RESEARCH PAPERS

STUDIES IN THE FIELD OF DIURETIC AGENTS

PART V. A NEW ROUTE TO DISULPHAMYL DERIVATIVES OF BENZENE

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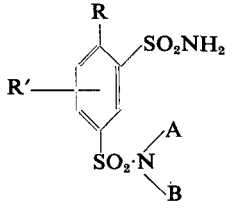
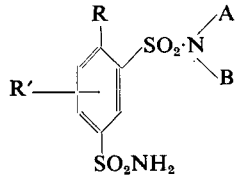
A procedure has been developed for converting sulphamyl derivatives of aniline into the corresponding sulphamyl-sulphonchlorides. The latter have been condensed with ammonia and with amines giving novel 1,2-, 1,3- and 1,4-disulphamyl derivatives of benzene, required for examination as diuretics.

WORK on disulphamyl derivatives of benzene is herein extended to some novel types containing one unsubstituted sulphamyl residue. Derivatives of 1,3-disulphamyl benzene in which only one sulphamyl group is alkylated (I; II) are not described in the literature. Their preparation presented initial difficulty. Alkylation of a disulphonamide with one equivalent proportion of alkylating agent gave a complex mixture from which a monoalkyl-derivative could not be isolated. Chlorosulphonation of a sulphonamide or *N*-substituted sulphonamide caused deamination of the sulphamyl group with formation of a 1,3-disulphonchloride (e.g., III) in place of the required 3-chlorosulphonyl sulphamylbenzene.

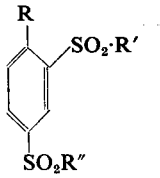
Steinkopf and others[1] have shown that sulphonfluorides are more stable than sulphonchlorides and, unlike the latter, are not readily attacked by ammonia in ether. This observation formed the starting point of our first method for the preparation of monoalkylated 1,3-disulphonamides. Toluene-4-sulphonfluoride[2] was chlorosulphonated in carbon tetrachloride solution to give toluene 2-sulphonchloride-4-sulphonfluoride (IV) in moderate yield. This reacted with ammonia in aqueous dioxan at $-10°$ to give a small yield of (V) which, with ethanolic methylamine, provided the required monomethyl disulphonamide (VI).



(I)



(II)

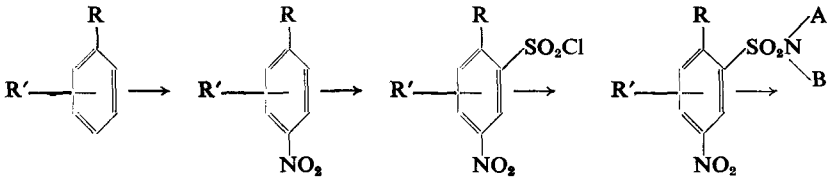


(III): $R' = R'' = Cl$
(IV): $R = Me$, $R' = Cl$, $R'' = F$
(V): $R = Me$, $R' = NH_2$, $R'' = F$
(VI): $R = Me$, $R' = NH_2$, $R'' = NH{\cdot}Me$

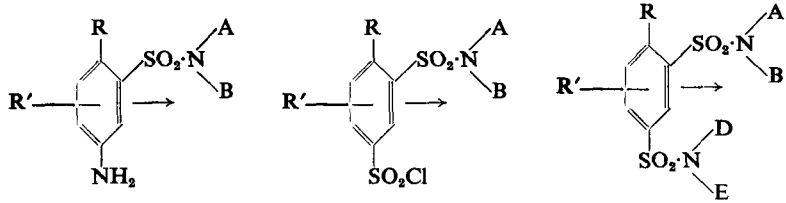
This method could not be extended to the preparation of 1,4-disulphamyl compounds because of the *m*-directive effect of the sulphonhalide group. A method of sufficiently wide scope was ultimately discovered by applying the reaction of Meerwein and others[3] for converting an aniline into the corresponding benzene sulphonchloride. Route (i) shows the stages in the preparation of a mixed alkylated 1,3-disulphonamide using this reaction. Conversion of (VII) to (XI) follows conventional routes. Compound (XI) is then converted into the diazonium chloride and treated with excess of a saturated solution of sulphur dioxide in glacial acetic acid, containing cupric chloride as catalyst, to give the sulphonchloride (XII). Conversion to (XIII) follows normal practice.

Several variations of this versatile method are immediately apparent. Thus by using a suitable benzene sulphonyl chloride (XIV) a 1,3-disulphamyl benzene derivative may be prepared according to route (ii). Numerous 1,3-disulphonamides (Table IV) were prepared in this way from benzene, toluene, ethyl, n-propyl and isopropylbenzene, 1,2- and 1,3-xylene, anisole, chlorobenzene, bromobenzene, 1,3-dichlorobenzene, 1,2- and 1,3-chlorotoluene.

Route (i)

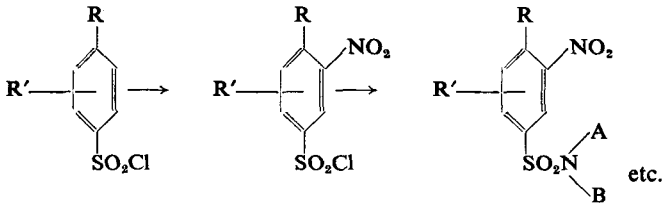


(VII) (VIII) (IX) (X)



(XI) (XII) (XIII)

Route (ii)

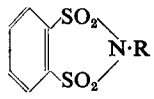


(XIV) (XV) (XVI)

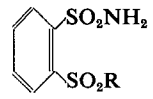
TABLE I

NITROSULPHONAMIDES

Substituent at position			N·RR'	Formula	m.p. °C.	Found				Required			
2	3	4				C	H	N	S	C	H	N	S
Me	—	—	NMe_2	$C_9H_{13}O_4N_3S$	92–94	44·4	5·2	11·2	12·7	44·3	5·0	11·5	13·1
Me	—	—	$N(CH_2)_5$	$C_{13}H_{17}O_4N_3S$	110–111	50·7	5·9	9·7	11·4	50·7	5·7	9·9	11·3
Et	—	—	NH_2	$C_8H_{11}O_4N_3S$	128–129	42·1	4·3	12·0	13·9	41·7	4·4	12·2	13·9
Pr^i	—	—	NH_2	$C_9H_{13}O_4N_3S$	123–124	44·0	4·6	11·8	13·2	44·3	5·0	11·5	13·1
Pr^i	—	—	NHMe	$C_{10}H_{15}O_4N_3S$	113–115	46·1	5·2	11·0	12·5	46·5	5·5	10·9	12·4
H	—	OMe	NHMe	$C_{10}H_{15}O_5N_3S$	178–180	39·0	4·2	11·2	13·2	39·0	4·1	11·4	13·0
H	—	OMe	NH_2	$C_9H_{13}O_5N_3S$	223–225	36·6	3·6	12·1	13·7	36·2	3·5	12·1	13·8
Cl	—	—	NH_2	$C_7H_7O_4N_3SCl$	70–72	33·3	3·0	11·2	12·8	33·5	2·8	11·2	12·8
Cl	—	—	NHMe	$C_8H_9O_4N_3SCl$	103–104	36·2	3·1	10·8	12·3	36·3	3·4	10·6	12·5
Cl	—	—	NMe_2	$C_9H_{11}O_4N_3SCl$	204–205	25·8	1·8	10·0	11·6	25·6	1·8	10·0	11·4
Cl	—	Br	NH_2	$C_7H_6O_4N_3SBr$	176–178	26·6	1·4	10·1	11·9	26·6	1·5	10·3	11·8
Cl	—	Cl	NH_2	$C_7H_6O_4N_3SCl_2$	127–129	36·4	3·5	11·1	12·9	36·3	3·4	10·6	12·5
Cl	Me	—	NHMe	$C_8H_9O_4N_3SCl$	158–160	34·0	3·2	11·5	13·1	33·6	2·8	11·2	12·8
Cl	—	Me	NH_2	$C_7H_7O_4N_3SCl$	134–136	36·3	3·6	10·6	12·8	36·3	3·4	10·6	12·5
PhO	—	—	NMe_2	$C_{14}H_{14}O_4N_3S$	105	52·0	4·3	8·8	—	52·2	4·4	8·7	—



(XVII)



(XVIII)

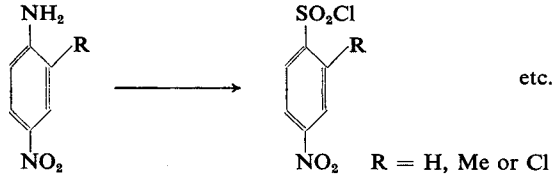
Important features of this new method of preparation of 1,3-disulphamyl benzenes include high overall yields even when using crude intermediates in the earlier stages. Thus, 2-n-propylnitrobenzene was chlorosulphonated in carbon tetrachloride solution. The crude chlorosulphonyl derivative was converted directly into the sulphonmethylamide. This, also without purification, was reduced to 3-amino-4-propylbenzene sulphonmethylamide, which was readily isolated as the crystalline hydrochloride in 60 per cent overall yield. Again, the 4-sulphonchloride of isopropyl benzene was nitrated at 40–45° with a mixture of concentrated nitric and sulphuric acids. After pouring on to ice, collecting, and washing with water, the total crude nitration product was treated directly with ammonia or with methylamine to give the appropriate sulphamyl derivatives in 63 and 65 per cent yield, respectively.

The method was applied to the synthesis of 1,2- and 1,4-disulphamyl derivatives of benzene.

The literature on the 1,2-disulphamyl derivatives of benzene is scanty. The reaction of benzene-1,2-disulphonyl chloride with ammonia or with primary amines, however, is known to lead to cyclic 1,2-disulphonimides (XVII)[4,5]. Though this ring closure occurs easily, we successfully prepared 2-chlorosulphonyl benzene sulphonamide (XVIII; R = Cl), which surprisingly proved to be a relatively stable crystalline compound. With ammonia it gave a small yield of benzene-1,2-disulphonamide (XVIII; R = NH_2), together with the cyclic imide (XVII; R = H), as the major product. The sulphonchloride (XVIII; R = Cl) condensed with dimethylamine to give 2-sulphamylbenzene sulphondimethylamide (XVIII; R = NH_2) additionally prepared from 2-nitrobenzenesulphondimethylamide by the processes already described.

Only 1,4-disulphamyl derivatives of benzene, toluene and chlorobenzene were prepared. In each case one sulphamyl group carried mono- and dimethyl substituents. Methods were essentially the same as described above. The nitrobenzene-4-sulphonchlorides (XX) required as starting materials, however, could not be obtained by nitration of sulphonchlorides or by chlorosulphonation of nitrobenzenes because of the *m*-directive effect of the $-SO_2Cl$ or $-NO_2$ substituents. They were prepared from

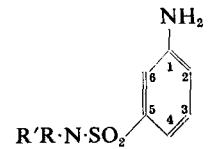
Route (iii)



(XIX) (XX)

TABLE II

AMINOSULPHONAMIDES



Substituent at position			N·RR'	Formula	m.p. °C.	Found				Required			
2	3	4				C	H	N	S	C	H	N	S
Me	—	—	NH_2	$C_7H_{10}O_2N_2S$	175	44·7	5·5	15·2	17·1	45·1	5·4	15·1	17·2
Me	—	—	NHMe	$C_{10}H_{14}O_2N_2S$	163 (*a*)	49·5	5·6	11·4	12·9	49·6	5·8	11·6	13·2
Me	—	—	NMe_2	$C_9H_{14}O_2N_2S$	172–174	50·6	6·3	12·8	14·7	50·4	6·6	13·1	15·0
Me	—	—	$N(CH_2)_5$	$C_{12}H_{18}O_2N_2S$	117–118	56·7	7·3	11·3	12·7	56·7	7·1	11·0	12·6
Et	—	—	NH_2	$C_8H_{12}O_2N_2S$	130–132	47·6	5·9	14·0	16·5	48·0	6·0	14·0	16·0
Et	—	—	NH_2	$C_8H_{12}O_2N_2S$;HCl	226–228 (*d*)	40·7	5·7	12·0	13·3	40·7	5·6	11·9	13·6
Et	—	—	NHMe	$C_9H_{14}O_2N_2S$;HCl	210–212 (*d*)	43·6	5·6	11·4	12·9	43·1	6·0	11·2	12·8
Pr^n	—	—	NH_2	$C_9H_{14}O_2N_2S$;HCl	193–195	43·3	5·9	11·3	12·7	43·1	6·0	11·2	12·8
Pr^n	—	—	NHMe	$C_{10}H_{16}O_2N_2S$;HCl	208–210	45·3	6·3	10·7	12·4	45·4	6·5	10·6	12·1
Pr^i	—	—	NH_2	$C_9H_{14}O_2N_2S$;HCl	215 (*d*)	43·3	6·0	11·0	12·8	43·1	6·0	11·2	12·8
Pr^i	—	—	NHMe	$C_{10}H_{16}O_2N_2S$	103–105	52·7	7·0	12·0	14·4	52·6	7·1	12·3	14·1
Me	Me	—	NH_2	$C_8H_{12}O_2N_2S$	159–160	48·1	6·1	14·2	—	48·0	6·0	14·0	—
Me	Me	—	NHMe	$C_9H_{14}O_2N_2S$;HCl	242–244 (*d*)	43·4	5·7	11·2	13·0	43·1	6·0	11·2	12·8
Me	—	Me	NH_2	$C_8H_{12}O_2N_2S$	189–190	48·2	6·1	14·0	16·2	48·0	6·0	14·0	16·0
—	—	OMe	NH_2	$C_7H_{10}O_3N_2S$	190	41·2	5·2	13·8	15·8	41·6	5·0	13·9	15·9
—	—	OMe	NHMe	$C_8H_{12}O_3N_2S$	176–178	44·8	5·3	13·0	15·0	44·4	5·6	13·0	14·8
Cl	—	—	NH_2	$C_6H_7O_2N_2SCl$	157–159	34·9	3·5	13·6	15·1	34·9	3·4	13·6	15·5
Cl	—	—	NHMe	$C_7H_9O_2N_2SCl$	85–86	38·2	4·4	12·6	14·6	38·1	4·0	12·4	14·1
—	—	Cl	NH_2	$C_6H_7O_2N_2SCl$	168–170	35·2	3·3	13·7	15·5	34·9	3·4	13·6	15·5
Cl	—	—	NMe_2	$C_8H_{11}O_2N_2SCl$	149–151	41·3	4·9	11·7	13·7	41·0	4·7	11·9	13·7
Br	—	—	NH_2	$C_6H_7O_2N_2SBr$	160–162	28·8	2·6	11·0	13·0	28·7	2·8	11·1	12·7
—	—	Br	NH_2	$C_6H_7O_2N_2SBr$;HCl	202 (*d*)	25·0	2·8	—	39·9*	25·1	2·8	—	40·1*
Cl	—	Cl	NH_2	$C_6H_6O_2N_2SCl_2$	216–218	30·2	2·4	11·4	13·3	29·9	2·5	11·6	13·3
Cl	Me	—	NH_2	$C_7H_9O_2N_2SCl$	144–145	38·4	4·1	12·7	14·4	38·1	4·1	12·7	14·5
Cl	Me	—	NHMe	$C_8H_{11}O_2N_2SCl$;HCl	202–204	35·4	4·1	10·5	11·9	35·4	4·1	10·3	11·8
Cl	—	Me	NH_2	$C_7H_9O_2N_2SCl$	213	38·0	4·2	12·9	—	38·1	4·1	12·7	—
Cl	—	Me	NHMe	$C_8H_{11}O_2N_2SCl$	131–133	40·8	4·7	12·4	14·1	41·0	4·7	12·0	13·7
PhO	—	—	NMe_2	$C_{14}H_{16}O_3N_2S$	97–99	57·8	5·6	9·5	10·8	57·5	5·5	9·6	11·0

(*a*) Acetyl derivative.

* Total halogen.

the readily available 4-nitroanilines (XIX), which were converted into the corresponding 4-nitrosulphonchlorides (XX) by means of the diazo-reaction [Route (iii)].

Study of the above compounds as oral diuretics in the saline loaded rat (for which we are indebted to Dr. A. David and his colleagues) revealed certain correlations of structure and biological activity.

Compounds of type (I) were uniformly more potent than their isomers of type (II). As expected, the *N*-substituted disulphonamides possessed lower carbonic anhydrase inhibiting activity than the corresponding disulphamyl-derivatives, but, as with the latter group of compounds, there was no simple relation between carbonic anhydrase inhibiting activity *in vitro* and oral diuretic activity.

Many of the 1,4-disulphamyl benzene derivatives listed in Table V possessed appreciable diuretic activity, but their relatively high potency as carbonic anhydrase inhibitors led to enhanced potassium excretion, thus rendering them inferior to 5-chlorotoluene-2,4-disulphonamide (disulphamide).

EXPERIMENTAL

2-*Sulphamyltoluene*-4-*sulphonfluoride*. A mixture of toluene-4-sulphonfluoride[2] (97·5 g.), chlorosulphonic acid (130 g.) and carbon tetrachloride (173 g.) was heated under reflux for 3 hours on the steam bath. The mixture was cooled, poured on to ice, and the product extracted with carbon tetrachloride. The extract was washed with water and the solvent removed. Distillation of the residual oil at 0·6 mm. yielded crude 2-chlorosulphonyltoluene-4-sulphonfluoride (55 g.) b.p. 146–156° which solidified and had m.p. 41–44°. It was used without further purification.

The foregoing crude product (10 g.) was added in portions with vigorous stirring and cooling to −10°, to a mixture of ammonia solution (7·4 ml., d = 0·880), water (90 ml.) and dioxan (50 ml.) and stirring was continued at −10° for 1 hour after addition was complete. The cold mixture was acidified with hydrochloric acid and the solid (5·4 g.) which separated was collected and crystallised from aqueous ethanol to yield 2-*sulphamyltoluene*-4-*sulphonfluoride* (0·95 g.), m.p. 212–214°. Found: C, 34·2; H, 3·2; N, 5·5. $C_7H_8O_4NS_2F$ requires C, 33·2; H, 3·2; N, 5·5 per cent. The mother liquors deposited toluene-2,4-disulphonamide (2·95 g.) m.p. 185°.

2-*Sulphamyltoluene*-4-*sulphonmethylamide*. The foregoing compound (0·4 g., m.p. 212–214°) was added to 25 per cent aqueous methylamine (5 ml.) and the solution allowed to stand at room temperature for 1½ hours. Excess of methylamine was distilled off and the liquid cooled and acidified. 2-*Sulphamyltoluene*-4-*sulphonmethylamide* separated and had m.p. 172–174° after crystallisation from aqueous ethanol. Found: C, 36·2; H, 4·6; N, 10·7; S, 24·4. $C_8H_{12}O_4N_2S_2$ requires C, 36·4; H, 4·5; N, 10·6; S, 24·3 per cent. The melting point was not depressed on admixture with authentic material (see below).

The following examples illustrate methods of preparation used for products listed in the Tables, which include the analyses.

TABLE III

CHLOROSULPHONYL SULPHONAMIDES

Substituent at position			N·RR'	Formula	m.p. °C.	Found				Required			
2	3	4				C	H	N	Cl	C	H	N	Cl
—	—	—	NH_2	$C_6H_6O_4NS_2Cl$	154–156	28·4	2·4	5·3	13·5	28·2	2·4	5·5	13·9
Me	—	—	NH_2	$C_7H_8O_4NS_2Cl$	162–164	31·1	2·9	5·3	13·2	31·2	3·0	5·2	13·1
—	—	Me	NH_2	$C_7H_8O_4NS_2Cl$	203–205	31·3	2·8	5·2	13·2	31·2	3·0	5·2	13·1
Me	—	—	NHMe	$C_8H_{10}O_4NS_2Cl$	126–127	34·1	3·3	4·8	—	33·9	3·6	4·9	—
Me	—	—	$N(CH_3)_2$	$C_9H_{12}O_4NS_2Cl$	155–156	42·5	4·5	4·3	10·9	42·7	4·8	4·2	10·5
Pr^n	—	—	NH_2	$C_9H_{12}O_4NS_2Cl$	181–183	36·4	4·0	4·5	12·3	36·3	4·1	4·7	11·9
Pr^n	—	—	NHMe	$C_{10}H_{14}O_4NS_2Cl$	93–94	38·9	4·3	4·6	11·8	38·5	4·5	4·5	11·4
Pr^i	—	—	NH_2	$C_9H_{12}O_4NS_2Cl$	205	36·5	4·1	21·4*	12·4	36·3	4·1	21·5*	11·9
Pr^i	—	—	NHMe	$C_{10}H_{14}O_4NS_2Cl$	99–101	21·0*	—	4·7	11·9	20·6*	—	4·5	11·4
Pr^i	—	OMe	NH_2	$C_9H_{12}O_5NS_2Cl$	183–185	29·8	3·0	5·4	12·4	29·4	2·8	4·9	12·4
Cl	—	—	NH_2	$C_6H_5O_4NS_2Cl_2$	191–192	25·1	2·1	5·1	24·3	24·8	1·7	4·8	24·4
Cl	—	Cl	NH_2	$C_6H_5O_4NS_2Cl_2$	186–188	25·2	2·1	4·9	24·2	24·8	1·7	4·8	24·4
Cl	—	—	NMe_2	$C_8H_9O_4NS_2Cl_2$	128–130	30·7	3·0	4·4	21·8	30·2	2·9	4·4	22·3
Br	—	—	NH_2	$C_6H_5O_4NS_2BrCl$	202–204	21·9	2·0	4·1	19·2*	21·5	1·5	4·1	19·2*
Cl	—	Cl	NH_2	$C_6H_5O_4NS_2Cl_2$	197–199	22·6	1·0	4·4	32·6	22·2	1·2	4·3	32·8
PhO	—	—	NMe_2	$C_{14}H_{13}O_5NS_2Cl$	119–121	45·0	3·7	4·2	17·5*	44·7	3·8	3·7	17·1*

* = Sulphur.

Toluene-2,4-disulphamyl Derivatives

(i) *N^2-Substituted Compounds*

2-Amino-4-sulphamyl toluene[6]. (*a*) A solution of 2-nitro-4-sulphamyl toluene[6] (55 g.) in warm ethanol (500 ml.) containing Raney nickel catalyst (5 g.) was hydrogenated at 100° and 30 atmospheres pressure. Reaction was complete in 1½ hours, when the mixture was boiled and filtered. The product (35 g.) separated on cooling and had m.p. 175° after crystallisation from water.

(*b*) A mixture of the nitro-compound (124·8 g.), iron powder (116 g.), acetic acid (8 ml.) and water (800 ml.) containing octanol (1 ml.), was stirred and heated under reflux for 6 hours. Ethanol (3 litres) was then added, the mixture boiled and filtered through "Hyflo". The product (93·5 g. yield) which separated had m.p. 160–162° and was sufficiently pure for the next stage of the preparation.

2-Chlorosulphonyl toluene-4-sulphonamide. A solution of 2-amino-4-sulphamyl toluene (9·3 g.) in 24 per cent hydrochloric acid was diazotised at 0–5° by the addition of a solution of sodium nitrite (3·8 g.) in water (9 ml.). The solution was added at once without cooling and with vigorous stirring to a saturated solution of sulphur dioxide in glacial acetic acid (80 ml.) containing cupric chloride dihydrate (3·5 g.). After 5 minutes the mixture was diluted with ice-water to complete precipitation of the sulphonchloride, which was collected, washed with ice-water and dried. It crystallised from 1,2-dichloroethane-light petroleum (b.p. 60–80°), m.p. 162–164° (10.4 g.).

4-Sulphamyltoluene-2-sulphonpiperidide. The foregoing sulphonchloride (13·5 g.) was added in portions with stirring, at room temperature to a mixture of piperidine (12·8 g.), water (100 ml.) and chloroform (60 ml.). After the addition was complete stirring was continued for 30 minutes when chloroform and excess piperidine were distilled off under reduced pressure. The resulting aqueous solution was acidified with hydrochloric acid when the *product* separated on cooling. It had m.p. 160–162° after crystallisation from aqueous ethanol.

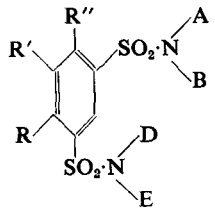
(ii) *N^4-Substituted Compounds*

4-Nitro-2-sulphamyl toluene[7]. Sodium 4-nitrotoluene-2-sulphonate dihydrate (100 g.) was added in portions with shaking to a mixture of formdimethylamide (10 ml.) and thionyl chloride (100 ml.) and the reaction completed by heating the mixture on the steam bath for 10 minutes. Residual thionyl chloride was distilled off under reduced pressure. The residue was dissolved in chloroform (400 ml.) and added with stirring to aqueous ammonia (800 ml., d = 0·880) at room temperature. After stirring for 1 hour, excess of ammonia and chloroform were boiled off, and the aqueous solution was cooled and acidified with hydrochloric acid. The product (76 per cent) had m.p. 186–187° after crystallisation from water.

4-Amino-2-sulphamyltoluene[8] was obtained in 85 per cent yield by reduction of the foregoing nitro-compound with iron powder in acidulated water. It had m.p. 164° after crystallisation from water.

TABLE IV

SUBSTITUTED-1,3-DISULPHONAMIDES



Substituent						m.p. °C.	Found				Required			
R	R′	R″	N·AB	N.DE	Formula		C	H	N	S	C	H	N	S
—	—	—	NHMe	NH_2	$C_7H_{10}O_4N_2S_2$	138–140	33·9	3·7	11·0	25·0	33·6	4·0	11·2	25·6
—	—	—	NHBu	NH_2	$C_{10}H_{16}O_4N_2S_2$	124–125	41·2	5·5	9·4	21·6	41·1	5·5	9·6	21·9
—	—	—	NH·CH_2·CH_2·OH	NH_2	$C_8H_{12}O_5N_2S_2$	132–133	34·2	4·5	10·2	22·3	34·3	4·3	10·0	22·9
—	—	—	NHPh	NH_2	$C_{12}H_{12}O_4N_2S_2$	147–149	46·2	3·9	8·7	20·1	46·1	3·9	9·0	20·5
—	—	—	NMe_2	NH_2	$C_9H_{12}O_4N_2S_2$	177–178	36·5	4·5	10·7	24·5	36·4	4·6	10·6	24·3
—	—	—	THP[1]	NH_2	$C_{11}H_{14}O_4N_2S_2$	157–159	43·6	4·7	9·2	21·0	43·7	4·7	9·3	21·2
—	—	Me	NHMe	NH_2	$C_8H_{12}O_4N_2S_2$	128–130	36·3	4·6	10·8	24·2	36·4	4·6	10·6	24·3
—	—	Me	NHEt	NH_2	$C_9H_{14}O_4N_2S_2$	143–144	39·2	5·0	9·9	22·7	38·9	5·1	10·1	23·1
—	—	Me	NHC_2H_5	NH_2	$C_{10}H_{14}O_4N_2S_2$	130–131	—	—	10·0	22·4	—	—	9·7	22·1
—	—	Me	NH·CH_2·CH_2·OH	NH_2	$C_9H_{14}O_5N_2S_2$	144–145	37·1	4·9	9·7	21·6	36·7	4·8	9·5	21·8
—	—	Me	NHPh	NH_2	$C_{13}H_{14}O_4N_2S_2$	123–125	47·5	4·3	8·9	19·8	47·8	4·3	8·6	19·7
—	—	Me	NMe_2	NH_2	$C_9H_{14}O_4N_2S_2$	136–138	39·3	5·1	10·0	22·7	38·9	5·1	10·1	23·0
—	—	Me	$N(CH_2)_5$	NH_2	$C_{13}H_{18}O_4N_2S_2$	160–162	44·7	5·7	8·9	20·3	45·3	5·7	8·8	20·1
—	—	Me	PTHP[2]	NH_2	$C_{18}H_{30}O_4N_2S_2$	176–177	55·1	5·5	7·0	16·4	55·1	5·1	7·1	16·3
—	—	Me	NH_2	NHMe	$C_8H_{12}O_4N_2S_2$	172–174	36·6	4·6	10·6	24·1	36·4	4·6	10·6	24·3
—	—	Me	NH_2	NHEt	$C_9H_{14}O_4N_2S_2$	133–135	38·9	5·1	9·9	23·0	38·9	5·1	10·1	23·0
—	—	Me	NH_2	NHBu	$C_{11}H_{18}O_4N_2S_2$	123–124	43·4	6·1	9·1	20·7	43·1	5·9	9·1	20·9
—	—	Me	NH_2	NH·CH_2·CH_2·OH	$C_9H_{14}O_5N_2S_2$	162–164	36·9	5·1	9·5	—	36·7	4·8	9·5	—
—	—	Me	NH_2	NHPh	$C_{13}H_{14}O_4N_2S_2$	150–152	48·2	4·4	8·7	19·4	47·8	4·3	8·6	19·7
—	—	Me	NH_2	NH·CH_2·CH_2·Ph	$C_{15}H_{18}O_4N_2S_2$	130–131	51·3	5·2	7·8	17·8	51·0	5·1	7·9	18·0
—	—	Me	NH_2	NMe_2	$C_9H_{14}O_4N_2S_2$	161–163	39·0	5·1	10·2	22·7	38·9	5·1	10·1	23·0
—	—	Me	NH_2	NMe·CH_2·CH_2·OH	$C_{10}H_{16}O_5N_2S_2$	142–144	39·0	5·2	9·3	20·7	38·9	5·2	9·1	20·8
—	—	Me	NH_2	$N(CH_2)_5$	$C_{13}H_{18}O_4N_2S_2$	150–152	45·3	5·8	9·1	20·1	45·3	5·7	8·8	20·1
—	—	Me	NH_2	THP[1]	$C_{13}H_{16}O_4N_2S_2$	126–128	45·2	5·1	9·0	20·2	45·5	5·1	8·9	20·3
—	—	Me	NMe_2	NHMe	$C_{10}H_{16}O_4N_2S_2$	89–90	41·1	5·4	9·7	22·1	41·1	5·5	9·6	21·9
—	—	Me	NHMe	$N(CH_2)_5$	$C_{13}H_{20}O_4N_2S_2$	118–119	47·1	6·2	8·6	19·3	47·0	6·1	8·4	19·3
—	—	Me	$N(CH_2)_4O$	$N(CH_2)_5$	$C_{16}H_{24}O_4N_2S_2$	150–151	49·5	6·2	7·4	—	49·5	6·2	7·2	—
—	—	Et	NHMe	NH_2	$C_9H_{14}O_4N_2S_2$	127–129	38·6	5·4	10·2	22·8	38·8	5·1	10·1	23·0
—	—	Et	NH_2	NHMe	$C_9H_{14}O_4N_2S_2$	157–159	38·8	5·2	10·4	23·0	38·8	5·1	10·1	23·0
—	—	Pr^n	NHMe	NH_2	$C_{10}H_{16}O_4N_2S_2$	153–155	41·1	5·7	9·6	22·0	41·1	5·5	9·6	21·9
—	—	Pr^n	NH_2	NHMe	$C_{10}H_{16}O_4N_2S_2$	145–146	41·3	5·7	9·5	22·0	41·1	5·5	9·6	21·9

4-*Chlorosulphonyl*-2-*sulphamyltoluene*. The foregoing aminosulphonamide (23 g.) was diazotised and added to a saturated solution of sulphur dioxide in acetic acid (320 ml.) at 15° as described above. The *product* precipitated by dilution with ice-water, had m.p. 203–205° after crystallisation from 1,2-dichloroethane-light petroleum (b.p. 60–80°) (yield 76 per cent).

2-*Sulphamyltoluene*-4-*sulphonethylamide*. The foregoing sulphonchloride (8·2 g.) was added in portions with stirring to a mixture of 10 per cent aqueous ethylamine (70 ml.) and chloroform (30 ml.) at 20°. After the addition was complete excess of chloroform and ethylamine were boiled off. The residual liquid was cooled and acidified with hydrochloric acid to yield the *product* which had m.p. 133–135° after crystallisation from water (yield 95 per cent).

2-*Aminotoluene*-4-*sulphonmethylamide*. A solution of 2-nitrotoluene-4-sulphonmethylamide[9] (68 g.) in ethanol (500 ml.) was hydrogenated in the presence of Raney nickel at 100° and 50 atmospheres pressure for 1 hour. The *product* (70 per cent yield), m.p. 80–83° was characterised by conversion into its *acetyl* derivative which had m.p. 163°, after crystallisation from water.

2-*Chlorosulphonyltoluene*-4-*sulphonmethylamide*. Diazotisation of the foregoing amine followed by reaction with sulphur dioxide-acetic acid yielded the *product* which had m.p. 126–127°, after crystallisation from 1,2-dichloroethane-light petroleum (b.p. 60–80°) (yield 85 per cent).

2-*Sulphamyltoluene*-4-*sulphonmethylamide* obtained by reaction of the foregoing compound with an aqueous ammonia (d = 0·880)-carbon tetrachloride two phase mixture, had m.p. 172–174°, after crystallisation from aqueous ethanol (yield 90 per cent).

2-*Nitrotoluene*-4-*sulphondimethylamide* was obtained in 80 per cent yield by reaction of the corresponding sulphonchloride[6,9] with aqueous dimethylamine-carbon tetrachloride. It had m.p. 92–94°, after crystallisation from methanol.

2-*Aminotoluene*-4-*sulphondimethylamide*, prepared in 83 per cent yield by hydrogenation of the foregoing nitro-compound in ethanol, using Raney nickel as catalyst at 100° and 40 atmospheres pressure, had m.p. 172–174°, after crystallisation from ethanol.

2-*Sulphamyl toluene*-4-*sulphondimethylamide*, prepared in 75 per cent yield from the foregoing amine by conversion into the sulphonchloride and reaction with ammonia solution (d = 0·880) (described above) had m.p. 161–163°, after crystallisation from aqueous ethanol.

2-*Nitrotoluene*-4-*sulphonpiperidide*, prepared *via* the sulphonchloride, had m.p. 110–111°, after crystallisation from aqueous ethanol.

2-*Aminotoluene*-4-*sulphonpiperidide*, obtained in 64 per cent yield by reduction of the foregoing nitro-compound with iron powder in acidulated 20 per cent ethanol, had m.p. 117–118°, after crystallisation from aqueous ethanol.

2-*Chlorosulphonyltoluene*-4-*sulphonpiperidide*, prepared from the foregoing amine, had m.p. 155–156°, after crystallisation from 1,2-dichloroethane-light petroleum (b.p. 60–80°). It was condensed with methylamine

TABLE IV—*continued*

Substituent						m.p. °C.	Found				Required			
R	R′	R″	N.AB	N.DE	Formula		C	H	N	S	C	H	N	S
—	—	Pr^i	NHMe	NH_2	$C_{10}H_{18}O_4N_2S_2$	157–159	41·2	5·5	10·0	22·2	41·1	5·5	9·6	21·9
—	—	Pr^i	NH_2	NHMe	$C_{10}H_{18}O_4N_2S_2$	172–174	41·4	5·3	9·9	21·7	41·1	5·5	9·6	21·9
—	Me	Me	NHMe	NH_2	$C_9H_{14}O_4N_2S_2$	184–186	38·9	5·2	10·2	23·1	38·9	5·1	10·1	23·0
—	Me	Me	NH_2	NHMe	$C_9H_{14}O_4N_2S_2$	157–159	38·8	5·2	10·4	23·0	38·9	5·1	10·1	23·0
Me	—	Me	NHMe	NH_2	$C_9H_{14}O_4N_2S_2$	171–173	38·7	5·1	10·0	22·6	38·9	5·1	10·1	23·0
—	—	MeO	NHMe	NH_2	$C_8H_{12}O_5N_2S_2$	208–209	34·6	4·5	9·8	—	34·3	4·3	10·0	—
—	—	MeO	NH_2	NHMe	$C_8H_{12}O_5N_2S_2$	203–204	34·2	4·7	10·0	—	34·3	4·3	10·0	—
—	—	Cl	NHMe	NH_2	$C_7H_9O_4N_2S_2Cl$	139–141	30·0	3·2	9·6	12·0*	29·5	3·2	9·8	12·5*
—	—	Cl	NH_2	NHMe	$C_7H_9O_4N_2S_2Cl$	177–179	30·0	3·2	10·1	22·2	29·5	3·2	9·8	22·5
—	—	Cl	NH_2	NHEt	$C_8H_{11}O_4N_2S_2Cl$	146–148	32·1	3·6	9·3	21·4	32·2	3·7	9·4	21·4
—	—	Cl	NH_2	$NH{\cdot}CH_2{\cdot}CH_2{\cdot}OH$	$C_8H_{11}O_5N_2S_2Cl$	162–164	30·8	3·6	9·1	20·2	30·5	3·5	8·9	20·4
—	—	Cl	NH_2	NMe_2	$C_8H_{11}O_4N_2S_2Cl$	182–184	32·6	3·8	11·9*	21·4	32·2	3·7	11·9*	21·4
—	—	Cl	NH_2	$N(CH_2)_5$	$C_{11}H_{15}O_4N_2S_2Cl$	172–174	39·1	4·4	8·4	18·9	39·0	4·5	8·3	18·9
—	—	Cl	NEt_2	NHMe	$C_{11}H_{17}O_4N_2S_2Cl$	98–100	39·0	4·8	8·2	18·8	38·7	5·0	8·2	18·8
—	—	Br	NHMe	NH_2	$C_7H_9O_4N_2S_2Br$	165–166	25·4	2·6	8·4	19·6	25·5	2·8	8·5	19·5
—	—	Br	NH_2	NHMe	$C_7H_9O_4N_2S_2Br$	175–176	25·5	2·8	8·6	19·5	25·5	2·8	8·5	19·5
Cl	—	Cl	NHMe	NH_2	$C_7H_8O_4N_2S_2Cl_2$	210–211	26·5	2·7	9·0	20·3	26·3	2·5	8·8	20·1
—	Me	Cl	NHMe	NH_2	$C_8H_{11}O_4N_2S_2Cl$	179–180	32·6	3·7	9·2	11·8*	32·2	3·7	9·4	11·9*
—	Me	Cl	NH_2	NHMe	$C_8H_{11}O_4N_2S_2Cl$	182–184	32·5	4·0	9·8	21·7	32·2	3·7	9·4	21·4
Cl	—	Me	NHMe	NH_2	$C_8H_{11}O_4N_2S_2Cl$	223–225	32·3	3·8	9·7	21·0	32·2	3·7	9·4	21·4
Cl	—	Me	NH_2	NHMe	$C_8H_{11}O_4N_2S_2Cl$	192–194	—	—	9·2	21·0	32·2	3·7	9·4	21·4
—	—	PhO	NH_2	NHMe	$C_{14}H_{16}O_5N_2S_2$	163–165	47·5	4·5	7·8	17·8	47·2	4·5	7·9	18·0

1 = 1,2,3,6-Tetrahydropyridine.
2 = 4-Phenyl-1,2,3,6-tetrahydropyridine.
* = Chlorine.

and with morpholine to yield the mixed substituted sulphonamides described in Table IV.

2-*Methoxy*-5-*nitrobenzene sulphonchloride* was prepared in 71 per cent yield by diazotisation of 2-amino-4-nitroanisole, followed by reaction of the diazonium solution with a solution of sulphur dioxide in acetic acid as described above. It had m.p. 119–120°, after crystallisation from 1,2-dichloroethane-light petroleum (b.p. 60–80°). Found: C, 33·7; H, 2·0; N, 5·8; Cl, 14·0; S, 12·8. $C_7H_6O_5NSCl$ requires C, 33·4; H, 2·4; N, 5·6; Cl, 14·1; S. 12·7 per cent.

Bromobenzene-2-*sulphonchloride*[10] was prepared in 87 per cent yield from *o*-bromoaniline by the diazo route.

2-*Bromo*-5-*nitrobenzene sulphonchloride*[11] was obtained in 93 per cent yield by nitration of the foregoing sulphonchloride with a mixture of concentrated nitric and sulphuric acids at 25–35°. It had m.p. 92°. after crystallisation from 1,2-dichloroethane-light petroleum (b.p.60–80°),

5-*Chloro*-4-*nitrotoluene*-2-*sulphonchloride*. *m*-Chlorotoluene (126·5 g.) was added with stirring to chlorosulphonic acid (300 ml.), the temperature was kept below 30° and stirring was continued for 2 hours after the addition was complete. The mixture was added slowly with stirring to crushed ice and the sulphonchloride collected, washed with ice-water and dried in air. The crude, dry sulphonchloride was added slowly with stirring to fuming nitric acid (200 ml., d = 1·50) and when the addition was complete, concentrated sulphuric acid (50 ml.) was slowly stirred into the mixture. The mixture was warmed to 40° for 1 hour when it was cooled and added with stirring to ice-water. The *product* was collected and washed with cold water. It had m.p. 108–110°, after crystallisation from light petroleum (b.p. 80–100°). Found: C, 31·4; H, 1·9; N, 5·5. $C_7H_5O_4NSCl_2$ requires C, 31·1; H, 1·9; N, 5·2 per cent.

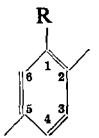
3-*Nitro*-4-*phenoxybenzene sulphondimethylamide*. A solution of 4-chloro-3-nitrobenzene sulphondimethylamide (6·6 g.) in ethanol (35 ml.) was treated with a solution of phenol (2·35 g.) in water (5 ml.) containing potassium hydroxide (1·4 g.) and the mixture heated under reflux for 4 hours. The *product* (7·4 g.) which separated on cooling and slight dilution with water had m.p. 105°, after crystallisation from ethanol. The melting point was depressed on admixture with the starting material.

2-*Chlorosulphonylbenzene sulphonamide*. A solution of 2-sulphamylaniline (17·2 g.) in 24 per cent hydrochloric acid (120 ml.) was diazotised at 0–5° by the addition of a solution of sodium nitrite (7·5 g.) in water (20 ml.), and the resultant diazonium solution added with stirring to a saturated solution of sulphur dioxide in glacial acetic acid (160 ml.) containing cupric chloride dihydrate (7 g.) at 25°. After the addition was complete, stirring was continued for a further 15 minutes when precipitation of the product was completed by the addition of ice-water. It was purified by crystallisation from 1,2-dichloroethane and had m.p. 176°. Found: C, 28·5; H, 2·5; N, 5·4; Cl, 13·6; S, 25·4. $C_6H_6O_4NS_2Cl$ requires C, 28·2; H, 2·4; N, 5·5; Cl, 13·9; S, 25·0 per cent.

(*a*) *Reaction with ammonia*. A suspension of the foregoing compound (2·0 g.) in chloroform (40 ml.) was stirred vigorously and treated at once

TABLE V

2,5-DISUBSTITUTED DERIVATIVES OF BENZENE, TOLUENE AND CHLOROBENZENE



R	Substituent at position 2	Substituent at position 5	Formula	m.p. °C.	Found C	Found H	Found N	Found S	Required C	Required H	Required N	Required S
H	SO_2NH_2	SO_2Cl	$C_6H_6O_4NS_2Cl$	155–157	28·6	2·5	5·5	13·7*	28·2	2·4	5·5	13·9*
H	SO_2NH_2	SO_2NHMe	$C_7H_{10}O_4N_2S_2$	160–161	33·4	4·0	11·1	—	33·6	4·0	11·2	—
H	SO_2NH_2	$SO_2NH{\cdot}CH_2{\cdot}CH_2{\cdot}OH$	$C_8H_{12}O_5N_2S_2$	150–151	34·4	4·5	10·1	23·3	34·3	4·3	10·0	22·9
H	SO_2NH_2	SO_2NMe_2	$C_8H_{12}O_4N_2S_2$	203	36·5	4·5	10·5	24·3	36·4	4·6	10·6	24·3
H	SO_2NHMe	SO_2NHMe	$C_8H_{12}O_4N_2S_2$	223–225	36·2	4·3	10·4	24·5	36·4	4·6	10·6	24·3
Me	SO_2Cl	NO_2	$C_7H_6O_4NSCl$	68–69	36·0	2·3	6·1	13·7	35·7	2·6	5·9	13·6
Me	SO_2NHMe	NO_2	$C_8H_{10}O_4N_2S$	172–174	41·8	4·2	12·5	13·8	41·7	4·4	12·2	13·9
Me	SO_2NHMe	NH_2	$C_8H_{12}O_2N_2S$	117–118	48·0	6·0	14·2	15·9	48·0	6·0	14·0	16·0
Me	SO_2NHMe	SO_2Cl	$C_8H_{10}O_4NS_2Cl$	117–119	33·8	3·4	5·1	12·7*	33·9	3·6	4·9	12·5*
Me	SO_2NHMe	SO_2NH_2	$C_8H_{12}O_4N_2S_2$	125–126	36·0	4·8	10·8	24·0	36·4	4·6	10·6	24·3
Me	SO_2NH_2	NO_2	$C_7H_8O_4N_2S$	155–156	39·3	3·6	12·9	14·5	38·9	3·7	13·0	14·8
Me	SO_2NH_2	NH_2	$C_7H_{10}O_2N_2S$	170–172	45·5	5·1	14·8	17·4	45·1	5·4	15·0	17·2
Me	SO_2NH_2	SO_2Cl	$C_7H_8O_4NS_2Cl$	134–136	31·4	2·9	5·2	23·9	31·2	3·0	5·2	23·8
Me	SO_2NH_2	SO_2NH_2	$C_7H_{10}O_4N_2S_2$	228–229	33·9	4·1	11·1	25·4	33·6	4·0	11·2	25·6
Me	SO_2NH_2	SO_2NHMe	$C_8H_{12}O_4N_2S_2$	149–151	36·3	4·9	10·6	23·9	36·4	4·6	10·6	24·3
Me	SO_2NH_2	SO_2NMe_2	$C_9H_{14}O_4N_2S_2$	173–175	39·0	5·1	10·2	22·6	38·9	5·1	10·1	23·0
Cl	SO_2Cl	NO_2	$C_6H_3O_4NSCl_2$	66–68	28·3	1·2	5·7	13·1	28·1	1·2	5·5	12·5
Cl	SO_2NHMe	NO_2	$C_7H_7O_4N_2SCl$	190–191	34·0	3·0	11·2	13·1	33·6	2·8	11·2	12·8
Cl	SO_2NHMe	NH_2	$C_7H_9O_2N_2SCl$	164–166	38·0	3·9	12·6	14·3	38·1	4·1	12·7	14·5
Cl	SO_2NHMe	SO_2Cl	$C_7H_7O_4NS_2Cl_2$	126–128	27·4	2·1	4·9	21·2	27·6	2·3	4·6	21·1
Cl	SO_2NHMe	SO_2NHMe	$C_8H_{11}O_4N_2S_2Cl$	144–145	32·0	3·8	9·4	11·6*	32·2	3·7	9·4	11·9*
Cl	SO_2NHMe	SO_2NH_2	$C_7H_9O_4N_2S_2Cl$	177–178	30·0	3·1	10·2	12·9*	29·5	3·2	9·8	12·5*
Cl	SO_2NH_2	NO_2	$C_6H_5O_4N_2SCl$	149–150	30·4	2·1	11·7	13·1	30·5	2·1	11·8	13·6
Cl	SO_2NH_2	NH_2	$C_6H_7O_2N_2SCl$	180–182	35·0	3·8	13·4	17·1*	34·9	3·4	13·6	17·2*
Cl	SO_2NH_2	SO_2Cl	$C_6H_5O_4NS_2Cl_2$	162–164	25·1	1·9	4·8	22·1	24·8	1·7	4·8	22·1
Cl	SO_2NH_2	SO_2NH_2	$C_6H_7O_4N_2S_2Cl$	229–231	26·7	2·6	10·4	24·0	26·6	2·6	10·4	23·7
Cl	SO_2NH_2	SO_2NHMe	$C_7H_9O_4N_2S_2Cl$	187–189	29·7	3·2	10·2	13·1*	29·5	3·2	9·8	12·5*
Cl	SO_2NH_2	SO_2NMe_2	$C_8H_{11}O_4N_2S_2Cl$	186–188	32·2	4·0	9·7	21·4	32·2	3·7	9·4	21·5

* = Chlorine.

with ammonia solution (3 ml., d = 0·880), when the solid dissolved and pasty material separated. The chloroform and ammonia were boiled off, the residue was acidified with hydrochloric acid and boiled with 50 per cent ethanol. The insoluble 1,2-disulphamylbenzene (0·1 g.) was collected and had m.p. 343° (decomp.). Found: C, 30·8; H, 3·2; N, 11·9; S, 27·1. *Benzene*-1,2-*disulphonamide*, $C_6H_8O_4N_2S_2$, requires C, 30·5; H, 3·4; N, 11·9; S, 27·1 per cent.

(*b*) *Reaction with dimethylamine.* A suspension of 2-chlorosulphonyl benzene sulphonamide (2 g.) in chloroform was stirred vigorously and treated with ethanolic dimethylamine (5 ml.; 33 per cent) when the solid dissolved immediately. The mixture was evaporated to dryness and the residue crystallised from ethanol-benzene to yield 2-sulphamylbenzene sulphondimethylamide (1·2 g.), m.p. 145–147°. The m.p. was not depressed on admixture with authentic material (see below).

2-*Nitrobenzene sulphondimethylamide* prepared by reaction of *o*-nitrobenzene sulphonchloride with 30 per cent ethanolic dimethylamine, had m.p. 80–82° after crystallisation from ethanol. Found: N, 12·0; S, 13·8. $C_8H_{10}O_4N_2S$ requires N, 12·2; S, 13·9 per cent.

2-*Aminobenzene sulphondimethylamide.* Reduction of the foregoing nitro-compound with iron powder in 1 per cent acetic acid furnished the *product* which had m.p. 85–86°, after crystallisation from aqueous ethanol. Found: C, 47·6; H, 5·9; N, 14·1. $C_8H_{12}O_2N_2S$ requires C, 48·0; H, 6·0; N, 14·0 per cent.

2-*Sulphamylbenzene sulphondimethylamide.* A solution of the foregoing compound (20 g.) in 24 per cent hydrochloric acid (240 ml.) was diazotised at 0–5° by the addition of a solution of sodium nitrite (7·6 g.) in water (18 ml.). The diazonium solution was added with stirring at 15–20° to a saturated solution of sulphur dioxide in acetic acid (160 ml.) containing cupric chloride dihydrate (7 g.). Sulphur dioxide was passed into the solution until the addition was complete, when stirring was continued for a further 20 minutes. The mixture was diluted with ice-water to complete precipitation of the sulphonchloride which was collected, washed with ice-water and dried.

The sulphonchloride (23·5 g., m.p. 96–98°) was added in portions to ammonia solution (300 ml., d = 0·880) with stirring. Stirring was continued for 1 hour after the addition was complete. The solution was boiled to remove excess of ammonia, cooled and neutralised with hydrochloric acid. The *product* (17·9 g.), had m.p. 145–147°, after crystallisation from water. Found: C, 36·2; H, 4·3; N, 10·9; S, 24·5. $C_8H_{12}O_4N_2S_2$ requires C, 36·4; H, 4·6; N, 10·6; S, 24·3 per cent.

2-*Sulphamyl*-4-*methylsulphamyl*-(*β*-*hydroxyethyl*)-*aniline.* A solution of 4-chloro-3-sulphamylbenzene sulphonmethylamide (28·5 g.) in 2-hydroxyethylamine (30 ml.) was heated at 150° for 1·5 hours when excess of amine was removed at 100° and 0·1 mm. pressure. The residue was dissolved in hot aqueous ethanol when the *product* crystallised on cooling. It had m.p. 162–164° after crystallisation from methanol. Found: C, 35·1; H, 4·7; N, 13·9. $C_9H_{15}O_5N_3S_2$ requires C, 34·9; H, 4·9; N, 13·6 per cent.

4-*Sulphamyl*-2-*methylsulphamyl*-(*β*-*hydroxyethyl*)-*aniline*, was obtained

by reaction of 2-chloro-5-sulphamylbenzene sulphonmethylamide with 2-hydroxyethylamine as described in the preceding example. It had m.p. 143–144° after crystallisation from 25 per cent methanol. Found: C, 35·3; H, 5·2; N, 13·7. $C_9H_{15}O_5N_3S_2$ requires C, 34·9; H, 4·9; N, 13·6 per cent.

5-*Methyl*-2-*sulphamyl*-4-*methylsulphamyl*-(*β-hydroxyethyl*)*aniline*, prepared by reaction of the corresponding chloro compound with 2-hydroxyethylamine at 145° for 1·5 hours, had m.p. 178–179° after crystallisation from water. Found: C, 37·3; H, 5·6; N, 12·9; S, 19·7. $C_{10}H_{17}O_5N_3S_2$ requires C, 37·1; H, 5·3; N, 13·0; S, 19·8 per cent.

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