; R = OH) (Meyer, *J. pr. Chem.*, 1901, **63**, 168) with various amines. In this way *N*-methyl-*N*-(toluene-*p*-sulphonylmethyl)aniline (IV; R = NMePh), 4-(toluene-*p*-sulphonylmethyl)morpholine (IV; R = N<[CH_2]$_4$>O), N^4-(toluene-*p*-sulphonylmethyl)sulphanilamide (IV; R = NH·C_6H_4·SO_2·NH_2-*p*) and 2-methyl-5-(toluene-*p*-sulphonylmethylamino)-1 : 3 : 4-oxadiazole (IV; R = NH·C:N·N:CMe, O) were obtained. These compounds were inactive and unstable, readily evolving formaldehyde when warmed with dilute acid. The failure to isolate anything but fission products by oxidation of diethylaminomethyl methyl sulphide (cf. McLeod and Robinson, *J.*, 1921, **119**, 1470), under the mildest possible conditions, indicates that alkyl diethylaminomethyl sulphones are even less stable.

A few compounds of the Bunte salt type were also prepared. 2-Diethylaminoethyl bromide or chloride condensed readily with sodium thiosulphate to give the monoester sodium salt (V; R = CH_2·CH_2·NEt_2). No tendency could be detected, even in the presence of a large excess of the halide, for the formation of any diester (VI; R = CH_2·CH_2·NEt_2). It was, therefore, surprising to find that with 2-dioctylaminoethyl chloride the sole product was the diester [VI; R = CH_2·CH_2·N(C_8H_{17})$_2$], half the sodium thiosulphate remaining unchanged when equivalent quantities of the reactants were used. This appears to be the first diester of thiosulphuric acid to have been described.

The preparation of sodium octyl and hexadecyl thiosulphates (V; R = C_8H_{17} and $C_{16}H_{33}$) is also described, since these have been found convenient sources of the corresponding thiols which are readily obtained by acid hydrolysis (cf. Westlake and Dougherty, *J. Amer. Chem. Soc.*, 1941, **63**, 658; 1942, **64**, 149). Sodium butyl thiosulphate (V; R = Bu), hydrolysed without isolation, is a less favourable source of butanethiol.

The highly active butyl 2-diethylaminoethyl sulphide (I; X = S, R = Bu) was selected for trial *in vivo* in guinea-pigs but no activity could be detected (Croshaw and Dickinson, *Brit. J. Pharmacol.*, 1950, **5**, 178).

Experimental.

The activities recorded refer to the standard conditions detailed on p. 3291 (footnote *). The symbol (*s*) indicates that the inhibition is in the presence of 10% serum.

Sodium Octyl Thiosulphate.—A solution of sodium thiosulphate (25 g.) in water (110 c.c.) was added to octyl bromide (20 g., 1 mol.) and ethanol (110 c.c.). The mixture was heated under reflux for 3½ hours, by which time it was homogeneous and sodium thiosulphate could no longer be detected. The ethanol was removed under diminished pressure, finally over sulphuric acid. The residual solid was extracted with hot acetone. On cooling, the extract deposited *sodium octyl thiosulphate monohydrate* in plates (16 g.), further purified by recrystallisation from ethanol (Found: H_2O, 6·7. $C_8H_{17}O_3S_2Na,H_2O$ requires H_2O, 6·7%) (activity = <1). Drying at 40° *in vacuo* over phosphoric oxide afforded the anhydrous *salt* (Found: S, 25·6; Na, 9·1. $C_8H_{17}O_3S_2Na$ requires S, 25·8; Na, 9·3%).

Sodium Hexadecyl Thiosulphate.—A mixture of hexadecyl iodide (7·0 g.), sodium thiosulphate (5·0 g., 1 mol.), ethanol (15 c.c.), and water (11 c.c.) was heated under reflux until it became homogeneous

(3 hours). On cooling, the product separated in translucent plates as a *dihydrate* (5·9 g.) and was recrystallised from ethanol (Found: S, 16·5; Na, 5·7; H_2O, loss *in vacuo* at 70°, 10·0. $C_{16}H_{33}O_3S_2Na,2H_2O$ requires S, 16·2, Na, 5·8; H_2O, 9·1%).

Sodium 2-Diethylaminoethyl Thiosulphate.—2-Diethylaminoethyl bromide hydrobromide (20 g., 1 mol.), N-sodium hydroxide (76·6 c.c., 1 equiv.), and sodium thiosulphate (19 g., 1 mol.) were stirred together at 35—40°, and the reaction was followed by titration of 3-c.c. aliquots with 0·1N-iodine at intervals. Reaction was almost complete after 20 minutes. The solution was evaporated to dryness *in vacuo*, and the residue extracted with hot acetone. The extract, on cooling, deposited *sodium 2-diethylaminoethyl thiosulphate* as plates, further purified by crystallisation from ethanol (yield, 11·8 g.) (Found: N, 5·8. $C_6H_{14}O_3NS_2Na$ requires N, 5·95%) (activity <1). The product decomposed appreciably at 100°. The same compound was obtained by using diethylaminoethyl chloride but the reaction was slower.

Bis-2-dioctylaminoethyl Thiosulphate.—2-Dioctylaminoethyl chloride hydrochloride (4·8 g.) (Part I, *J.*, 1949, 2680) was dissolved in ethanol (12 c.c.), and 0·1N-sodium hydroxide (13·95 c.c., *i.e.*, almost 1 equiv.) added to give a solution neutral to phenolphthalein. A solution of sodium thiosulphate (3·5 g., 1 mol.) in water (7 c.c.) was then added, and the two-phase mixture stirred at room temperature. At intervals, aliquots (1 c.c.) of the lower, aqueous layer were titrated with 0·01N-iodine. The titre fell steadily during 8 hours to 50% of its original value where it remained constant. The same result was obtained at temperatures as varied as 0° and 75°. The reaction mixture was evaporated to dryness *in vacuo*, and the residue extracted with warm ethanol. Sodium thiosulphate (1·7 g.) was left as residue. The extract was evaporated *in vacuo*, and the residue dissolved in ether containing a little ethanol. Slow evaporation of this solution afforded *bis-2-dioctylaminoethyl thiosulphate* (3·2 g.) as waxy plates, m. p. 138° (Found: C, 66·9; H, 11·75; N, 4·3; S, 10·2; Na, 0·1. $C_{36}H_{76}O_3N_2S_2$ requires C, 66·6; H, 11·7; N, 4·3; S, 9·9%) (activity = 5). The *monopicrate* separated from ether as a granular, yellow precipitate (Found: N, 8·2. $C_{42}H_{79}O_{10}N_5S_2$ requires N, 8·0%).

Alkyl 2-Diethylaminoethyl Sulphides.—2-Diethylaminoethyl chloride (48 g., 1·2 mols.) was added to a solution of sodium methyl sulphide (1 mol.), prepared by passing methanethiol into a cooled solution of sodium (7 g.) in absolute ethanol (200 c.c.) (Windus and Shildneck, *Org. Syn.*, 1943, Coll. Vol. II, p. 345), and the mixture warmed gently. A vigorous reaction set in at *ca.* 50° and sodium chloride was precipitated. The reaction was completed by 1 hour's heating under reflux with mechanical stirring. The reaction mixture was filtered, the filtrate evaporated *in vacuo*, and the residue extracted with ether. The ethereal solution was washed with water, dried (Na_2SO_4), and evaporated. Distillation of the residue afforded *2-diethylaminoethyl methyl sulphide* (28 g.) as a colourless oil, b. p. 141—145°/150 mm. (Found: N, 9·5. $C_7H_{17}NS$ requires N, 9·5%) (activity = <1 to 1). The hydrochloride crystallised from ethanol–ether in needles but was too hygroscopic for satisfactory analysis.

In the same way butanethiol (b. p. 97—99°; prepared in 25% yield by hydrolysis of sodium butyl thiosulphate with boiling dilute sulphuric acid) gave *butyl 2-diethylaminoethyl sulphide* (80%), b. p. 82°/2·5 mm. (Found: N, 7·4. $C_{10}H_{23}NS$ requires N, 7·4%) [activity = 500—1000; (*s*) 100 (500)]. Octanethiol (b. p. 75—78°/8 mm., prepared in 90% yield by the hydrolysis of sodium octyl thiosulphate) gave *2-diethylaminoethyl octyl sulphide* (89%), b. p. 116—118°/0·7 mm. (Found: N, 5·9. $C_{14}H_{31}NS$ requires N, 5·7%) [activity = >500; (*s*) 50] (Reineckate, m. p. 101—102°), and hexadecanethiol (b. p. 120°/0·7 mm., prepared in 71% yield by hydrolysis of sodium hexadecyl thiosulphate) gave *2-diethylaminoethyl hexadecyl sulphide* (83%), b. p. 184°/0·2 mm. (Found: N, 4·05. $C_{22}H_{47}NS$ requires N, 3·95%) [activity = 100 (500); (*s*) 10] (Reineckate, m. p. 122°).

Butyl 2-diethylaminoethyl sulphide was also prepared in 95% yield from 2-diethylaminoethanethiol (Albertson and Clinton, *J. Amer. Chem. Soc.*, 1945, **67**, 1222) and butyl bromide.

3-Diethylaminopropyl Propyl Sulphide.—Propanethiol (24·5 g.) (Ellis and Reid, *J. Amer. Chem. Soc.*, 1932, **54**, 1684) and trimethylene chlorohydrin (30·7 g.) were added to a solution of sodium (7·5 g.) in absolute ethanol (200 c.c.), and the solution heated under reflux for 1½ hours. The ethanol was removed *in vacuo*, and the product isolated with ether. Distillation gave 3-hydroxypropyl propyl sulphide as a colourless oil (35·0 g.), b. p. 115°/16 mm.

A mixture of this compound (10·0 g.), pyridine (6·0 g., 1 mol.), and chloroform (8 c.c.) was added slowly to thionyl chloride (8·9 g., 1 mol.) in chloroform (8 c.c.) at 10—13°. After 30 minutes the mixture had separated into two layers but became homogeneous on addition of further chloroform (10 c.c.). Next morning, the solution was heated under reflux for 1½ hours, the chloroform was removed *in vacuo*, and the residue was extracted with ether. Distillation of the extract afforded 3-chloropropyl propyl sulphide as a colourless oil (9·0 g.), b. p. 104°/34 mm. This was heated in a sealed tube with diethylamine (16·0 g., 4 mols.) at 120—130° for 5 hours. Diethylammonium chloride was removed, and the filtrate evaporated *in vacuo*. The residual oil was dissolved in light petroleum, and the solution extracted with dilute hydrochloric acid. The acid extracts were basified and the oil was isolated with ether. Distillation gave *3-diethylaminopropyl propyl sulphide* as a colourless oil (4·1 g.), b. p. 138—139°/38 mm. (Found: N, 7·5. $C_{10}H_{23}NS$ requires N, 7·4%) [activity = 10—50; (*s*) 5—10].

Butaldehyde Bis-2-diethylaminoethyl Mercaptal.—2-Diethylaminoethanethiol hydrochloride (12·6 g., 2 mols.) was dissolved in warm chloroform (15 c.c.) and butaldehyde (2·7 g., 1 mol.) was added. The solution was saturated at 10—15° with dry hydrogen chloride, kept overnight, and then warmed to 50° for 1 hour. The chloroform was removed *in vacuo*, and the residue taken up in water and basified with sodium hydroxide. The resultant oil was isolated with ether. Distillation gave the *mercaptal* as a yellow oil (7 g.), b. p. 151—152°/0·7 mm. (Found: N, 8·3. $C_{16}H_{36}N_2S_2$ requires N, 8·7%). The *dihydrochloride* crystallised from ethanol–ether in needles, m. p. 188—189° (Found: N, 7·05. $C_{16}H_{38}N_2Cl_2S_2$ requires N, 7·1%) [activity = 10; (*s*) 5]. The *monohydrochloride*, prepared with one

equivalent of hydrogen chloride, also crystallised from ethanol–ether in needles, m. p. 209—210° (Found : N, 8·3. $C_{16}H_{37}N_2ClS_2$ requires N, 7·9%).

The same product was obtained, but in poorer yield, by condensation of 1 : 1-dichlorobutane with sodium 2-diethylaminoethyl sulphide in methanol.

2-Diethylaminoethyl Octyl Sulphoxide.—The corresponding sulphide (15·0 g.) was dissolved in N-hydrochloric acid (61 c.c., 1 equiv.), 18% (w/v) hydrogen peroxide (13 c.c., 1·33 mols.) was added at such a rate that the temperature did not rise above 28° during the addition, and the mixture was kept overnight. Water and excess of hydrogen peroxide were removed under reduced pressure and the free base was liberated with dilute aqueous ammonia. The *sulphoxide*, isolated with ether, distilled at 138—140°/0·1 mm. as a colourless oil (11 g.) which darkened when kept (Found : C, 63·4; H, 11·6; N, 4·95. $C_{14}H_{31}ONS$ requires C, 64·4; H, 11·9; N, 5·4%) [activity = 10 (100); (*s*) 10 (50)]. The analysis suggests that the compound was contaminated with sulphone. Its Reineckate, crystallised from ethyl acetate–ether, had m. p. 106—107°. This depressed the m. p. of the Reineckate of the original sulphide to 94°.

Alkyl 2-Diethylaminoethyl Sulphones.—Butyl 2-diethylaminoethyl sulphide (7·0 g.) was dissolved in 50% aqueous acetic acid (5 c.c.), and a 3% solution of potassium permanganate in 50% aqueous acetic acid (160 c.c., 5% excess) added with stirring at 0—3°. Oxidation was rapid. The solution was finally decolorised with a little sulphur dioxide and concentrated *in vacuo*, and the residue made alkaline with aqueous ammonia. The resulting oil was isolated with ether and distilled, affording *butyl 2-diethylaminoethyl sulphone* (3·2 g.) as a colourless oil, b. p. 144°/3 mm. (Found : N, 6·3. $C_{10}H_{23}O_2NS$ requires N, 6·3%) [activity = 10; (*s*) 10].

In a similar manner the corresponding *octyl sulphone*, b. p. 152°/0·1 mm. (Found : C, 60·9; H, 10·9; N, 5·0. $C_{14}H_{31}O_2NS$ requires C, 60·65; H, 11·2; N, 5·05%) [activity = 10; (*s*) 5 (10)], was obtained in 80% yield. It gave a Reineckate, m. p. 122°, depressed by the Reineckate of both the sulphide and the sulphoxide. The corresponding *hexadecyl sulphone*, b. p. 205—206·5°/0·07 mm. (Found : N, 3·5. $C_{22}H_{47}O_2NS$ requires N, 3·6%) (activity = 5), was obtained in 58% yield. It gave a Reineckate, m. p. 132°, depressed to 117° by the Reineckate of the sulphide.

Methylbis-2-octylsulphonylethylamine.—Octanethiol (5·84 g., 2 mols.) was added to a solution of sodium (0·92 g., 2 atoms) in absolute ethanol (50 c.c.). At the same time bis-2-chloroethylmethylammonium chloride (3·85 g., 1 mol.) was added to a solution of sodium (0·46 g., 1 atom) in absolute ethanol (50 c.c.), and the two solutions were mixed and heated under reflux for 2 hours. The product, methyldi-(2-octylthioethyl)amine, was isolated as described for the analogous alkyl 2-diethylaminoethyl sulphides and obtained as a colourless oil (5·5 g.), b. p. 175—190°/0·5 mm. Refractionation gave 3·9 g., b. p. 180—186°/0·5 mm. The product was still impure (Found : N, 4·6. Calc. for $C_{21}H_{45}NS_2$: N, 3·7%) but was oxidised directly as described for the corresponding alkyl 2-diethylaminoethyl sulphones. Crystallisation of the product from water gave *methyldi-(2-octylsulphonylethyl)amine* (1·9 g.) as long needles, m. p. 185° after shrinking at 140° (Found : N, 3·0. $C_{21}H_{45}O_4NS_2$ requires N, 3·15%) [activity = 50; (*s*) 10]. The *hydrochloride* separated from ethanol in needles, m. p. 197° after shrinking at 140° (Found : N, 3·0; Cl, 7·1. $C_{21}H_{46}O_4NClS_2$ requires N, 2·9; Cl, 7·4%).

Butyl 2-Diethylaminoethyl Ether.—Sodium (6·9 g.) was dissolved in butanol (300 c.c.), and 2-diethylaminoethyl chloride (40 g.) added. The mixture was heated on the steam-bath, sodium chloride rapidly separating. After 15 hours the mixture was cooled, acidified to Congo-red with concentrated hydrochloric acid, filtered, and evaporated under reduced pressure. The residue was dissolved in water, basified with sodium hydroxide, and isolated with ether. The crude product (38 g.) distilled at 144—148°/200—210 mm. Redistillation failed to afford an analytically pure specimen. It was therefore converted into the *Reineckate*, m. p. 122° (decomp.) after repeated recrystallisation from aqueous methanol (Found : N, 19·6. $C_{14}H_{30}ON_7S_4Cr$ requires N, 19·9%). The free *base* recovered from the Reineckate had b. p. 144°/200 mm. (Found : N, 8·0. $C_{10}H_{23}ON$ requires N, 8·1%) [activity = 1—5; (*s*) 5].

2-Diethylaminoethyl Octyl Ether.—A solution of sodium (2·3 g.) in octanol (175 c.c.) was heated for 20 hours at 100° with 2-diethylaminoethyl chloride (13 g.). The mixture was cooled, diluted with light petroleum (100 c.c.), and extracted with excess of dilute hydrochloric acid. No product was precipitated on basification of the acid extract. The solvent layer was accordingly evaporated *in vacuo*, and the residual solid hydrochloride shaken with ether and dilute sodium hydroxide. Distillation of the ether afforded the pure *ether* (10·9 g.), b. p. 130—133°/10 mm. after redistillation (Found : N, 6·1. $C_{14}H_{31}ON$ requires N, 6·1%) [activity = 50—100; (*s*) 10].

Diethylheptylamine.—A mixture of heptyl bromide (6 g.) and diethylamine (12 g., 5 mols.) was heated in a sealed tube for 4 hours at 130°. The contents of the tube were diluted with ether, and diethylammonium bromide (5·0 g., 98%) filtered off. Distillation of the ethereal extract gave a crude product (4·8 g.), b. p. 154—156°/200 mm., of low nitrogen content (Found : N, 6·6. Calc. for $C_{11}H_{25}N$: N, 8·2%). The crude material was distributed between light petroleum and N-hydrochloric acid. The basic material, re-isolated from the acid extract, gave the pure amine, b. p. 156°/200 mm. (Found : N, 8·4%) [activity = 50; (*s*) 10—50]. Mannich and Davidson (*Ber.*, 1936, **69**, 2106) record b. p. 198°/760 mm. for this compound.

Diethylundecylamine.—A mixture of undecyl bromide (10 g.), diethylamine (7 g., 2·25 mols.), and xylene (10 c.c.) was heated in a sealed tube for 5 hours at 170°. *Diethylundecylamine*, isolated and purified as above, was obtained as a colourless liquid (7·5 g.), b. p. 85—88°/2 mm. (Found : N, 6·4. $C_{15}H_{33}N$ requires N, 6·2%) (activity = 5—10). The only solid derivative obtained was a Reineckate, m. p. 71°.

2-Diethylaminoethyl Nonyl Ketone.—This was prepared by Fry's method (*J. Org. Chem.*, 1945, **10**, 259). A mixture of methyl nonyl ketone (8·5 g., 1 mol.), paraformaldehyde (3·0 g., 2 mols.), diethyl-

ammonium chloride (5·5 g., 1 mol.), concentrated hydrochloric acid (0·2 c.c.), benzene (20 c.c.), and nitrobenzene (20 c.c.) was heated under reflux with stirring. A clear solution was obtained after 15 minutes. After 45 minutes the bath-temperature was raised from 110° to 145°, a water-trap was introduced into the condensing system, and heating was continued for 15 minutes. After cooling, the solution was filtered from a small quantity of crystalline diethylammonium chloride and evaporated *in vacuo*. The residual brown oil only partly solidified. It was accordingly made alkaline, and the free base isolated with ether. Distillation afforded 2-*diethylaminoethyl nonyl ketone* as a colourless oil (6·9 g.), b. p. 118—122°/0·5 mm. (Found : N, 5·7. $C_{16}H_{33}ON$ requires N, 5·5%) (activity = 1—5).

Bis-2-diethylaminoethyl Sulphoxide.—Bis-2-diethylaminoethyl sulphide (4·6 g.; b. p. 106—110°/2 mm.) (Gilman, Plunkett, Tolman, Fullhart, and Broadbent, *J. Amer. Chem. Soc.*, 1945, **67**, 1846) was suspended in ice-cold water (15 c.c.), and bromine water added with stirring in slight excess as shown by a faint yellow colour. The solution was evaporated *in vacuo*, and the residue dissolved in boiling ethanol (300 c.c.). On cooling, the *sulphoxide dihydrobromide* separated as colourless small needles (5·5 g.), m. p. 224° (decomp.) (Found : N, 6·8. $C_{12}H_{30}ON_2Br_2S$ requires N, 6·8%) (activity = <1). Titration with acid potassium permanganate resulted in the uptake of almost exactly two atoms of oxygen, corresponding to oxidation of the sulphoxide to sulphone and of the hydrogen bromide to bromine.

Bis-2-diethylaminoethyl Sulphone.—A solution of potassium permanganate (3 g., 10% excess) in 50% acetic acid (200 c.c.) was added with stirring at 0° to a solution of bis-2-diethylaminoethyl sulphide (10 g.) in 50% acetic acid (10 c.c.) during 45 minutes. After a further 20 minutes, the brown solution was decolorised with sulphur dioxide and evaporated to dryness *in vacuo*. The residue was dissolved in hot absolute ethanol and treated with excess of ethanolic ammonia. The inorganic salts were removed and re-extracted with absolute ethanol, and the united filtrates evaporated to dryness. The residual gum was extracted with warm absolute ethanol and filtered. Addition of ethanolic hydrogen chloride to the filtrate gave the *sulphone dihydrochloride* as colourless needles (6·0 g.), m. p. 202° after recrystallisation from ethanol (Found : N, 8·3. $C_{12}H_{30}O_2N_2Cl_2S$ requires N, 8·3%) (activity = <1).

Bis-2-diethylaminoethyl Disulphide.—2-Diethylaminoethanethiol hydrochloride, needles, m. p. 172—173°, from ethanol–ether, was exposed to air overnight. Crystallisation of the resulting solid from ethanol–ether gave the disulphide dihydrochloride as needles, m. p. 220° (Found : N, 8·5. Calc. for $C_{12}H_{30}N_2Cl_2S_2$: N, 8·3%) [activity = 10; (*s*) 5]. Gilman *et al.* (*loc. cit.*) record m. p. 216—217°.

p-*Aminophenyl* 2-*Diethylaminoethyl Sulphone.*—2-Diethylaminoethyl chloride (27·0 g., 1·1 mols.) was added to a solution of sodium *p*-acetamidobenzenesulphinate (1 mol.), prepared by adding *p*-acetamidobenzenesulphinic acid (35 g.; Smiles and Bere, *Org. Synth.*, 1941, Coll. Vol. I, p. 7) to a solution of sodium (4·0 g.) in absolute ethanol (500 c.c.), and the mixture was heated under reflux. Sodium chloride began to separate after about 5 minutes. After 1½ hours the reaction mixture was cooled, filtered from sodium chloride, and concentrated *in vacuo* to about half its volume. At this point a *substance* (3 g.) of unknown composition separated as fine needles, m. p. 284° (Found : N, 7·2%). The filtrate from this solid was further evaporated to dryness and the residual gum treated with 2N-hydrochloric acid (100 c.c.). The insoluble residue consisted of a mixture of *p*-acetamidobenzenesulphinic acid (3·5 g.) and the above compound, m. p. 284° (1·5 g.). The acid-soluble p-*acetamidophenyl* 2-*diethylaminoethyl sulphone* was precipitated by sodium hydroxide as a colourless solid, crystallising from benzene in needles (16 g.), m. p. 93—94° (Found : N, 8·9. $C_{14}H_{22}O_3N_2S$ requires N, 9·4%).

The above compound (7 g.) was heated under reflux for 1 hour with 2N-hydrochloric acid (180 c.c.). The cooled solution was made alkaline to litmus with sodium hydroxide. The oily precipitate solidified on cooling to 0° and was collected and redissolved in boiling water (250 c.c.). On cooling, p-*aminophenyl* 2-*diethylaminoethyl sulphone* (4·7 g.) separated in long needles, m. p. 55° (Found : N, 10·8. $C_{12}H_{20}O_2N_2S$ requires N, 10·9%) (activity = <1).

Toluene-p-*sulphonylmethylamines.*—A solution of hydroxymethyl *p*-tolyl sulphone (2·0 g.) (Meyer, *loc. cit.*) and methylaniline (1·14 g., 1 mol.) in ether (75 c.c.) quickly deposited N-(*toluene*-p-*sulphonylmethyl*)*aniline* (2·05 g.), needles, m. p. 109° (Found : N, 5·5. $C_{15}H_{17}O_2NS$ requires N, 5·4%). The following compounds were prepared similarly, the solvent for the condensation being given in parentheses : N^4-(*toluene*-p-*sulphonylmethyl*)*sulphanilamide* (from methanol), flat needles, m. p. 166—167° (Found : N, 8·6. $C_{14}H_{16}O_4N_2S_2$ requires N, 8·25%) (activity = <1); 2-*methyl*-5-(*toluene*-p-*sulphonylmethylamino*)-1 : 3 : 4-*oxadiazole*, fine needles (from chloroform), m. p. 170° (Found : N, 15·8. $C_{11}H_{13}O_3N_3S$ requires N, 15·7%) (activity = <1); 4-(*toluene*-p-*sulphonylmethyl*)*morpholine*, plates (from ether), m. p. 86—88° (Found : N, 5·5. $C_{12}H_{17}O_3NS$ requires N, 5·5%).

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