Elimination-Addition. Part XVII.[1] Elimination Pathways in Derivatives of β-Sulphonylsulphonic Acids

By **E. J. Miller** and **C. J. M. Stirling,*** King's College, Strand, London, W.C.2.

In reactions of alkyl esters of 2-*p*-tolylsulphonylethanesulphonic acid with alkoxides, elimination of the *p*-tolylsulphonyl group occurs to a greater extent than the competitive elimination of the alkoxysulphonyl group; the difference is attributed to the greater activation of elimination by the alkoxysulphonyl group. Both products of elimination undergo addition of alkoxide.

2-*p*-Tolylsulphonylethanesulphonyl chloride reacts with piperidine to give the piperidide in high yield but a small amount of sulphinic acid resulting from elimination is also obtained. In reactions with alkoxides the sulphonyl chloride gives the alkyl esters when equimolecular proportions of the reagents are used. With excesses of alkoxides, the product distributions are very similar to those found with the esters, showing that very little direct elimination occurs in reactions of the chloride.

NEARLY eighty years ago it was shown [2] that 1,2-bis-sulphones, on treatment with aqueous hydroxides yield a mixture of sulphinic acid and β-hydroxy-sulphone. Subsequently, in the first paper of this series, this reaction was interpreted [3] as an elimination–addition sequence in which elimination of one sulphonyl group is powerfully promoted by the other; the sulphonyl group may act as both leaving group and activating group. In an unsymmetrical bis-sulphonyl system (I), elimination under basic conditions may occur in two directions; the *p*-tolylsulphonyl group may promote departure of the group $-SO_2Z$ or conversely, the *p*-tolylsulphonyl group may depart, as sulphinate ion, under the activating influence of the group $-SO_2Z$ (Scheme).

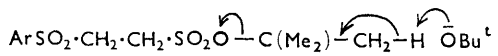
Earlier, we reported [4] that in reactions of β-sulphonylsulphonamides (I; $Z = NR_2$) with bases, the arylsulphonyl and sulphonamido-groups both act as leaving and as activating groups. In this paper, we report on a similar investigation of the chloride and alkyl esters of 2-*p*-tolylsulphonylethanesulphonic acid (I; $Z = OH$). The purpose of the investigation was three-fold: (i) to discover whether the chlorosulphonyl and alkoxysulphonyl groups would activate elimination or whether, in the chloride, nucleophilic displacement of chlorine from sulphur would predominate; (ii) to compare the alkoxysulphonyl group with the arenesulphonyl group in terms of their effects upon the direction of elimination; (iii) to study the effect of change of base on the direction of elimination.

Reactions with 2-p-*Tolylsulphonylethanesulphonyl Chloride.*—The chloride was conveniently obtained by addition of sulphite ion to *p*-tolyl vinyl sulphone and subsequent treatment of the resulting sulphonic acid [5] with phosphorus pentachloride.

With piperidine the predominant product (Table) is the piperidide (I; $Z = NC_5H_{10}$) derived from nucleophilic displacement of chloride from sulphur as with simple sulphonyl chlorides. In addition, however, a small amount of sulphinic acid is obtained and the yield of this product is not sensibly affected when a large excess of amine is used showing, as expected, that the amide is stable in the presence of excess of amine. The most likely explanation for the formation of sulphinic acid is that elimination of the *p*-tolylsulphonyl group under the influence of the chlorosulphonyl group competes to a very small extent with formation of the sulphonamide. Elimination of halogen situated β- to a chlorosulphonyl group probably occurs in similar reactions of amines with β-chlorosulphonyl chlorides.[6,7] Similar behaviour is found in reactions with dibenzylamine.

Products from reactions of the sulphonyl chloride with alcoholic solutions of alkoxides are listed in the Table. With equimolecular proportions of methoxide and of ethoxide, the sole product in each case is the alkyl sulphonate. It is clear that nucleophilic displacement at sulphur in these reactions is much faster than elimination of either leaving group. When an excess of methoxide or ethoxide is used, the distribution of products is very similar to that obtained with the corresponding sulphonate esters, and establishes the role of the esters as intermediates. The results are considered in the next section.

Reaction of the chloride with an equimolecular amount of potassium t-butoxide in t-butyl alcohol gave the sulphonic acid (41%) and half of the chloride was recovered. By analogy with the methoxide and ethoxide reactions, it is probable that the t-butyl ester is first formed. Tertiary sulphonates,[8] behaving like tertiary halides [9] are, however, very prone to the elimination of sulphonic



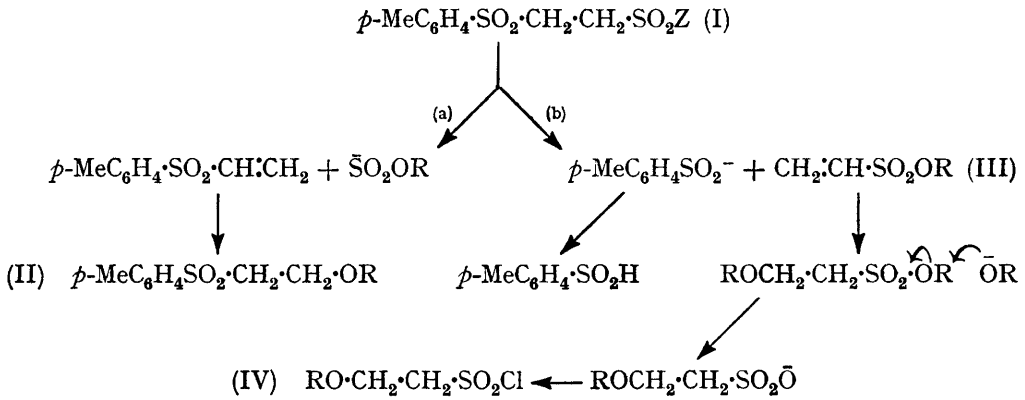
acid. Formation of the t-butyl ester and subsequent elimination consumes two moles of base for each mole of sulphonic acid obtained, so that half the chloride is recovered.

Treatment of the sulphonic acid with an excess of methoxide or ethoxide gave no reaction other than salt formation.

Reactions of Alkyl 2-p-*Tolylsulphonylethylsulphonates*

[1] Part XVI, A. W. Miller and C. J. M. Stirling, *J. Chem. Soc.* (*C*), 1968, 2612.
[2] E. Stuffer, *Ber.*, 1890, **23**, 1408, 3226.
[3] A. T. Kader and C. J. M. Stirling, *J. Chem. Soc.*, 1962, 3686.
[4] D. S. Campbell and C. J. M. Stirling, *J. Chem. Soc.*, 1964, 5869.
[5] W. Reppe, *Annalen*, 1956, **601**, 81.
[6] C. S. Rondestvedt, *J. Amer. Chem. Soc.*, 1954, **76**, 1926.
[7] A. A. Goldberg, *J. Chem. Soc.*, 1945, 464.
[8] H. M. R. Hoffmann, *J. Chem. Soc.*, 1965, 6748.
[9] C. K. Ingold, 'Structure and Mechanism in Organic Chemistry,' Bell, London, 1953, p. 439.

with Alkoxides.—Three types of product have been isolated from these reactions (Scheme). 2-Alkoxyethyl *p*-tolyl sulphones (II) result from nucleophilic addition of alkoxide ion to the vinyl sulphone obtained initially by elimination of the alkoxy-sulphonyl group [path (a)]. In path (b), toluene-*p*-sulphinate ion is eliminated and the free acid is isolated. The complementary product is the vinyl ester (III). As 2-alkoxyethanesulphonyl chlorides (IV) are obtained by treatment of the water-soluble, non-extractable products with phosphorus pentachloride, we interpret the subsequent reactions of the vinyl ester as shown in the Scheme. Formation of the sulphonate ion by attack of alkoxide ion on the α-carbon atom of the ester alkoxy-group may, of course, occur before or after addition of alkoxide to the carbon–carbon double bond. We favour the latter alternative in view of the high reactivity of vinylsulphonic esters to nucleophilic addition.[10]



In reactions with t-butoxide ion (Table), 2-hydroxyethyl and not 2-t-butoxyethyl *p*-tolyl sulphone is isolated. Contact with acid during the work up procedure hydrolyses the ether to the alcohol; when *p*-tolyl vinyl sulphone is treated under the same conditions but with omission of strong acid from the work up, a mixture of the hydroxy-sulphone and of its t-butyl ether in the ratio of 1 : 2 (by ^{1}H n.m.r. spectroscopy) is obtained.

The yields of sulphinic acid and of alkoxy (hydroxy)-sulphone (Table) denote the proportions of elimination by paths (a) and (b) respectively. As expected, there is little difference between the results obtained for the methyl and ethyl esters in a particular base–solvent system. For reactions with ethanolic ethoxide, path (b) is favoured by a factor of three over path (a). This may be ascribed either to better activation of elimination by the alkoxysulphonyl groups and/or to the fact that the *p*-tolylsulphonyl group is a better leaving group than the alkoxysulphonyl group. In this connection, elimination reactions of a series of β-phenoxyethyl compounds have recently been studied:[11]

$$\underset{\text{(V)}}{\text{XCH}_2\cdot\text{CH}_2\cdot\text{OPh}} \xrightarrow[\text{EtOH}]{\text{EtO}^-} \text{XCH:CH}_2 + \bar{\text{O}}\text{Ph}$$

and it has been found that the rate of elimination in the

Products obtained from reactions of derivatives of 2-*p*-tolylsulphonylethanesulphonic acid

Substrate	Reagent [a] (mol.)	Products (%)			
		p-TolylSO$_2$H	RO[CH$_2$]$_2$·SO$_2$·tolyl-*p*	RO[CH$_2$]$_2$·SO$_2$Cl	Others
p-TolylSO$_2$·[CH$_2$]$_2$·SO$_2$OH	MeONa (5)	0	0	0	*b*
,,	EtONa (5)	0	0	0	*c*
p-TolylSO$_2$·CH$_2$]$_2$·SO$_2$Cl	Piperidine (2)	2			*d*
,,	Piperidine (5)	3			*e*
,,	Dibenzylamine (2)	6			*f*
,,	MeONa (1)	0	0	0	*g*
,,	MeONa (5)	42	36	18 [h]	
,,	EtONa (1)	0	0	0	*i*
,,	EtONa (5)	79	16	49	
,,	t-BuOK (1)	0	0	0	*j*
,,	t-BuOK (5)	47	46 [k]	40 [l]	
p-TolylSO$_2$·[CH$_2$]$_2$·SO$_2$·OMe	MeONa (5)	46	44	17	
,,	EtONa (5)	63	24	45	
,,	t-BuOK (5)	91	5 [k]	82 [l]	
p-TolylSO$_2$·[CH$_2$]$_2$·SO$_2$·OEt	MeONa (5)	50	43	44 [h]	
,,	EtONa (5)	75	18	43	
,,	t-BuOK (5)	77	20 [k]	66 [l]	

[a] Alkoxides used in corresponding alcohol. [b] Sole product *p*-tolylSO$_2$·[CH$_2$]$_2$·SO$_2$Cl (97%). [c] Sole product *p*-tolylSO$_2$·[CH$_2$]$_2$·SO$_2$Cl. [d] Piperidide (95%). [e] Piperidide (90%). [f] Dibenzylamide (85%). [g] Methyl ester (94%). [h] As anilide. [i] Ethyl ester (93%). [j] Sulphonyl chloride recovered (45%); sulphonic acid isolated as the chloride (41%). [k] Hydroxy-sulphone. [l] Ethylenesulphonyl chloride.

[10] H. Distler, *Angew. Chem. Internat. Edn.*, 1965, **4**, 300.
[11] J. Crosby and C. J. M. Stirling, *J. Amer. Chem. Soc.*, to be published.

compound (V; X = $EtO{\cdot}SO_2$) is roughly twice that in the compound (V; X = $PhSO_2$). We broadly infer, therefore, that the predominant effect is one of differential activation, rather than of differential leaving group ability.

Another feature of the results is that in both esters, the yield of sulphinic acid increases and the yield of alkoxysulphone decreases when the medium is changed from the solvent system containing methanolic sodium methoxide to that containing potassium t-butoxide in t-butyl alcohol. Change of orientation of elimination with variation in the basicity of the base has been observed in other systems.[12] In this connection it was shown that transesterification does not occur before elimination when, for example, the methyl ester is treated with ethanolic sodium ethoxide.

EXPERIMENTAL

The light petroleum used had b.p. 40—60°. Methanol and ethanol were dried.[13] t-Butyl alcohol was distilled from sodium. Tetrahydrofuran was passed down a column of activated alumina and was subsequently distilled from lithium aluminium hydride. ^1H N.m.r. spectra were obtained using a Varian HR100 instrument operating at 100 MHz.

2-p-Tolylsulphonylethanesulphonyl Chloride.—The following method is superior to that [4] previously used. *p*-Tolyl vinyl sulphone [14] (18·2 g., 0·1 mole) was stirred under reflux with sodium hydrogen sulphite (50 g., 0·2 moles) in water (125 c.c.) for 7 hr. The mixture was evaporated to dryness and the residue was stirred under reflux for 4 hr. with phosphorus pentachloride (41·7 g.) in dry toluene (350 c.c.). Toluene and phosphoryl chloride were distilled off under reduced pressure and crushed ice was added to the residue. Extraction with dichloromethane gave the sulphonyl chloride (96%), m.p. and mixed m.p. 164—165°.

2-p-Tolylsulphonylethanesulphonic Acid.—The preceding chloride (9·9 g.) in methanol (200 c.c.) was heated under reflux for 2 hr. Evaporation gave the *acid* (92%), m.p. 157° (from ethyl acetate) (Found: C, 38·2; H, 5·1. $C_9H_{12}O_5S_2,H_2O$ requires C, 38·3; H, 5·0%). The *S*-benzylthiuronium salt had m.p. 175° (lit.,[4] m.p. 174—175°).

Esters of 2-p-Tolylsulphonylethanesulphonic Acid.—The acid chloride (9·6 g.) in tetrahydrofuran (75 c.c.) was treated with methanolic 0·2N-sodium methoxide (175 c.c.). The mixture was stirred at 20° for 2 hr., added to acidified (HCl), saturated brine and extracted with chloroform. The extracts were washed with aqueous sodium hydrogen carbonate and evaporation gave the *methyl ester* (94%), m.p. 120° (from chloroform–light petroleum) (Found: C, 43·1; H, 5·2. $C_{10}H_{14}O_5S_2$ requires C, 43·3; H, 5·0%). The *ethyl ester* obtained (93%) in the same way had m.p. 98° (from chloroform–light petroleum) (Found: C, 45·1; H, 5·8. $C_{11}H_{16}O_5S_2$ requires C, 45·2; H, 5·5%).

2-Methoxyethyl p-Tolyl Sulphone.—2-Methoxyethyl bromide [15] (12·1 g., 1·2 mol.) was added to a solution of toluene-*p*-thiol (11 g.) in ethanolic N-sodium ethoxide (87 c.c.). The mixture was heated under reflux for 30 min. and poured into water. Extraction with chloroform gave *2-methoxyethyl p-tolyl sulphide* (10·6 g. 66%), b.p. 140°/14 mm., n_D^{17} 1·5514 (Found: C, 65·6; H, 7·6. $C_{10}H_{14}OS$ requires C, 65·9; H, 7·7%). The sulphide (8·3 g.) was kept with 30% hydrogen peroxide (25 c.c.) in acetic acid (50 ml.) at 90° for 1 hr. The mixture was poured into saturated brine and extracted with chloroform. The chloroform extracts were washed with saturated aqueous sodium hydrogen carbonate and evaporation gave the *sulphone* (8·6 g. 88%), b.p. 133°/0·08 mm., n_D^{17} 1·5332 (Found: C, 55·6; H, 6·5. $C_{10}H_{14}O_3S$ requires C, 56·1; H, 6·55%).

2-Methoxyethanesulphonyl Chloride.—Ethylenesulphonyl chloride [6] (900 mg.) in tetrahydrofuran (15 c.c.) was stirred with methanolic N-sodium methoxide (35·5 c.c.) at 20° for 2 hr. The mixture was added to acidified, saturated brine and the subsequent work up as for the sulphone-sulphonyl chloride (above) gave the chloride (1·01 g., 90%), b.p. 103°/10 mm., n_D^{20} 1·4653 (lit.,[16] b.p. 103°/18 mm.). Treatment of the chloride with aniline (2 mol.) in ether gave the anilide (94%), m.p. 91° (Found: C, 50·2; H, 6·2; N, 6·3. $C_9H_{13}NO_3S$ requires C, 50·2; H, 6·1; N, 6·5%).

2-Ethoxyethanesulphonyl Chloride.—Treatment of ethylenesulphonyl chloride with ethanolic sodium ethoxide as in the preceding preparation gave the *chloride* (89%), b.p. 74°/5 mm., n_D^{25} 1·4550 (lit.,[17] b.p. 75—76°/4 mm., n_D^{25} 1·4552).

Reactions of 2-p-Tolylsulphonylethanesulphonyl Chloride.—(a) *With dibenzylamine.* The chloride (2 g.) was stirred with dibenzylamine (2·8 g. 2 mol.) in tetrahydrofuran (35 c.c.) for 1 hr. at 20° and then added to acidified saturated brine; the mixture was then extracted with chloroform. The extracts were washed with aqueous sodium hydrogen carbonate and evaporated. The residue, with light petroleum, gave *NN*-dibenzyl 2-*p*-tolylsulphonylethanesulphonamide (85%) m.p. and mixed m.p. 131° (lit.,[4] m.p. 132°). The alkaline washings were acidified, saturated with sodium chloride and extracted with dichloromethane. Evaporation gave the crude sulphinic acid which was converted [3] to the *p*-nitrobenzyl sulphone (6%), m.p. and mixed m.p. 186—187°.

(b) *With piperidine.* Similar treatment of the sulphonyl chloride with piperidine (2 mol.) in tetrahydrofuran gave the sulphonylpiperidide [4] (95%), m.p. and mixed m.p. 145—146° together with toluene-*p*-sulphinic acid (2%). When the molar ratio of piperidine to sulphonyl chloride was 5, the yield of amide was 90% and that of sulphinic (3%).

Reactions of 2-p-Tolylsulphonylethanesulphonyl Derivatives with Alkoxides. The derivative (0·0071 mole) in tetrahydrofuran (15 c.c.) was stirred with a N-solution of the alkoxide (5 mol.) in the alcohol (35·5 c.c.) at 20° for 2 hr. The mixture was added to acidified (HCl), saturated brine and extracted with chloroform. The extracts were washed with aqueous sodium hydrogen carbonate and evaporation gave the neutral product, the 2-alkoxy- or 2-hydroxyethyl sulphone. Acidification of the alkaline washings and extraction with chloroform gave free sulphinic acid which was either weighed directly or converted to the *p*-nitrobenzyl sulphone.[3]

The original aqueous solution was basified ($NaHCO_3$) and evaporated to dryness. The residue was kept at 100°/10 mm. for 4 hr. and was then stirred with phosphorus pentachloride (2·9 g.) in toluene (50 c.c.) for 4 hr. at 110°. Toluene and phosphoryl chloride were removed under reduced

[12] D. H. Froemsdorf and M. D. Robbins, *J. Amer. Chem. Soc.*, 1967, 1737.
[13] A. I. Vogel, ' A Text-Book of Practical Organic Chemistry,' Longmans, 3rd edn., 1956.
[14] L. I. Smith and H. R. Davis, *J. Org. Chem.*, 1950, **15**, 824.
[15] R. C. Tallman, *J. Amer. Chem. Soc.*, 1934, **56**, 126.
[16] A. S. Matlack, *J. Org. Chem.*, 1959, **23**, 729.
[17] C. Ziegler and J. M. Sprague, *J. Org. Chem.*, 1951, **16**, 621.

pressure and crushed ice was added to the residue. Extraction with dichloromethane gave ethylenesulphonyl chloride or the alkoxyethane sulphonyl chloride. All products were authenticated by comparison of i.r. spectra and/or mixed m.p.s. In experiments with the sulphonic acid, no sulphinic acid or alkoxy-(hydroxy-) ethyl sulphone was obtained. The sole product was 2-*p*-tolylsulphonylethanesulphonyl chloride.

Test of Exchange in Ester-Alkoxide Reactions.—Methyl 2-*p*-tolylsulphonylethanesulphonate (0·5 g.) in tetrahydrofuran (4 ml.) was treated with ethanolic 0·1N-sodium ethoxide (9 c.c., 0·5 mol.) dropwise with stirring during 30 min. After 1 hr., the mixture was added to acidified saturated brine and extracted with chloroform. The extracts were washed with saturated, aqueous sodium hydrogen carbonate and evaporation gave the neutral product (0·37 g.), m.p. 90—105°. The ^{1}H n.m.r. spectrum showed this material to be recovered methyl ester contaminated with a small amount of *p*-tolyl vinyl sulphone. There was no sign of the characteristic triplet–quartet pattern which would be given by ethyl ester produced by transesterification.

Reaction of p-*Tolyl Vinyl Sulphone with Potassium* t-*Butoxide.*—The sulphone (0·92 g.) was treated with potassium t-butoxide in t-butyl alcohol under the standard conditions. The mixture was neutralised with acetic acid, diluted with water and extracted with dichloromethane. Evaporation of the extracts gave a residue (0·919 g.), b.p. 135°/0·05 mm. The i.r. spectrum showed the presence of a hydroxy-group and comparison of the integrals of the t-butyl (τ 9·05) and nuclear methyl (τ 7·65) protons showed that the mixture consisted of one part of hydroxy-sulphone and two parts of its t-butyl ether.

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