1120. *Elimination–Addition. Part VI.*[1] *Elimination of Sulphonamido-Groups.*

By D. S. Campbell and C. J. M. Stirling.

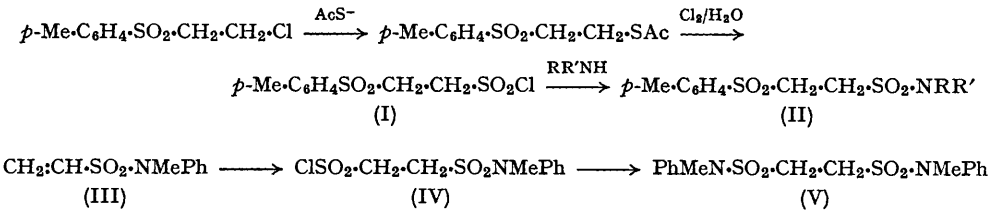
Two types of reaction are observed when β-arylsulphonylethanesulphonamides are treated with sodium ethoxide: elimination of a proton and aryl sulphinate gives an ethylenesulphonamide, and elimination of a proton and sulphimate gives aryl vinyl sulphone; nucleophilic addition to both vinyl sulphonamide and aryl vinyl sulphone follows. Attempts to characterise sulphimate ions have failed; immediate decomposition to sulphite and amine occurs.

With sulphonamides of secondary amines, relatively slight changes in the distribution of products are caused by variation of the amine. With sulphonamides of primary amines, however, elimination of the sulphonamido-group occurs almost exclusively and the reaction constitutes a potential method for the protection of primary amino-groups.

The ready replacement of certain β-substituents in sulphones under basic conditions has been known for some time,[2] and more recently the mechanisms of such reactions have received attention.[3–6] In the present investigation, reactions of β-arylsulphonylethanesulphonamides have been studied in order to determine whether the sulphonamido-group, like the sulphonyl group,[3,4] can behave as a leaving group, and also whether it can behave as an activating group for the elimination of β-substituents. Elimination of sulphonamido-groups, in which C–N fission is involved, have been observed previously.[7,8] This Paper is concerned with eliminations in which C–S fission occurs and there appear to be no previous instances of this type of reaction. Elimination of β-substituents in sulphonamides has not been studied and, although treatment of 2-chloroethanesulphonyl chloride with aromatic amines is known to give ethylenesulphonamides,[9,10] this reaction probably involves an initial dehydrohalogenation and subsequent reaction of ethylenesulphonyl chloride with the amine. There is evidence from the reactions of 2-chloroethanesulphonyl chloride[10] and of ethane-1,2-disulphonyl chloride[11,12] that the chlorosulphonyl group strongly promotes β-elimination and is a good leaving group in such reactions. This topic will be the subject of a subsequent Paper.

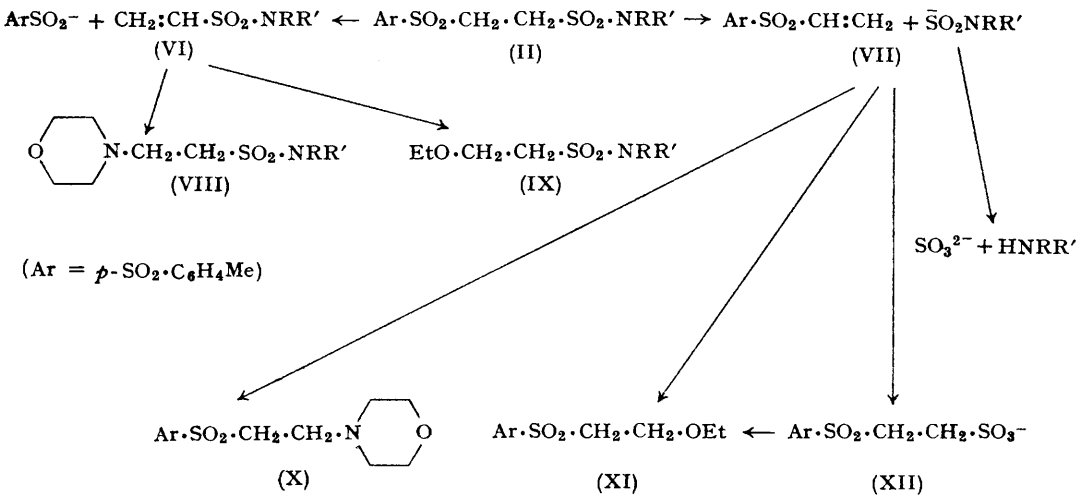
1 Part V, C. J. M. Stirling, preceding Paper
2 C. M. Suter, "Organic Chemistry of Sulfur," Wiley, New York, 1944.
3 C. J. M. Stirling, *Chem. and Ind.*, 1960, 933.
4 A. T. Kader and C. J. M. Stirling, *J.*, 1962, 3686.
5 A. T. Kader and C. J. M. Stirling, *J.*, 1964, 258.
6 P. Mamalis and H. N. Rydon, *J.*, 1955, 1049.
7 C. J. M. Stirling, *J.*, 1962, 3676.
8 Y. Takata, *J. Pharm. Soc. Japan*, 1952, **72**, 321.
9 A. A. Goldberg, *J.*, 1945, 464.
10 C. S. Rondestvedt, *J. Amer. Chem. Soc.*, 1954, **76**, 1926.
11 P. W. Clutterbuck and J. B. Cohen, *J.*, 1922, 120.
12 S. M. McElvain, A. Jelinek, and K. Rorig, *J. Amer. Chem. Soc.*, 1954, **76**, 1578.

The β-arylsulphonylethanesulphonamides studied in the present work were obtained by the sequence of reactions shown in the scheme below. Reactions of aniline and of methylaniline with 2-*p*-tolylsulphonylethanesulphonyl chloride (I) proceeded normally, but with piperidine and dibenzylamine poor yields were obtained, unless reactions were carried out at −40°. Eliminations involving the chlorosulphonyl group evidently occur. Formation of the diphenylamide (II; R = R′ = Ph) required forcing conditions. The bis-sulphonamide (V)



is not obtained directly from *N*-methylaniline and ethane-1,2-disulphonyl chloride; the product of this reaction is *N*-methylethylenesulphonanilide[13] (III). Addition of sulphite to this amide and treatment of the resulting sulphonic acid with phosphorus pentachloride gave the sulphonyl chloride (IV); this, on subsequent treatment with *N*-methylaniline, gave the bis-amide (V).

Treatment of β-arylsulphonylethanesulphonamides (II) with an excess of ethanolic sodium ethoxide gave, in general, five products: toluene-*p*-sulphinic acid, 2-ethoxyethanesulphonamide (IX), sulphite, amine, and 2-ethoxyethyl *p*-tolyl sulphone (XI). These products can, in theory, be accounted for, either by direct substitution, or by elimination–addition.[4] A simple sulphonamide such as *NN*-dibenzylmethanesulphonamide was quite unaffected by the reaction conditions, suggesting that the first alternative must be discounted.



Evidence for the latter mechanism was obtained by carrying out reactions of the dibenzylamide (II; R = R′ = CH_2Ph) in the presence of morpholine. This amine did not react with the amide in the absence of sodium ethoxide, but in the presence of this strong base, the morpholino-compounds (VIII) and (X) were formed. The routes to these various products are indicated in the Scheme. It is clear that a sulphonamido-group powerfully assists β-elimination, and that it can itself act as a leaving group. In the bis-sulphonamide (V), one sulphonamido-group undergoes elimination under the influence of the other; *N*-methyl-2-ethoxy-

[13] W. Autenrieth and P. Rudolph, *Ber.*, 1901, **34**, 3467.

ethanesulphonanilide (IX: R = Ph; R′ = Me) and methylaniline are obtained in high yields from the reaction with sodium ethoxide. The subsequent stage, involving nucleophilic addition to the vinyl sulphone, has been discussed previously;[4] additions to vinyl sulphonamides have been observed by other workers.[9,11]

When a sulphonamido-group is eliminated, the departing anion is presumably that of a sulphimic acid (R_2NSO_2H). The 1:1 complexes formed between primary and secondary amines and sulphur dioxide[14] were originally assigned this structure.[15] These complexes are stable in the absence of water, with which they rapidly react to give the hydrogen sulphite of the amine. In an attempt to isolate the salt of the sulphimic acid produced by elimination, the sulphonamide (II; R = R′ = CH_2Ph) was treated with one equivalent of ethanolic sodium ethoxide, and the salts produced were precipitated with ether. Addition of acid to the precipitate yielded sulphur dioxide but no amine was isolated. A negligible amount of amine was present, therefore, as sulphimate ion, which evidently decomposes under the reaction conditions giving sulphite and free amine. The products obtained were dibenzylamine, 2-ethoxyethyl *p*-tolyl sulphone (XI), *NN*-dibenzylethylenesulphonamide (VI; R = R′ = CH_2Ph), toluene-*p*-sulphinic acid, and 2-*p*-tolylsulphonylethanesulphonic acid (XII), together with recovered starting material (20%). The sulphonic acid and ethylenesulphonamide are intermediates (Scheme); each reacts further with excess of base to give ethoxy-sulphone and ethoxy-sulphonamide, respectively. The recovery of some starting material is due to the consumption of base in the conversion of sulphimate into sulphite.

It was of interest to determine the effect of change of the amino-component of the sulphonamide upon the preferred direction of elimination. The yields of ethoxy-sulphone and ethoxy-sulphonamide obtained from each of a series of five sulphonamides are given in Table 1. It can be seen that a large change in basicity has no systematic effect on the direction of elimination. There are two possible ways in which the basicity of the amine can affect the

TABLE 1.

Orientation of elimination in β-sulphonyl-sulphonamides.

	% Yield		
Sulphonamide (II)	Ethoxy-sulphone	Ethoxy-sulphonamide	pK_a of amine*
R = R′ = Ph	43	50	0·9
R = Ph; R′ = H	87	3†	4·6
R = Ph; R′ = Me	46	44	4·85
R = R′ = CH_2Ph	63	35	8·4
R = R′ = $[CH_2]_5$	33	57	11·0

* As conjugate acids. † Yield of ethylenesulphonanilide.

direction of elimination. In sulphonamides of strong bases, the lone-pair electrons on nitrogen can better satisfy the electron demand of the sulphonyl group, which should thus have a weaker inductive effect on C–H bonds adjacent to it; the tendency for elimination of toluene-*p*-sulphinic acid should thus be reduced. On the other hand, amine basicity can affect the ease with which the sulphonamido-group is eliminated, and this is not readily predictable. Further work is required to separate these effects. In the anilide (II; R = Ph; R′ = H), however, elimination of the sulphonamido-group occurs almost exclusively. This acidic[16] (p$K \sim 10$) sulphonamide must be almost completely dissociated in the reaction medium. The negative charge at the sulphonamido-group deflects ethoxide ion from the vicinity of the group and preferential removal of protons from carbon adjacent to the *p*-tolylsulphonyl group occurs. Formation of vinyl- and not ethoxy-ethanesulphonamide in this instance is also understandable, since the negative charge on the sulphonamido-group inhibits nucleophilic addition to the double bond.

[14] L. C. Bateman, E. D. Hughes, and C. K. Ingold, *J.*, 1944, 243.
[15] A. Michaelis and O. Storbek, *Annalen*, 1893, **274**, 187, and refs. there cited.
[16] A. V. Willi, *Helv. Chim. Acta*, 1956, **39**, 46.

Preferential elimination of the sulphonamido-group in 2-*p*-tolylsulphonylethanesulphonamides of primary amines suggests a method for the protection of primary amino-groups. The β-sulphonyl-sulphonamide would be stable in acidic or neutral media and towards catalytic hydrogenation, but on treatment with bases, the free amine would be liberated. This type of procedure is under investigation; a similar procedure involving elimination of carbamoyloxy-groups has been described recently.[5]

Experimental

Solvents were dried and redistilled. Extracts were dried over $MgSO_4$. The light petroleum used had b. p. 40—60° unless otherwise stated. Alumina was Spence's Type H and "neutral alumina" was obtained from it by treatment with 5% w/w of 10% aqueous acetic acid.

Liquid amines were dried over sodium hydroxide, distilled from zinc dust, and stored over sodium hydroxide. Diphenylamine had m. p. 52—54° (from light petroleum). 2-Ethoxyethanesulphonyl chloride[17] had b. p. 75—76°/4 mm., n_D^{25} 1·4552.

The identities of products from elimination reactions were confirmed by comparison of their infrared spectra with those of authentic specimens.

Infrared-spectroscopic Analysis.—Standard solutions (7% w/v in benzene) of the components were mixed so as to obtain an accurate match with the spectrum of a 7% solution of the unknown mixture. An Infracord model 137 spectrophotometer was used, with cells of 0·1 mm. path-length and sodium chloride windows.

2-p-*Tolylsulphonylethyl Thiolacetate.*—Cunneen's[18] method gave poor results, and the following alternative method was employed. 2-Chloroethyl *p*-tolyl sulphone[19] (0·16 mole) was refluxed for 2 hr. with thiolacetic acid (0·24 mole) in N-ethanolic sodium ethoxide (200 ml.). The mixture was poured into 5% aqueous sodium hydrogen carbonate (500 ml.), and extraction with methylene chloride gave a red oil which, on recrystallisation (charcoal) from benzene–light petroleum, gave 2-p-*tolylsulphonylethyl thiolacetate* (80%), m. p. 64·5—66° (Found: C, 51·1; H, 5·7. $C_{11}H_{14}O_3S_2$ requires C, 51·1; H, 5·5%).

2-p-*Tolylsulphonylethanesulphonyl Chloride.*[20]—Chlorine was passed into a vigorously stirred suspension of the preceding ester in water at 5—10° until an excess was present. Extraction was with methylene chloride, and the extracts were washed with aqueous sodium hydrogen sulphite. Evaporation gave the sulphonyl chloride (89%), m. p. 164·5—166° from benzene (Found: C, 38·3; H, 4·1. Calc. for $C_9H_{11}ClO_4S_2$: C, 38·2; H, 3·9%).

General Procedures for the Preparation of Amides.—(*a*) The amine (0·071 mole) in tetrahydrofuran (100 ml.) was added dropwise with stirring during 1 hr. to the sulphonyl chloride (0·0355 mole) in tetrahydrofuran (150 ml.) at −40°. The mixture was stirred for a further 2 hr. at −40° and poured into methylene chloride. The solution was washed with hydrochloric acid and evaporated to yield the amide.

(*b*) The sulphonyl chloride (0·025 mole) and the amine (0·05 mole) were kept in benzene (100 ml.) containing pyridine (0·05 ml.) at 20°. When reaction was complete, the mixture was diluted with methylene chloride and washed with hydrochloric acid. Evaporation gave the amide.

Amides obtained by these procedures are listed in Table 2.

NN-*Diphenyl*-2-p-*tolylsulphonylethanesulphonamide.*—2-*p*-Tolylsulphonylethanesulphonyl chloride (0·04 mole) was kept at 120° with diphenylamine (0·2 mole) under nitrogen at 10 mm. for 6 hr. The green mixture was extracted with boiling light petroleum (b. p. 30—40°) (300 ml.). The residue was extracted with boiling carbon tetrachloride; evaporation of the extracts and recrystallisation of the residue from ethanol gave the *amide* (33%), m. p. 146—147° (Found: C, 60·5; H, 5·2; N, 3·5. $C_{21}H_{21}NO_4S$ requires C, 60·7; H, 5·1; N, 3·4%).

NN-*Diphenyl*-2-*ethoxyethanesulphonamide.*—2-Chloroethanesulphonyl chloride[21] (0·02 mole), diphenylamine (0·1 mole), and toluene (2 ml.) were kept under nitrogen at 120° for 12 hr. Ether was added to the cooled mixture, which was then filtered. Evaporation of the filtrates gave a residue which was extracted with boiling light petroleum (b. p. 30—40°) (2 × 200 ml.). Distil-

[17] C. Ziegler and J. M. Sprague, *J. Org. Chem.*, 1951, **16**, 621.
[18] J. I. Cunneen, *J.*, 1947, 134.
[19] J. Heyna and W. Reimenschneider, G. P. 887,505.
[20] Cf. I. B. Douglass and T. B. Johnson, *J. Amer. Chem. Soc.*, 1938, **60**, 1486.
[21] D. Klamann and H. Bertsch, *Chem. Ber.*, 1955, **88**, 201.

TABLE 2.

Sulphonamides.

No.	Sulphonamide	Cryst. solvent	Yield (%)	M. p.	Procedure
1.	(II); R = R′ = CH_2Ph	EtOH	77	132°	*a*
2.	(II); R = R′ = $[CH_2]_5$	EtOH	55	145—146	*a*
3.	(II); R = Ph; R′ = Me	EtOH–Et_2O	78	144—145	*b*
4.	(II); R = H; R′ = Ph	PhH–MeOH	80	165—166	*b*
5.	(IX); R = R′ = CH_2Ph		80	[a]	*b*
6.	(IX); R = R′ = $[CH_2]_5$	Pet[b]	95	38—39[c]	*b*[d]
7.	(IX); R = Ph; R′ = Me	Pet[b]	82	38—39[e]	*b*
8.	(IX); R = H; R′ = Ph	Pet[f]	96	68—69	*b*
9.	(V)	$CHCl_3$–Pet[f]	85	225	*b*[g]
10.	$MeSO_2·N(CH_2Ph)_2$	Pet[h]	82	85	*b*[d]

	Reaction	Found (%)				Required (%)		
No.	time	C	H	N	Formula	C	H	N
1.	2 hr.	62·3	5·6	3·1	$C_{23}H_{25}NO_4S_2$	62·3	5·7	3·1
2.	2 hr.	50·9	6·5	4·4	$C_{14}H_{21}NO_4S_2$	50·7	6·4	4·2
3.	36 hr.	54·2	5·2	4·1	$C_{16}H_9NO_4S_2$	54·3	5·4	4·0
4.	3 days	53·3	5·2	4·4	$C_{15}H_{17}NO_4S_2$	53·1	5·1	4·1
5.	30 min.	65·1	6·8	4·1	$C_{18}H_{23}NO_3S$	64·8	7·0	4·2
6.	4 hr.	48·9	8·4	6·2	$C_9H_{19}NO_3S$	48·8	8·7	6·3
7.	3 days	54·3	7·2	5·9	$C_{11}H_{17}NO_3S$	54·3	7·1	5·8
8.	3 days	52·4	6·8	6·3	$C_{10}H_{15}NO_3S$	52·4	6·6	6·1
9.	5 days	51·8	5·5	7·8	$C_{16}H_{20}N_2O_4S_2$	52·1	5·5	7·6
10.	90 min.	65·5	6·3	5·3	$C_{15}H_{17}NO_2S$	65·4	6·2	5·1

[a] n_D^{18} 1·5513; b. p. 170°/0·1 mm. [b] B. p. 30—40°. [c] B. p. 120°/0·6 mm. [d] Pyridine omitted. [e] B. p. 142°/0·4 mm. [f] B. p. 40—60°. [g] From $PhMeN·SO_2·CH_2·CH_2·SO_2Cl$. [h] B. p. 80—100°

lation of the residue gave first diphenylamine, b. p. 95—100°/0·1 mm., and then NN-*diphenylethylenesulphonamide* (19%), b. p. 150°/0·1 mm., m. p. 102° (from isopropyl ether) (Found: C, 64·6; H, 5·1; N, 5·1. $C_{14}H_{13}NO_2S$ requires C, 64·8; H, 5·1; N, 5·4%). This sulphonamide (0·002 mole) was treated with 0·4N-ethanolic sodium ethoxide (10 ml.). After 30 min. at 20°, the solution was diluted with saturated brine and extracted with ether to give the *ethoxy-sulphonamide* (98%), m. p. 65—66° (from light petroleum) (Found: C, 63·0; H, 6·1; N, 4·8. $C_{16}H_{19}NO_3S$ requires C, 62·9; H, 6·3; N, 4·6%).

NN-*Dibenzyl-2-morpholinoethanesulphonamide*.—Dibenzylamine (0·08 mole) in benzene (50 ml.) was added dropwise with stirring during 30 min. to 2-chloroethanesulphonyl chloride (0·02 mole) in benzene (100 ml.) at 20°. After 75 min., the mixture was washed with hydrochloric acid and evaporation of the organic layer gave NN-*dibenzylethylenesulphonamide* (65%), m. p. 59—60° [from light petroleum (b. p. 60—80°)] (Found: C, 66·8; H, 6·2; N, 4·9. $C_{16}H_{17}NO_2S$ requires C, 66·8; H, 6·0; N, 4·9%). The sulphonamide (0·025 mole) was treated with morpholine (0·025 mole) in ethanol (30 ml.) and after 2 hr. the mixture was diluted with ether and extracted with 4N-hydrochloric acid. The aqueous extracts were basified (Na_2CO_3) and extracted with ether to give NN-*dibenzyl-2-morpholinoethanesulphonamide* (90%), m. p. 91—92° [from light petroleum (b. p. 60—80°)] (Found: C, 64·2; H, 7·1; N, 7·7. $C_{20}H_{26}N_2O_3S$ requires C, 64·1; H, 7·0; N, 7·5%).

N-*Methyl-2-chlorosulphonylethanesulphonanilide*.—*N*-Methylethylenesulphonanilide[13] (63%) was obtained from ethane-1,2-bis-sulphonyl chloride.[22] The amide (0·0304 mole) and sodium pyrosulphite (0·0228 mole) were refluxed in 50% aqueous ethanol (150 ml.) for 15 hr. Extraction with ether gave recovered ethylenesulphonamide (7%), m. p. and mixed m. p. 75—77°. The aqueous layer was acidified with concentrated hydrochloric acid and re-neutralised with saturated aqueous sodium hydrogen carbonate. Evaporation to dryness gave a residue, which was kept with phosphorus pentachloride (5·8 g.) and toluene (50 ml.) for 4 hr. at 110°. Toluene and phosphoryl chloride were removed under reduced pressure and ice was added to the residue. Extraction with methylene chloride gave the *amido-sulphonyl chloride* (67%), m. p. 120—121° (from carbon tetrachloride) (Found: C, 36·2; H, 4·0; N, 4·9. $C_9H_{12}ClNO_4S_2$ requires C, 36·3; H, 4·1; N, 4·7%).

S-*Benzylthiouronium* 2-p-*Tolylsulphonylethanesulphonate*.—Treatment of an aqueous solution

[22] J. Lichtenberger and P. Tritsch, *Bull. Soc. chim. France*, 1961, 363.

of the sodium salt[23] with *S*-benzylthiouronium hydrochloride gave the *salt*, m. p. 174—175° (from water) (Found: C, 47·3; H, 5·2; N, 6·7. $C_{17}H_{22}N_2O_5S_3$ requires C, 47·4; H, 5·2; N, 6·6%).

Reactions of β-Sulphonyl-sulphonamides with Sodium Ethoxide.—General procedure. The β-sulphonyl-sulphonamide (0·005 mole) in (warm) benzene (10 ml.) was added to 0·83N-ethanolic sodium ethoxide (30 ml.). The mixture was kept at 20° for 1 hr. and poured into saturated brine. The ethereal extract was washed with acidified (HCl) brine and evaporated. The residue, a mixture of 2-ethoxyethyl *p*-tolyl sulphone and the 2-ethoxyethanesulphonamide of the relevant amine, was analysed by the infrared-spectroscopic procedure (above). The acid washings were basified and extracted with ether. Evaporation gave the free amine produced in the reaction; this was usually characterised as a derivative.

The original aqueous layer was brought to pH 2 with sulphuric acid. Sulphur dioxide was liberated, and extraction with ether gave toluene-*p*-sulphinic acid, which was determined as *p*-nitrobenzyl *p*-tolyl sulphone.[4]

(a) NN-*Dibenzyl*-2-p-*tolylsulphonylethanesulphonamide.* (i) Fractionation of the neutral products gave 2-ethoxyethyl *p*-tolyl sulphone (59%), b. p. 115°/0·15 mm., n_D^{20} 1·5230, and *NN*-dibenzyl-2-ethoxyethanesulphonamide (35%), b. p. 165°/0·15 mm., n_D^{20} 1·5430. Infrared analysis gave 63 and 35%, respectively. Dibenzylamine (58%), b. p. 90°/0·2 mm., n_D^{20} 1·5740, was converted into the *N*-2,4-dinitrophenyl derivative, m. p. and mixed m. p. 102—104°. Toluene-*p*-sulphinic acid (25%) was obtained as *p*-nitrobenzyl *p*-tolyl sulphone, m. p. and mixed m. p. 187—189°.

(ii) When the reaction time was reduced to 5 min., no starting material was recovered. Dibenzylamine (64%), 2-ethoxyethyl *p*-tolyl sulphone (63%), and *NN*-dibenzyl-2-ethoxyethanesulphonamide (35%) were isolated.

(iii) Reaction with sodium ethoxide (1 mol.) was carried out as in the standard procedure and, after 1 hr., the volume of the mixture was reduced to 20 ml. Addition of ether (250 ml.) gave a precipitate, which evolved sulphur dioxide on treatment with hydrochloric acid. Extraction of the acidic solution with ether gave toluene-*p*-sulphinic acid (8%) but, on basification and re-extraction with ether, no dibenzylamine was obtained. The aqueous solution was then adjusted to pH 7, and addition of a slight excess of aqueous *S*-benzylthiouronium hydrochloride gave the thiouronium salt of 2-*p*-tolylsulphonylethanesulphonic acid (17%), m. p. and mixed m. p. 172—174°.

Evaporation of the original ethereal solution and treatment of the residue with a little ether gave recovered starting material (16%), m. p. and mixed m. p. 132—138°. Saturation of the filtrate with hydrogen chloride precipitated dibenzylamine hydrochloride (50%), m. p. and mixed m. p. 273—275°. The filtrate was chromatographed in 4:1 light petroleum–ether on neutral alumina. Elution with this solvent mixture gave *NN*-dibenzylethylenesulphonamide (24%), m. p. and mixed m. p. 57—59°, and then 2-ethoxyethyl *p*-tolyl sulphone (19%), n_D^{16} 1·5240. Elution with 1:1 light petroleum–ether gave further recovered starting material (4%), m. p. and mixed m. p. 133—139°.

(iv) The sulphonamide (0·005 mole) in benzene (10 ml.) was treated with morpholine (0·05 mole) and 0·33N-ethanolic sodium ethoxide (0·01 mole). After 1 hr. at 20°, the mixture was poured into ether (250 ml.) and extracted successively with sulphuric acid and aqueous sodium hydrogen carbonate. Evaporation of the ethereal solution gave 2-ethoxyethyl *p*-tolyl sulphone (38%), b. p. 108—110°/0·05 mm., n_D^{20} 1·5268, and *NN*-dibenzyl-2-ethoxyethanesulphonamide (17%), b. p. 150°/0·05 mm., n_D^{20} 1·5472.

The acid extract was basified (Na_2CO_3) and extracted with ether. Evaporation of the ether extract gave a residue which, on chromatography on alumina in ether, gave first, dibenzylamine (60%), b. p. 80—85°/0·05 mm., n_D^{16} 1·5757, followed by *NN*-dibenzyl-2-morpholinoethanesulphonamide (8%), m. p. and mixed m. p. 89—91°, and 2-*morpholinoethyl* p-*tolyl sulphone** (25%), m. p. and mixed m. p. 64—65° (Found: C, 57·9; H, 6·9; N, 4·8. $C_{13}H_{19}NO_3S$ requires C, 57·9; H, 7·1; N, 5·2%).

Acidification (H_2SO_4) of the alkaline extracts gave toluene-*p*-sulphinic acid (13%).

The sulphonamide was unaffected by morpholine in the absence of sodium ethoxide, and *NN*-dibenzylmethanesulphonamide did not react under the standard reaction conditions.

(b) N-*Methyl*-2-p-*tolylsulphonylethanesulphonanilide.* Infrared analysis of the neutral products, which could not be separated by distillation, gave ethoxy-sulphone (46%) and

* We thank Mr. S. T. McDowell for preparing this compound.

[23] W. Reppe, *Annalen*, 1956, **601**, 81.

ethoxysulphonamide (44%). *N*-methylaniline (45%), b. p. 70°/10 mm., n_D^{16} 1·5722, and toluene-*p*-sulphinic acid (40%) were also isolated.

(c) N-2-p-*Tolylsulphonylethanesulphonylpiperidine*. The separation procedure was modified because of the solubility of piperidine in water. The reaction mixture was poured into ether and extracted with dilute sulphuric acid (evolution of sulphur dioxide). The aqueous extracts were basified (NaOH) and shaken with benzenesulphonyl chloride. Extraction with ether gave *N*-benzenesulphonylpiperidine (30%), m. p. and mixed m. p. 90—92°.

The original ethereal solution was washed with aqueous sodium hydrogen carbonate; acidification of the washings gave toluene-*p*-sulphinic acid (51%). Evaporation gave the neutral products, b. p. 100—130°/0·1 mm., which were shown by infrared spectroscopy to contain 2-ethoxyethyl *p*-tolyl sulphone (33%) and *N*-2-ethoxyethanesulphonylpiperidine (57%).

(d) NN-*Diphenyl*-2-p-*tolylsulphonylethanesulphonamide*. The procedure was modified because of the low basicity of diphenylamine. Toluene-*p*-sulphinic acid (48%) was obtained from the ethereal extract in the usual way. This extract was evaporated and the residue was dissolved in light petroleum and chromatographed on alumina. Elution with 20:1 light petroleum–ether gave diphenylamine (46%), m. p. and mixed m. p. 50—53°, and with 1:1 light petroleum–ether gave *NN*-diphenyl-2-ethoxyethanesulphonamide (29%), m. p. and mixed m. p. 64—65°. Subsequent mixed fractions were combined and chromatography on alumina of their benzene solution gave further ethoxy-amide (21%). Subsequent elution with 20:1 benzene–ether gave 2-ethoxyethyl *p*-tolyl sulphone (43%), n_D^{22} 1·5218.

(e) 2-p-*Tolylsulphonylethanesulphonanilide*. When the standard procedure was used, immediate precipitation of the sodium salt of the sulphonamide occurred, and the usual working up gave the starting material (85%). A homogeneous reaction mixture was obtained when the anilide was dissolved in pyridine (25 ml.) and 1·67N-ethanolic sodium ethoxide (15 ml.) was added. The usual working up gave, as the sole neutral product, 2-ethoxyethyl *p*-tolyl sulphone (87%), b. p. 125—129°/0·2 mm., n_D^{20} 1·5232. Aniline (81%) was characterised as benzanilide, m. p. and mixed m. p. 162—163°. The extract containing acidic products was washed with aqueous sodium hydrogen carbonate, and evaporated to give ethylenesulphonanilide[11] (3%), m. p. and mixed m. p. 67—69°. The alkaline washings yielded toluene-*p*-sulphinic acid (4%).

(f) N-*Methylethane*-1,2-*disulphonanilide*. Because of the low solubility of the sulphonamide, the reaction was carried out under reflux for 3 hr. The mixture was poured into acidified brine, and extracted with ether to give *N*-methyl-2-ethoxyethanesulphonanilide (95%), m. p. and mixed m. p. 37—38°. Basification of the aqueous phase and extraction with ether gave *N*-methylaniline (96%), n_D^{20} 1·5705, characterised as the *N*-2,4-dinitrophenyl derivative, m. p. and mixed m. p. 167—169°.

This work was supported by the U.S. Department of the Army through its European Office.

THE QUEEN'S UNIVERSITY OF BELFAST. [*Received, September 17th*, 1964.]