Elimination and Addition Reactions. Part 30.[1,2] Leaving Group Abilities in Alkene-forming Eliminations activated by Sulphonyl Groups

By **Donald R. Marshall, Patsy J. Thomas,** and **Charles J. M. Stirling,*** School of Physical and Molecular Sciences, University College of North Wales, Bangor LL57 2UW

Rates of elimination of the group Z from a series of β-substituted sulphones, $PhSO_2{\cdot}CH_2{\cdot}CH_2Z$, in ethanolic sodium ethoxide at 25 °C have been measured. For each substrate, the mechanism of the reaction has been shown to be the reversible carbanion mechanism $[(E_1cB)_R]$ by determination of the primary kinetic deuterium isotope effect or by demonstration that deuterium–hydrogen exchange at C_β is very much faster than elimination.

The k_{obs} values obtained for these substrates encompass the equilibrium constant for carbanion formation and the rate constant for ejection of the leaving group. The effect of the leaving group on the equilibrium constant, assessed from a Taft plot for sulphone detritiation, has been taken into account where possible in comparison of leaving group abilities.

All positively charged leaving groups depart very easily. Among neutral leaving groups the following order of familiar groups is found PhSe > PhO > PhS > $PhSO_2$ > PhSO > NMeTs > NMeAc > CN. The range of reactivity values spans *ca.* 10^{16}. Carbon-linked leaving groups such as cyano are exceptionally poor.

No simple correlation is obtained between leaving group order and pK_a of ZH, the dissociation energy of the C–Z bond, the inverse nucleophilicity of Z:, or the polar effect of Z as measured by values of $\sigma_I(CH_2Z)$ or the ^{13}C chemical shift of C_α–Z.

Comparisons are drawn between the present data and earlier, usually qualititative, observations on elimination reactions.

LEAVING group ability contributes to reactivity in three main reaction types: substitution, carbonyl-forming elimination, and alkene-forming elimination. For substitution, most work has been concentrated on nucleophilic substitution at carbon[3] and the main emphasis has been on the examination of nucleophilic reactivity[4] and substituent effects,[5] rather than on the leaving group. This is not surprising, because the range of examinable leaving groups is generally restricted to the halides,[6] 'onium groups, and esters of a limited range of strong proton acids.[7]

For nucleophilic substitution at sulphur, the range of leaving groups is wider[8,9] including such groups as ^-SR, SO_3^{2-}, ^-Cl, ^-CN, and ^-SCN. Comparisons of reactivity are, however, restricted.

For nucleophilic substitution, variation of nucleophile, solvent and reaction type may involve large effects on reactivity in which the leaving group is implicated, even with very closely related leaving groups such as bromine and chlorine.[3,5,10]

In carbonyl-forming elimination, the range of leaving group ability is much wider than for nucleophilic substitution. The hydrolysis of an acyl halide or an amide, and the reversions of cyanohydrin formation and

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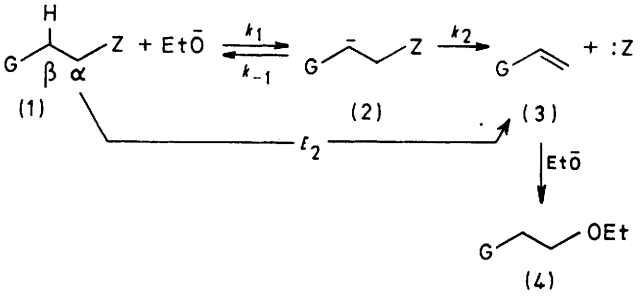
of the Claisen reaction are all of the same type. Determination of the rate constant for the process in which the leaving group–carbon bond is broken, however, is considerably complicated by associated equilibria. Some information is available from direct measurement [11,12] and from isotope exchange studies.[13,14]

Leaving Groups in Alkene-forming Eliminations.—Earlier work [15,16] has shown that a much wider range of leaving groups exists for unactivated alkene-forming elimination than for substitution, provided that very strongly basic media *e.g.* potassium t-butoxide in dimethyl sulphoxide, are used. Thus in the formation of propene from 2-substituted propanes the order Br^-, $^-SO_2Ph$, $PhSO^- > NO_3^- > SCN^- > RS^- > NO_2^- > {}^-CN$ is found.[15] In a later more quantitative study Bartsch and Bunnett [16] studied elimination in 2-substituted hexanes. They derived a reactivity index for leaving groups and it was assumed that reactions were concerted. For unfamiliar leaving groups, *e.g.* OPh, very severe conditions were required, *e.g.* to obtain a 0.48% yield of hexenes from 1-methylpentyl phenyl ether, treatment of the ether with M-potassium t-butoxide in t-butyl alcohol at 129.5 °C for 5 h was required. Other studies have been made of eliminations of arylsulphonyl,[17] sulphinyl,[18] bis(alkylsulphonyl)amino,[19] and even alkoxy-groups.[20] Again, the pattern of severe conditions in strongly basic media is generally maintained and no accurate quantitative comparisons of leaving group ability can be made.

Base-promoted alkene-forming eliminations are greatly accelerated by the insertion, β to the leaving group, of groups capable of stabilising a carbanion. Comparison of data for reactions of ethyl bromide [21] and 2-phenylsulphonylethyl bromide [22] with ethanolic sodium ethoxide suggests a rate enhancement of *ca.* 10^{12} for the sulphone. Such activation renders otherwise very slow reactions with unfamiliar leaving groups amenable to quantitative study. A number of leaving groups in activated eliminations have been examined: alkoxycarbonyl,[23,24] aryloxy,[25,26] arylsulphonyl,[27,28] phenylthio,[29] and alkoxy,[30,31] but no accurate comparisons of reactivity have been made. This is largely because of the imprecise knowledge of the mechanism of the reactions which, as seen below, is a prerequisite for the estimation of leaving group ability from gross reactivity measurements. In this paper we present, for the first time, accurately comparable data on relative magnitudes of leaving group abilities derived from elimination reactions of known mechanism activated by a common activating group.

The System.—An ideal system for evaluation of leaving group ability should allow the rate constant for the process in which the C–Z bond is broken to be separated from others involved in pre-equilibria.

For an elimination, the concerted * process E_2 (Scheme 1), as typified by the phenethyl system



SCHEME 1

(G = Ph),[32] is not capable of yielding the required information, because C_β–H and C_α–Z bond cleavages are coupled.

For a stepwise * process (Scheme 1) the steady-state assumption for the carbanion (2) gives the expression [equation (1)] for the rate constant. Two extreme mechanisms [33] can operate.

(i) The $(E_1cB)_I$ mechanism, in which $k_2 \gg k_{-1}[BH]$ and k_1, the rate constant for the ionisation of the substrate, is rate-determining. This mechanism is only of interest where leaving group abilities are concerned in that k_1 is influenced by Z, and this must be allowed for when k_1 is part of a complex rate constant [equation (1)]. This point is developed further (below).

$$k_{obs} = k_1k_2/(k_{-1}[BH] + k_2) \qquad (1)$$

* The term ' concerted ' is applied to processes in which no evidence can be obtained for an intermediate between reactant and product. The term ' stepwise ' is applied to processes in which there is good evidence for an intermediate carbanion. It is recognised that, because of the involvement of the solvent, the species initially produced by removal of a proton from the substrate may differ from that which sheds the leaving group or recaptures a proton.

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(ii) The $(E_1cB)_R$ mechanism [33] in which $k_{-1}[BH] \gg k_2$, and consequently $k_{obs} = k_1k_2/k_{-1}[BH]$. This expression is essentially the product of the equilibrium constant for carbanion formation and the rate constant, k_2, for the process in which the leaving group, Z, is lost from the carbanion (2). This mechanism is easily detected and distinguished from the E_2 and $(E_1cB)_I$ mechanisms by the absence of a primary deuterium isotope effect, or by the observation of hydrogen–deuterium exchange at C_β occurring much more rapidly than elimination.

is *ca.* $1 : 10^3$. The much less reactive nitro-stabilised carbanion would be expected to be more selective and this may, in part, account for the higher ratio in the nitro-activated system.

We chose to measure rate constants for elimination in sulphones (1; G = $PhSO_2$) substituted with a series of leaving groups, Z (Table 1). The sulphonyl group was selected as activating group because adjacent carbanions are strongly stabilised (pK $PhSO_2Me$ = 29.0; pK PhCOMe = 24.7 in Me_2SO),[37] and it is itself unreactive

TABLE 1

Elimination in sulphones, $PhSO_2{\cdot}[CH_2]_2{\cdot}Z$ [a]

Z	k_{obs} [b]	$k_{H/D}$	Rank	pK of ZH [d]	$6 + \log k_{Nu}$ [e]
F	892	2.0 [f]		3.17	1.7
Cl	780	3.6		−7	4.5
Br	2 600	5.0		−8	4.9
OTs	6 700	2.0		−7	
$OPO(OEt)_2$ [g]	549 [g]	>1($k_e > k_{exch}$)		1.4	
OAc	21.3	1.9		4.7 (9.6)	4.6
OCSPh [g]	0.20 [h]	*j*		3	
OSOPh [g]	0.25	*j*		2	7.6 [k]
OPh	0.35 [u]	*j*	8.94	10	4.8
OMe	4.3×10^{-5}	*j*	6.14	16	5.4
OH	V. slow [q]			15.7	
$^+SMe(C_6H_4Me\text{-}p)$	6.2×10^5	(k_i evidence)	9.79	−7	4.0 [i]
SCOPh [g]	0.22 [h]	*j*		3	
SO_2Ph	1.05 [m]	1.01	8.67	2	7.6 [k]
SOPh	0.26	*j*	7.05	5	
SPh	0.021 [n]	1.03	8.68	8	9.0
SePh	0.31	0.98	10.39		9.8
$^+NMe_2Ph$	5.23×10^4	0.98	9.17	5	4.7
N(Me)Ts [g]	3.4×10^{-5}	*j*	5.41	*ca.* 10	5.3
N(Me)Ac	4.6×10^{-6} [p]	*j*	5.02	16	2.3
NMe_2	V. slow [q]	*j*		*ca.* 30	
$^+PPh_3$	8.8×10^3 [r]	1.02		0	6.1
$P(O)(OEt)_2$	1.2×10^{-5} [s]	*j*			6.1
CN	$<10^{-8}$ [t]	*j* (k_i evidence)	<0.5	10	5.8
$C(Me)_2NO_2$	$<10^{-10}$	*j*	<0.5	*ca.* 10	

[a] Reactions in ethanolic sodium ethoxide at 25 °C. [b] Units 1 mol^{-1} s^{-1}. [c] $\log k_{obs} - \log k_i + 11$. [d] Values in H_2O (EtOH in parentheses). [e] Values from ref. 59. [f] Lit. for MeO^-–HOMe (V. Fiandanese, G. Marchese, and F. Naso, *J.C.S. Perkin II*, 1973, 1538). [g] *p*-Tolylsulphonyl instead of phenylsulphonyl activation. [h] Value estimated from Bu^tOK–Bu^tOH reactions. [i] Value for $(PhCH_2)_2S$. [j] $k_{exch} \gg k_e$. [k] Value for sulphite. [m] Statistically corrected. [n] R. P. Redman and C. J. M. Stirling, *Chem. Comm.*, 1970, 633. [p] Value at 40 °C divided by 5. [q] No elimination after 5 days reflux in 10 mol excess EtO^-–EtOH. [r] Calculated from value for $CN{\cdot}[CH_2]_2{\cdot}\overset{+}{P}Ph_3$ with Et_3N–EtOH. [s] Value for $PhCO{\cdot}[CH_2]_2{\cdot}P(O)(OEt)_2$ divided by 100. [t] Value for $CN[CH_2]_2CN$; see text. [u] Value from J. Crosby and C. J. M. Stirling, *J. Chem. Soc.* (*B*), 1970, 671.

If the activating group, G, renders the carbanion very stable, as, for example, when G = NO_2, then in strongly basic media, the substrate is converted entirely into the carbanion. The only rate process then observable is that corresponding to k_2. A few measurements [34-36] of this type have been made and direct comparison of k_2 values should then yield relative leaving group abilities. Data are too restricted for accurate comparison to be made but we note that expulsion of methoxide [34] from a nitro-stabilised carbanion occurs *ca.* 10^5 times less rapidly than expulsion of phenoxide.[35] The activating group undoubtedly affects relative leaving group abilities, and for a sulphone-activated system (this paper) a corrected leaving group ability ratio OMe : OPh in the conditions required for elimination reactions except when it is acting as a leaving group. Further, as the reprotonation of sulphonyl stabilised carbanions is inherently rapid,[38] *i.e.* $k_{-1}[BH]$ is large, $(E_1cB)_R$ mechanisms, capable of yielding information on leaving group ability, are favoured.

For the series of sulphones (Table 1), reactions with ethanolic sodium ethoxide at 25 °C were overall of the second order, first order in substrate and first order in base. Each sulphone gave a high yield of the alkene (3) or the derived ethoxy-compound (4) together with, in appropriate cases, products derived from the leaving group. Details are in Table 2.

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Some of the initial work was carried out with *p*-tolylsulphonyl rather than phenylsulphonyl compounds. The difference that this makes is very small [39] and results for *p*-tolylsulphonyl compounds have been multiplied by 1.93 (the phenyl : *p*-tolyl ratio is 1.93 : 1 for the phenoxy leaving group).

TABLE 2

Product analyses for elimination reactions

Z	% p-$MeC_6H_4SO_2$·CH:CH_2 or p-$MeC_6H_4SO_2$·$[CH_2]_2$·OEt	Z (%)
$OPO(OEt)_2$	95 [a]	$(EtO)_2P(:O)$·O^-·$^+NH_2$:$C(NH_2)$·SCH_2Ph (98)
OCSPh	78 [c]	
OSOPh	88	(79) [d]
OPh	99	PhOH (91)
OMe	79 (of reacted starting material)	
^+SMePh [e]	91 [b,e]	p-MeC_6H_4·SMe (98)
SCOPh	73 [c]	
SO_2Ph	98 [a]	(72) [d]
SOPh	78 [a]	
SPh	96 [a]	PhSH (88)
SePh	96 [a]	PhSeSePh (79)
$^+NMe_2Ph$	98 [b]	
NMeTs	94 [a]	p-MeC_6H_4·SO_2·NHMe (80)
NCH_2PhAc	85 [a]	$PhCH_2$·NH·COMe (91)
NMe_2	91% recovery after 48 h at 80 °C	
Ph_3P^+	89% NC·$[CH_2]_2$·OEt	
$P(O)(OEt)_2$ [g]	93% PhCO·$[CH_2]_2$·OEt	
CN [g]	100% recovery after 7 days at 25 °C	
CN [f]	100% recovery after 8 days at 25 °C	
CMe_2NO_2	98% recovery after 48 h at 80 °C	

[a] $PhSO_2$·$[CH_2]_2$·OEt. [b] $PhSO_2$·CH:CH_2. [c] As mixture of $PhSO_2$·$[CH_2]_2$·OH and $PhSO_2$·$[CH_2]_2$·OBu^t. [d] As *p*-nitrobenzyl phenyl sulphone. [e] *p*-Tolyl compound. [f] G = CN. [g] G = PhCO.

Reaction of the most reactive substrate, the sulphonium salt (1; Z = $^+SMe_2$) was too rapid to be followed even by using a stopped flow spectrometer. The rate with ethanolic triethylamine was measured and the rate constant was multiplied by the ethoxide : triethylamine ratio for the ammonium salt (1; Z = $^+NMe_3$).

The thioesters (1; Z = SCOPh or OCSPh) underwent rapid transesterification on treatment with ethanolic sodium ethoxide. Accordingly, reactions were carried out with potassium t-butoxide in t-butyl alcohol and the rate constants were divided by the t-butoxide : ethoxide ratio for the sulphone phenyl ether (1; Z = OPh).

In some substrates, the leaving group is itself an activating group, and elimination of sulphinate rather than of the intended leaving group occurred. This was true of the sulphones [1; Z = CN, Ph_3P^+, or $P(O)(OEt)_2$]. In these cases, the carbanion formed in the smaller concentration initiates the reaction. Accordingly, the phenylsulphonyl activating group was replaced by either a cyano or benzoyl group and the rate constant was multiplied by the activation ratio in the phenoxy series.[25]

For the sulphoxide sulphone (1; Z = SOPh) the reaction was followed spectroscopically at 250 nm (appearance of vinyl sulphone) but formation of the alkene was accompanied by a rapid appearance and disappearance of a species absorbing at 325 nm. We suspect that this species is the sulphenate ion expelled from the sulphonyl carbanion; its characterisation will be reported in a later paper.

A possible difficulty in measuring elimination rates of nucleophilic leaving groups, especially phenylthio, was expected because of re-addition. Elimination in the sulphone sulphide (1; Z = SPh) was, therefore, carried out in the presence of an equivalent of toluene-α-thiol. No change in the rate constant was detected.

RESULTS AND DISCUSSION

Those results in Table 1 which showed $k_{H/D} = 1.0 \pm 0.1$, or showed hydrogen–deuterium exchange at C_β to occur more rapidly than elimination, are assigned the $(E_1cB)_R$ mechanism. A considerable number of those sulphones examined showed substantial primary deuterium isotope effects or did not undergo hydrogen–deuterium exchange at C_β more rapidly than elimination. The reactivity of these substrates is not directly related to leaving group ability and they are discussed in an accompanying paper.[22] Results for some familiar leaving groups are, however, included in Table 1 for comparison.

Although the rate constants obtained give a broad idea of the ease with which the C–Z bond is cleaved, these rate constants include the equilibrium constant for dissociation of the substrate in the particular solvent–base system. This constant varies with the leaving group by virtue of the differential polar effect of different leaving groups. It is not possible to obtain pK_a data for sulphones in the medium used, because they are insufficiently acidic. Instead, the effect of the leaving group on the *rate* of ionisation has been estimated, where possible, from a Taft plot constructed [40] from rates of detritiation of model β-substituted sulphones under the same conditions. Division of k_{obs} values by calculated $k_{ionisation}$ values then gives values of k_2/k_{-1}. This function is an index of leaving group ability (leaving group rank), if the assumption is made that the differential polar effects of the leaving groups on k_{-1} are small by comparison with those on k_2. Values of k_{-1} are very large for sulphones [38] and we consider that the differential effect of the leaving group on k_{-1} is likely to be correspondingly small.

The substrates studied may be divided broadly into three categories on the basis of k_{obs} values: (i) substrates with powerfully inductive leaving groups [$\sigma^*(CH_2Z)$ *ca.* 2] for which elimination occurs by the reversible mechanism. This category is typified by the 'onium substituents. In these cases, the ionisation rate k_1 is fractionated by the k_2/k^-_1 ratio ($\ll$1) but because the ionisation rate of sulphones is so very sensitive to polar

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[40] P. J. Thomas, and C. J. M. Stirling, following paper (Part 31).

effects,[40] k_1 is very large when $\sigma^*(CH_2Z)$ is large. This effect gives the largest k_{obs} values for 'onium salts notwithstanding fractionation of the ionisation rate constant, and substrates of this type have been studied in more detail by using buffer systems.[41] (ii) Next, in order of reactivity, are substrates with moderately inductive leaving groups [$\sigma^*(CH_2Z) = 0.8$—1.4]. This group is typified by the familiar leaving groups Z = OTs, I, Cl, and Br which have been shown not to react by the $(E_1cB)_R$ mechanism. For groups such as OTs, OAc, and F (but not I) comparison of elimination and ionisation rates shows[22] them probably to eliminate *via* the $(E_1cB)_I$ mechanism and for these groups k_2 is high and $> k_{-1}$. In these cases, relative magnitudes of k_2 (≡ leaving group ability) are not calculable but the conclusion can be drawn that as, for example, $k_1(^+NMe_3) > k_1(OTs)$,[40] then probably $K(^+NMe_3) > K(OTs)$ and $k_{-1}(^+NMe_3) < k_{-1}(OTs)$. If these assumptions hold, then $k_2(^+NMe_3) < k_2(OTs)$ because the $(E_1cB)_I$ mechanism is followed for OTs and not for $^+NMe_3$. The conclusion thus follows that in elimination from a carbanion, OTs is a superior leaving group to $^+NMe_3$. This follows previous experience in, for example, the phenethyl series,[42,43] but the same conclusion probably holds for acetoxy. For acetoxy the k_{obs} value is quite modest because of the modest polar effect on the rate-determining ionisation which this leaving group occasions.

Our results for the acetoxy leaving group are directly in accord with those obtained by Fedor[23] for acetoxyketones.

(iii) The third category embraces the remainder of the leaving groups which have the lower k_{obs} values, and the reversible $(E_1cB)_R$ mechanism. The range of $\sigma^*(CH_2Z)$ values is wide and in this category it is clear that k_{obs} values are low because k_2 is low, a feature which also imposes the reversible mechanism. Notable examples are $PhSO_2$ [$\sigma^*(CH_2SO_2Ph) = 1.32$][44] and CN [$\sigma^*(CH_2CN) = 1.3$],[45] in which the k_1 and hence presumably K values are substantial and similar to values for OTs. Expulsion of the leaving group is, however, difficult.

For the PhO, PhS, and $PhSO_2$ leaving groups studied in the sulphone series the reversible mechanism operates but the same leaving groups in the ketone series (G = PhCO or MeCO) give much higher k_{obs} values and the $(E_1cB)_I$ or E_2 mechanisms are followed (Table 3).

The higher k_{obs} values are due to two factors: (i) the intrinsically higher rate of ionisation of ketones than sulphones for Z groups with $\sigma^*(CH_2Z) < 1.05$;[40] (ii) the fact that irreversible (or E_2) mechanisms give inherently higher k_{obs} values because in the case of the $(E_1cB)_R$ mechanism, $k_{obs} = k_1k_2/k_{-1}[BH]$ and $k_2/k_{-1}[BH] \ll 1$. Ketone-activated eliminations have an intrinsically greater tendency to show the irreversible mechanism because the reprotonation rate for ketones is less than that for sulphones with the same pK_a. Only, therefore, when the leaving group is 'poor,' *i.e.* k_2 is small, does $k_{-1}[BH]$ exceed k_2 and the reversible mechanism operate. This mechanism has been demonstrated for ketones[31] when OMe is the leaving group, and comparison of eliminations with different activating groups will be the subject of subsequent publications.

TABLE 3

Comparison of elimination rates and mechanisms in sulphones and ketones ($G[CH_2]_2Z$)

Z	G	k_{obs} [a,b]	Mechanism [c]
OPh	$PhSO_2$	0.35	R
OPh	MeCO	31.5	I [c]
SPh	$PhSO_2$	0.021	R
SPh	MeCO	29.4	I or E_2
SO_2Ph	$PhSO_2$	1.05	R
SO_2Ph	MeCO	620	I [c]

[a] Reactions in ethanolic sodium ethoxide at 25 °C. [b] Units $l\,mol^{-1}\,s^{-1}$. [c] R and I refer to (E_1cB) mechanisms. [d] See ref. 22 for assignment. This mechanism was previously assigned incorrectly (see ref. 26).

Before correlations with specific molecular parameters are considered, some general comparisons with previous observations are appropriate.

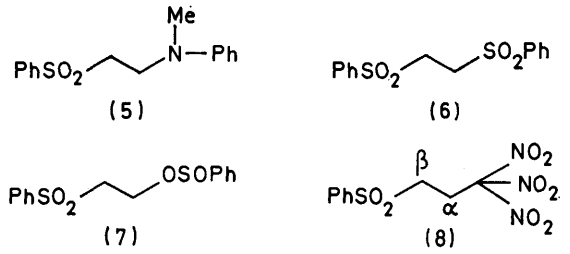
The outstandingly high reactivity of the 'onium salts is paralleled by the observation of rapid elimination reactions of cyano-activated phosphonium salts[46] with bases. Also, the rapid reactions of allylic arsonium salts with cyanide ion to give arsines[47,48] are readily interpreted as prototropy–addition–elimination sequences.

The very poor leaving group ability of cyano is striking. Rappoport and his colleagues[49,50] have made detailed studies of rapid 1,2-eliminations involving expulsion of cyanide ion, but the substrates used have possessed several activating groups and reactions have been carried out in aprotic media. Elimination of cyanide ion from 1,2-dinitriles has previously been shown[51] to be very slow in protic solvents but occurs readily in solutions of bases in hexamethylphosphoramide. Rappoport[52] has commented upon the substantially lower leaving ability of cyanide with respect to 2,2,2-trifluoroethoxide in activated eliminations, and

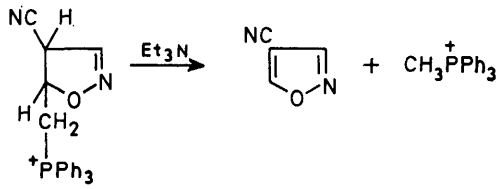
[41] K. N. Barlow, D. R. Marshall, and C. J. M. Stirling, accompanying paper (Part 33).
[42] W. H. Saunders, D. G. Bushman, and A. R. Cockerill, *J. Amer. Chem. Soc.*, 1968, **90**, 1775.
[43] C. H. De Puy and C. A. Bishop, *J. Amer. Chem. Soc.*, 1960, **82**, 2535.
[44] The value is derived from interpolation on the σ^* plot for dissociation constants of acetic acids (A. Chambers and C. J. M. Stirling, *J. Chem. Soc.*, 1965, 4558).
[45] R. W. Taft in 'Steric Effects in Organic Chemistry,' ed. M. S. Newman, Wiley, New York, 1956, ch. 13.
[46] W. B. Farnham and K. Mislow, *J.C.S. Chem. Comm.*, 1972, 469.
[47] L. Horner and W. Hofer, *Tetrahedron Letters*, 1966, 3321.
[48] J. J. Brophy and M. J. Gallagher, *Austral. J. Chem.*, 1969, **22**, 1405.
[49] Z. Rappoport and E. Shohamy, *J. Chem. Soc.* (*B*), 1971, 2060.
[50] Z. Rappoport, M. Albeck, and S. Hoz, *J.C.S. Perkin II*, 1972, 1248.
[51] R. Seux, G. Morel, and A. Foucaud, *Tetrahedron Letters*, 1972, 1003.
[52] M. Albeck, S. Hoz, and Z. Rappoport, *J.C.S. Perkin II*, 1975, 628.

another carbon-linked leaving group in the present series is also very feebly reactive. Reversal of the Michael reaction involving elimination of a carbon-linked leaving group activated (usually) by a carbonyl group is often alleged to occur readily. Examination of the conditions required, however, shows that these are severe.[53]

The very poor leaving group ability of carbon-linked groups is striking and we are currently examining a wider range of such groups where the derived ion has low proton basicity.[54] In this connection, a particularly suitable example (8) $\{pK_a[HC(NO_2)_3] = 0\}$ eliminates



nitrite ion with the proton being removed from the unactivated α-position. The preference for the expulsion of nitrite rather than of $^-C(NO_2)_3$ in such a situation bears further testimony to the difficulty of C–C bond cleavage in this type of reaction. The difficult reversal of the Michael reaction is referred to above. Conditions are extremely severe and these results qualitatively reinforce the present measurements. On the other hand, elimination of a phosphonium ylide occurs[55] under remarkably mild conditions (Scheme 2). Formation of an aromatic heterocycle may play a role here but C–Z bond cleavage is usually low in this type of reaction (above).



SCHEME 2

Hydroxy and dimethylamino are also extremely poor leaving groups and in the present work only an approximate upper limit can be set for their reactivity. In the case of hydroxy, the sulphonyl group is very powerfully inductive, raising the dissociation of the hydroxy-group to a level at which it is probably largely ionised[56] in the reaction medium. This would reduce leaving group ability relative to OMe by a factor of 10^2—10^3. Elimination of hydroxy activated by a fluorenyl group[57] occurs quite readily. Fluorenyl is poorly inductive but powerfully stabilises a carbanion, so that in this case elimination is activated but the proportion of ionised (inert) hydroxy-group is much less. Hydroxy β to a phosphonium group is also expelled[58] under basic conditions. This is the opposite situation: the activating group is very powerful[25] and highly inductive. Because of powerful activation, elimination proceeds notwithstanding the fact that the hydroxy-group is largely ionised. The very large difference in reactivity (factor of 1.6×10^5) between 4-hydroxypentan-2-one and its acetate towards elimination in aqueous sodium hydroxide has been pointed out.[23] The leaving group comparison is exaggerated because the former substrate probably eliminates by the $(E_1cB)_R$ mechanism whereas the mechanism for the acetate has been shown to be $(E_1cB)_I$.

The poor reactivity of the dimethylamino-sulphone is in contrast with results[59] obtained earlier which demonstrated elimination of secondary amines from β-dialkylamino-sulphones in ethanolic solutions of triethylamine. We interpret this apparent gross difference in reactivity as involving protonation of the amino-sulphone followed by elimination of the resulting (excellent) leaving group under the conditions described in a subsequent paper.[41] In agreement with this interpretation, the amino-sulphone (5) is stable both in ethanolic triethylamine and in ethanolic ethoxide solution. The amino-group is too feebly basic to undergo significant protonation in ethanolic triethylamine and, in the absence of a good leaving group, elimination does not occur.

Comparison of our results, so far as possible, with the Bartsch–Bunnett indices[16] gives the same qualitative order of leaving group ability, provided that it is borne in mind that in our work chloride, fluoride, tosylate, and acetate leaving groups have irreversible mechanisms. With those leaving groups that are susceptible to accurate ranking through the reversible mechanism, our order is PhO > SPh > SO_2Ph, while Bartsch and Bunnett's (concerted) order is SO_2Ph > OPh > SPh. The recent discovery[19] that $^-N(SO_2Ar)_2$ is readily eliminated in unactivated systems is striking in view of our present results with the monosulphonamide (Table 1).

Correlation of Leaving Group Abilities in Sulphone-activated Elimination.—We have examined a number of simple single parameter comparisons.

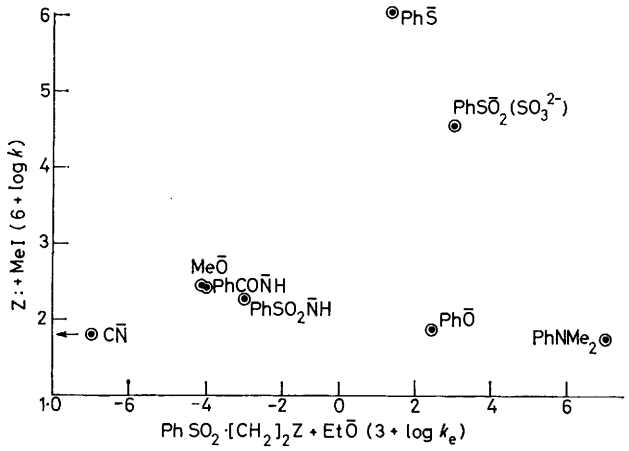
(i) p*K* *of* ZH. This criterion is often implied in over-simple discussions of leaving group ability. p*K* Data (in water) are in Table 1 and show no correlation between the pK_a of the conjugate acid of leaving group and k_{obs} or the leaving group rank, log k_{obs}/k_1. Previous experience of leaving group ability has been restricted to what must be regarded in present terms as only the most reactive groups, and within the narrow band the order

[53] C. K. Ingold and W. J. Powell, *J. Chem. Soc.*, 1921, **119**, 1976; C. K. Ingold and E. A. Perren, *J. Chem. Soc.*, 1922, **121**, 1414.
[54] D. R. Marshall, S. Monaghan, and C. J. M. Stirling, in preparation.
[55] P. dalla Croce and D. Pocar, *J.C.S. Perkin I*, 1976, 620.
[56] P. Ballinger and F. A. Long, *J. Amer. Chem. Soc.*, 1960, **82**, 795.
[57] R. A. More O'Ferrall and S. Slae, *J. Chem. Soc.* (*B*), 1970, 260.
[58] H. Christol, H. J. Cristau, and M. Soleiman, *Tetrahedron Letters*, 1975, 1381.
[59] R. Andrisano, A. S. Angeloni, and A. Fini, *Tetrahedron*, 1972, **28**, 2681.

$F < Cl < Br < I$ does hold *e.g.* for displacement reactions. Tosylate is reactive but has variable leaving group ability,[60] according to the reaction studied. A rectilinear Hammett plot is obtained [39] for eliminations in a series of 2-aryloxyethyl phenyl sulphones ($\rho = 1.5$), showing that for a specific type of group connected by a common atom there is a correlation between leaving group ability and pK of ZH over a narrow pK range.

For the present series of activated eliminations in which leaving group ability is accurately quantifiable over a much wider range, a striking failure of pK data to correlate leaving group ability is shown by the series CN, NMeTs, OPh, $^{+}NMe_3$. The conjugate acids of these groups all have pK values close to 10 and yet, as Table 1 shows, their k_{obs} values span a range of 10^{15}.

Carbon nucleophilicity of Z:. pK Data for the acids ZH reflect the proton basicity of Z:. More relevant to the ease of cleavage of the C–Z bond is the carbon



Plot of the nucleophilicity of the leaving group Z: towards methyl iodide against k_{obs} in a sulphone-activated β-elimination

nucleophilicity of the group Z. A measure of this nucleophilicity is obtained from the relative rate constants for nucleophilic displacement by Z: on methyl iodide.[61] The higher the relative value, the higher the carbon nucleophilicity and hence it seems reasonable to suppose that the lower should be the tendency for the C–Z bond to rupture in elimination. The Figure shows the relationship between log k_{obs} and log $k_{Nu(MeI)}$. Again no correlation exists. Phenylthio is striking in being a middle rank leaving group and yet is one of the most nucleophilic. Phenylseleno is both the highest ranked leaving group and extremely nucleophilic towards methyl iodide. Conversely, cyano is poorly nucleophilic towards methyl iodide but is one of the lowest ranked leaving groups.

An even more direct comparison to apply under this heading would be the reactivity of the group Z: in nucleophilic addition to electrophilic alkenes. Data on relative reactivities of different nucleophiles in this type of reaction are scarce, but the following order of reactivity has been found for additions to vinyl sulphones,[62] PhO : EtO : PhS = 1 : 378 : 37 800. The high reactivity of phenoxy as a leaving group is matched, in this series, by its low reactivity as a nucleophile but the reverse applies to PhS^-.

Against this background the reactivities of the sulphone (6) and the sulphinate ester (7) may be compared. These substrates have a common leaving group, the sulphinate ion, but this is attached through sulphur and oxygen respectively. In spite of the difference in linkage to the leaving group, the substrates have similar reactivities, and it was confirmed that conversion of sulphinate into sulphone does not occur under the reaction conditions.

The polar effect of Z. The tendency of the leaving group to accept the electron pair of the C–Z bond should contribute to leaving group ability. Values of $\sigma_I(Z)$ [63] give a measure of the polarity of the leaving group and if distortion of the C_α–Z bond is important, some correlation might be expected. None is found.

The correlation with ^{13}C chemical shifts of the carbon atoms in the substrates which bear the leaving group (Table 4) has also been tested. ^{13}C Chemical shifts are

TABLE 4

^{13}C N.m.r. data (p.p.m. from Me_4Si)

G	Z	α-^{13}C Chemical shift
$PhSO_2$	SPh	24.16
$PhSO_2$	SOPh	54.19
$PhSO_2$	SePh	17.93
$PhSO_2$	NPhAc	46.00
$PhSO_2$	OPh	61.34
$PhSO_2$	CN	11.95
NC	SO_2Ph	51.07
NC	OPh	62.50
NC	SOPh	50.16
NC	SOPh	30.15

sensitive to polar effects of substituent groups [64] but again no correlation with leaving group ability is found.

The C–Z *bond dissociation energy.* The dissociation energy of the C–Z bond must be a contributory factor in leaving group ability. Its importance will depend upon the degree of C–Z bond extension.[10] The evidence at present available [27,39,41] suggests that C–Z bond extension in the rate-determining step of $(E_1cB)_R$ reactions is small, so this factor is likely to be of low weight. In general, oxygen-connected leaving groups are superior to comparable sulphur-connected leaving groups, both in k_{obs} and in rank, *e.g.* OPh > SPh. D(C–O) is typically 80 kJ mol^{-1} larger than D(C–S) in the same type of connection,[65] suggesting that for this comparison the factor cannot be important.

[60] A. F. Cockerill, *Tetrahedron Letters*, 1969, 4913.
[61] R. G. Pearson, H. Sobel, and J. Songstad, *J. Amer. Chem. Soc.*, 1968, **90**, 319.
[62] P. De Maria and A. Fini, *J.C.S. Perkin II*, 1973, 1773.
[63] M. Charton, *J. Org. Chem.*, 1964, **29**, 1222.
[64] G. C. Levy, and G. L. Nelson, ' Carbon-13 Nuclear Magnetic Resonance for Organic Chemists,' Wiley, New York, 1972.
[65] V. I. Vedeneyev, L. V. Gurvich, V. N. Kondrat'yev, V. A. Medvedev, and Ye. L. Frankevich, ' Bond Energies Ionization Potentials and Electron Affinities,' Edward Arnold, London, 1966, Table 2, p. 56.

Carbon-linked leaving groups are ranked lowest and D(C–C), while variable, is usually similar to D(C–O). D(C–CN) at 430 kJ mol^{-1},[65] however, is exceptionally high, and this may account for the low leaving ability of this particular group.

These results present, so far as we are aware, the most comprehensive account of quantified leaving group abilities that is at present available. Comparisons with other systems are appropriate. We alluded earlier to the restricted range of leaving groups pertinent in nucleophilic substitution at sp^3-hybridized carbon and in unactivated alkene-forming eliminations. The only other reaction type with a comparable range of leaving groups is carbonyl-forming elimination, which embraces leaving groups from group 7 to group 4 of the periodic table. For this reaction type, very little work has been done on the isolation of the rate constants for the stage in which the leaving group separates. This is undoubtedly due to the mechanistic complexities of the reaction and the variability of the rate-determining steps. By comparison with the present results, it appears that, as expected, carbonyl-forming elimination in the system $^{-}$O–C–Z ⟶ C=O :Z is much faster than $^{-}$C–C–Z ⟶ C=C :Z. Thus hydrolysis of cyanohydrins occurs at readily observable rates, as does elimination of cyanide from diarylmethyl thiocyanates.[66] All alkene-forming eliminations with carbon-linked leaving groups, however, occur extremely slowly. The leaving group order for carbonyl groups, *i.e.* 7 > 6 > 5 > 4 also appears to apply. Much smaller differentials between leaving groups in carbonyl-forming eliminations are indicated by competitive isotope exchange experiments [13] which suggest the relative order of reactivities $PhCO_2 : MeO : NH_2 = 950 : 25 : 1$.

Some further information is available from an important correlation of reactions of nucleophiles with esters.[67] Ritchie's data give relative values for expulsion of groups from the tetrahedral intermediate of carbonyl substitution (carbonyl-forming elimination). His results correlate with ours in that relative to phenoxide, cyanide, and methoxide are poor leaving groups whereas fluoride, acetate, and (protonated) amino are good leaving groups.

Conclusions.—With the present information, it is not possible to delineate the properties of a good leaving group, but the following generalisations may be made.

(i) A positively charged leaving group departs rapidly even when the large effect on k_{obs} of the polar effect on ionisation is allowed for.

(ii) For uncharged groups, leaving group ability generally decreases from right to left across the periodic table. Carbon- and nitrogen-linked leaving groups are notably poor, irrespective of the proton basicity or carbon nucleophilicity of the ion produced by elimination.

Among the ranked leaving groups, *i.e.* those for which it is possible to apply ionisation corrections, dimethylsulphonium is notably better than trimethylammonium, in agreement with studies in poorly activated systems, *e.g.* phenethyl.[32] Surprisingly, phenoxy is better than phenylthio, notwithstanding that D(C–O) > D(C–S), but phenylseleno is the most reactive of all the ranked groups.

Perhaps the most surprising result is the rank of the $PhSO_2$ group. This is a powerfully inductive group and correction for its polar effect on ionisation rate depresses its rank even below that of PhS. The rank of the $PhSO_2$ group is hard to understand on the basis of its capability to accept the electron pair of the cleaved bond, the proton basicity or carbon nucleophilicity of the group, or the strength of the C–S bond, which is substantially stronger in sulphides than in sulphones.[68]

The term leaving group is casually employed in discussions of reactivity. It is often used without reference to the type of reaction involved and, even within a reaction type, without reference to mechanism. The possibility of comparisons being made of the ease of detachment of leaving groups is frequently not alluded to, but acquisition of information on the ease with which bonds to carbon and other atoms are broken in reactions is of the greatest importance to the understanding of molecular behaviour. It is also clear, however, that the applicability of such information may be restricted to specific reaction types.

Comparisons with other reactions may illuminate the general factors which control these reactions, and in future publications we shall present results of more detailed examination of leaving group abilities in which comparisons between closely related types of leaving group are drawn. Our present work shows that the problem is an extremely complex one, and that oversimplification of the term ' leaving group ability ' can produce confusion rather than enlightenment.

EXPERIMENTAL

Solids were recrystallised to constant m.p. (quoted in °C). Extraction was performed with dichloromethane unless otherwise stated, and extracts were dried over $MgSO_4$. Light petroleum had b.p. 40—60 °C. Ethanol was dried by the magnesium–iodine method. t-Butyl alcohol was refluxed over sodium and distilled.

Kinetics.—Sodium ethoxide solutions were prepared by dissolution of clean sodium in dry ethanol and were standardised against hydrochloric acid. Solutions of potassium t-butoxide in t-butyl alcohol were prepared and standardised similarly. Spectroscopic determinations of reaction rates were made using a Unicam SP 800A spectrophotometer fitted with a scale expander, and programme controller. Fast reactions were monitored using a Durrum–Gibson stopped flow spectrometer, the output of whose photomultiplier was connected *via* an analogue-digital converter to a Northern NS-600 Econ series multichannel analyser to a teletype producing punched tape data for computer processing. Substrate concentrations were

[66] A. Checcon, U. Miotti, U. Tonellato, and M. Padovan, *J. Chem. Soc.* (*B*), 1969, 1084.
[67] C. D. Ritchie, *J. Amer. Chem. Soc.*, 1975, **97**, 1170.
[68] W. K. Busfield, K. J. Ivin, H. Mackle, and P. A. G. O'Hare, *Trans. Faraday Soc.*, 1961, **57**, 1064.

typically 10^{-3}—10^{-4}M and base concentrations were generally tenfold greater. All solutions were adjusted to an ionic strength of 0.05M by addition of sodium perchlorate. Rapid reactions were followed by appearance of vinyl sulphone (λ 248 nm) or of leaving group as appropriate. Rate constants (Table 1) are means of 4—8 determinations in which initial concentrations of substrate and base were varied independently. Air was not excluded and the elimination reaction of 1-phenylsulphonyl-2-phenylthioethane in oxygen-saturated ethanol showed no rate effect.

For 2-cyanoethyltriphenylphosphonium bromide, a conductometric technique using a Wayne–Kerr Autobalance Universal Bridge B642 connected to an external recorder was used, with temperature control to within ±0.02 °C.

For compounds that eliminated very slowly rate constants were obtained by taking samples of a thermostatted reaction mixture and using quantitative g.l.c. to analyse the progress of the reaction with time (SE30 column at 201 °C).

Hydrogen–Deuterium Exchange Experiments.—In the general procedure employed, the substrate (2.5 mmol) in EtOD (3 ml) was treated with sodium ethoxide (1.25 mmol) in EtOD (1.5 ml). After the time specified (below) most of the solvent was removed *in vacuo* at 25 °C and the products were examined by ^{1}H n.m.r. spectroscopy.

Diethyl 2-p-*Tolylsulphonylethyl Phosphate.*—2-*p*-Tolylthioethanol (3.6 g, 20 mmol) in pyridine (10 ml) was treated with diethyl phosphorochloridate (20 mmol) added dropwise with stirring at 25 °C. After 12 h, the mixture was poured into saturated acidified brine and extraction gave the *sulphide ester* (5.71 g, 89%), b.p. 174° at 0.1 mmHg, n_D^{16} 1.5011 (Found: C, 51.1; H, 6.9. $C_{13}H_{21}O_4PS$ requires C, 51.3; H, 6.9%).

The sulphide ester (3.2 g, 10 mmol) in methanol (100 ml) was added to aqueous 30% hydrogen peroxide (20 ml) containing ammonium molybdate (0.3 g). The mixture was set aside for 12 h at 25 °C and extraction as before gave the *sulphone* (3.0 g, 84%), b.p. 179° at 10^{-3} mmHg, n_D^{20} 1.5005 (Found: C, 46.2; H, 6.3. $C_{13}H_{21}O_6PS$ requires C, 46.4; H, 6.3%).

The sulphone ester (1.68 g, 5 mmol) in ethanol (100 ml) was treated with ethanolic M-sodium ethoxide (50 ml, 50 mmol). After 30 min the mixture was extracted as before to give 2-ethoxyethyl *p*-tolyl sulphone (1.09 g, 95%), b.p. 141° at 0.25 mmHg, n_D^{19} 1.5221 (lit.,[26] b.p. 128° at 0.01 mmHg, n_D^{18} 1.5218).

The aqueous layer from extraction was adjusted to pH 7 and evaporated to dryness. The residue, in the minimum of hot water, was treated with *S*-benzylthiouronium chloride (3 g). On cooling, the solution deposited *S*-benzylthiouronium diethyl phosphate (1.42 g, 98%), m.p. 153.6° (lit.,[69] 153.2°).

No deuterium incorporation was observed in H–D exchange studies.

O-2-p-*Tolylsulphonylethyl Thiobenzoate.*—Dry hydrogen chloride was passed into a solution of 2-*p*-tolylsulphonylethanol [70,71] (2 g, 10 mmol) and benzonitrile (4.12 g, 40 mmol) in ether (100 ml) for 26 h. After 2 days, the resulting precipitate of the imino-ether hydrochloride was filtered off and suspended in ether (200 ml). The stirred suspension was saturated with hydrogen sulphide and aqueous M-sodium hydrogen sulphide (100 ml) was added. The mixture was stirred for 10 h under hydrogen sulphide and extraction with ether gave the *ester* (1.22 g, 92%), m.p. 96.7° (from toluene–petroleum) (Found: C, 60.0; H, 5.1. $C_{10}H_{16}O_3S$ requires C, 60.0; H, 5.0%).

The ester (1.6 g, 5 mmol) in t-butyl alcohol (75 ml) was treated with potassium t-butoxide in t-butyl alcohol (40 ml, 50 mmol). After 3.5 h at 30 °C, extraction gave a mixture of 2-t-butoxyethyl *p*-tolyl sulphone and 2-hydroxyethyl *p*-tolyl sulphone (78%), b.p. 130° at 0.1 mmHg, in the ratio 2 : 1 (^{1}H n.m.r.). Mixtures of ether and alcohol have previously been obtained from *p*-tolyl vinyl sulphone in reactions with potassium t-butoxide in t-butyl alcohol.[72]

Reactions were followed at 315 nm (disappearance of ester). A hydrogen–deuterium exchange experiment in Bu^{t}OD showed complete exchange at C_β in both starting material and product but none at C_α.

2-p-*Tolylsulphonylethyl Toluene*-p-*sulphinate.*—2-*p*-Tolylsulphonylethanol (5 g, 25 mmol) in anhydrous pyridine (15 ml) at −20 °C was treated with toluene-*p*-sulphinyl chloride [73,74] (5.3 g, 30 mmol) and the mixture was stirred until precipitation was complete. Aqueous M-hydrochloric acid (60 ml) at −20 °C was added with stirring and extraction was performed with dichloromethane at −20 °C. The extract was washed with ice-cold aqueous sodium hydrogen carbonate; evaporation gave the *sulphinate ester* (92%), m.p. 72° (from ethanol) (Found: C, 56.8; H, 5.3. $C_{16}H_{18}O_4S_2$ requires C, 56.8; H, 5.4%).

The ester (5.9 mmol) in ethanol (50 ml) was treated with sodium ethoxide (50 mmol) in ethanol (100 ml). After 1.5 h at 25 °C the mixture was poured into saturated brine and extracted. Evaporation of the extract gave 2-ethoxyethyl *p*-tolyl sulphone (88%), b.p. 138° at 0.2 mmHg, n_D^{19} 1.5218. The aqueous solution was acidified (H_2SO_4) and re-extracted. The residue from evaporation was refluxed for 4 h with an excess of 4-nitrobenzyl bromide and sodium carbonate. Extraction gave 4-nitrobenzyl *p*-tolyl sulphone (79%), m.p. 187.7° (lit.,[75] 185—189°).

A hydrogen–deuterium exchange experiment in EtOD showed complete exchange at C_β in both starting material and product but none at C_α.

Reactions were followed at 250 nm (appearance of *p*-tolylvinyl sulphone).

2-*Methoxyethyl Phenyl Sulphone.*—Phenyl vinyl sulphone (1.68 g, 10 mmol) in methanol (75 ml) was treated with methanolic sodium methoxide [from sodium (1.15 g, 50 mmol)] in methanol (75 ml). After 2 h at 20 °C extraction gave the *sulphone* (98%), b.p. 122—124° at 0.1 mmHg, n_D^{18} 1.5329 (lit.,[76] b.p. 125° at 0.1 mmHg, n_D^{17} 1.5332).

The ether (5 mmol) was kept with sodium ethoxide (50 mmol) in ethanol (150 ml) at 25 °C for 10 days. Extraction gave starting material and 2-ethoxyethyl phenyl sulphone (b.p. 128° at 0.1 mmHg, n_D^{22} 1.5204).

Methyl-(p-*tolyl*)-(2-p-*tolylethyl*)*sulphonium Fluorosulphate.*—*p*-Tolylthioethyl *p*-tolyl sulphone [77] (1.53 g, 5 mmol) in anhydrous dichloromethane was treated with methyl fluorosulphate (7.5 mmol) under nitrogen. The mixture was kept at 6 °C for 48 h and a dilute solution of methanol in ether was added. Evaporation gave the *salt* (63%),

[69] C. J. M. Stirling, *J. Chem. Soc.*, 1957, 3597.
[70] H. S. Schultz, H. B. Freyermuth, and S. R. Buc, *J. Org. Chem.*, 1963, **28**, 1140.
[71] J. Heyna and K. Karrenbauer, Ger. Pat., 944,607/1956.
[72] J. W. Batty, P. D. Howes, and C. J. M. Stirling, *J.C.S. Perkin I*, 1976, 1543.
[73] C. J. M. Stirling, *J. Chem. Soc.*, 1963, 5741.
[74] D. Barnard and E. J. Percy, *J. Chem. Soc.*, 1962, 1667.
[75] W. L. Troger and R. Nolte, *J. prakt. Chem.*, 1920, **101**, 136.
[76] E. J. Miller, Ph.D. Thesis, Belfast, 1966.
[77] W. Reppe, *Annalen*, 1956, **601**, 111.

m.p. 105.3° (decomp.) (from ethanol–ether) (Found: C, 62.8; H, 6.7. $C_{16}H_{20}O_2S_2$ requires C, 62.6; H, 6.5%).

The salt (1.05 g, 2.5 mmol) in ethanol (50 ml) was treated with triethylamine (25 mol); after 3 h at 25 °C under nitrogen, evaporation gave a residue which on extraction with pentane gave methyl *p*-tolyl sulphide (98%), b.p. 78° at 12 mmHg, n_D^{16} 1.5874 (lit.,[78] b.p. 74° at 10 mmHg, n_D^{20} 1.5863). The residue from extraction was extracted with chloroform to give *p*-tolyl vinyl sulphone (91%), m.p. and mixed m.p. 65.7° (lit.,[79] 65—66°).

Reactions were too rapid for measurement of kinetics in ethanolic sodium ethoxide ($t_{\frac{1}{2}} < 10$ ms) and triethylamine was used as base, with a correction factor of 2×10^5 being applied. [This factor is derived from comparison of elimination rates in Et_3N–EtOH and EtO^-–EtOH of (2-phenylsulphonylethyl)trimethylammonium iodide.]

Reactions were followed at 280 nm (appearance of methyl *p*-tolyl sulphide).

S-2-p-*Tolylsulphonylethyl Thiobenzoate*.—Potassium thiobenzoate (1.99 g, 12 mmol) in ethanol (75 ml) was added slowly with stirring and cooling to *p*-tolyl vinyl sulphone (2.0 g, 11 mmol) in ethanol (75 ml) containing acetic acid (20 mmol). After 2 h, the solution was evaporated and the residue was extracted with ether (3 × 100 ml). The extracts were washed with saturated aqueous sodium hydrogen carbonate; evaporation gave the *ester* (98%), m.p. 72.2° (from ethanol) (Found: C, 60.3; H, 5.2. $C_{16}H_{16}O_3S_2$ requires C, 60.0; H, 5.0%).

The ester (1.5 g, 4.7 mmol) was kept with sodium ethoxide (30 mmol) in ethanol (50 ml) at 25 °C for 2 h. The mixture was poured into acidified (H_2SO_4) brine; extraction gave a residue which on extraction with light petroleum gave ethyl benzoate (0.429 g, 62%), b.p. 86° at 12 mmHg, n_D^{17} 1.5021, and left a residue which was redissolved in chloroform. Addition of light petroleum to the chloroform solution gave *bis*-2-p-*tolylsulphonylethyl sulphide* (0.36 g, 40%), m.p. 160.6° [raised to 163.7° (from ethanol)] (Found: C, 54.4; H, 5.5. $C_{18}H_{22}O_4S_3$ requires C, 54.3; H, 5.5%), τ 1.7—2.5 (m), 6.7 (t), 7.1 (t), and 7.5 (s) (4 : 2 : 2 : 3).

The mother liquors from the above precipitation were evaporated to give crude 2-*p*-tolylsulphonylethanethiol (0.62 g), m.p. 69.5°, which was characterised by treatment with a 10% excess of benzyl chloride and sodium hydroxide in ethanol (12 ml). The mixture was kept at 80 °C for 1 h, and the residue from evaporation was extracted with ether to give benzyl 2-*p*-tolylsulphonyl ethyl sulphide (43%), m.p. 80.9°, alone or mixed with an authentic specimen prepared by addition of toluene-α-thiol to *p*-tolyl vinyl sulphone (98%), m.p. 81.0° (from methanol) (Found: C, 62.8; H, 5.8. $C_{16}H_{15}O_2S_2$ requires C, 62.7; H, 5.7%).

Treatment of the ester with potassium t-butoxide in t-butyl alcohol as for *O*-2-*p*-tolylsulphonylethyl thiobenzoate gave a mixture (73%) of alcohol and ether in the ratio 2 : 1.

Reactions (Bu^tOK in Bu^tOH) were followed at 315 nm (appearance of $PhCOS^-$).

1,2-*Bis*-p-*Tolylsulphonylethane*.—Preparation and analysis of products from reactions with ethanolic sodium ethoxide have been described previously.[27] 1,2-*Bisphenylsulphonylethane* was prepared as above from benzenethiol and dibromoethane; yield 98%, m.p. 201° (from ethanol) (Found: C, 54.2; H, 4.6. $C_{14}H_{14}O_4S_2$ requires C, 54.2; H, 4.5%). The tetradeuterio-compound was prepared by treatment of the isotopically normal compound (0.338 g) with an equimolar quantity of sodium benzenesulphinate in dimethyl sulphoxide (10 ml) and deuterium oxide (3 ml) at reflux for 24 h. Extraction and evaporation gave the sulphone, m.p. 201°, alone or mixed with isotopically normal material.

A hydrogen–deuterium exchange experiment with isotopically normal sulphone in MeOD showed quantitative exchange in 1 h.

Reactions were followed at 280 nm (appearance of benzenesulphinate ion).

Phenyl 2-p-Tolylsulphonylethyl Sulphoxide.—2-Phenylthioethyl *p*-tolyl sulphone [77] (2.5 g, 8.2 mmol) in methanol (120 ml) was added slowly to sodium periodate [80] (2.0 g, 9.3 mmol) in water (25 ml) at 0 °C. The mixture was stirred at 0 °C for 15 h and was then filtered. The residue was washed with dichloromethane; extraction of the combined filtrates and washings gave the *sulphoxide* (77%), m.p. 132.6° (from methanol) (Found: C, 58.4; H, 5.2. $C_{15}H_{16}O_3S_2$ requires C, 58.4; H, 5.3%).

Phenyl 2-phenylsulphonylethyl sulphoxide was prepared (79%) as above from phenyl 2-phenylthioethyl sulphone. It had m.p. 121.3° (from methanol) (Found: C, 57.2; H, 4.8. $C_{14}H_{14}O_3S_2$ requires C, 57.1; H, 4.7%).

The sulphoxide (1.54 g, 5 mmol) in ethanol (75 ml) was kept with sodium ethoxide (50 mmol) in ethanol (100 ml) at 20 °C for 1 h. Extraction as before gave 2-ethoxyethyl *p*-tolyl sulphone (79%), b.p. 133° at 0.15 mmHg, n_D^{21} 1.5213.

In an experiment as above but under nitrogen, methyl iodide (200 mmol) was added; work-up as before gave a residue which g.l.c. showed to contain 2-ethoxyethyl *p*-tolyl sulphone and methyl benzenesulphinate, but not methyl phenyl sulphoxide, methyl phenyl sulphone, or 2-phenylthioethyl *p*-tolyl sulphide.

Hydrogen–deuterium exchange experiments showed quantitative exchange adjacent to the sulphonyl group of the sulphone sulphoxide in 2 h.

Reactions were followed at 250 nm (formation of vinyl sulphone) but appearance of the absorption maximum at 250 nm was accompanied by rapid appearance (65.5 l mol^{-1} s^{-1}) and disappearance of absorption at 325 nm. An investigation of this phenomenon will be the subject of a later paper.

1-*Phenylsulphonyl*-2-*phenylthioethane*.—Preparation, product analysis, and kinetics have been reported previously.[29,81]

Hydrogen–deuterium exchange experiments showed complete exchange adjacent to the sulphonyl group in 1.5 h.

1-*Phenylsulphonyl*-2-*phenylthio*[1,1-$^2H_2$]*ethane*.—1-Chloro-2-phenylsulphonyl[2,2-$^2H_2$]ethane [22] (15 mmol) was stirred with triethylamine (6.3 g) in ethanol. Extraction gave phenyl [1-^{2}H]vinyl sulphone, m.p. and mixed m.p. (with isotopically normal sulphone) 62°.

Benzenethiol (30 mmol) and triethylamine (0.5 ml) were stirred with deuterium oxide (4 ml) for 12 h. Extraction and repetition of the exchange gave PhSD, b.p. 48° at 12 mmHg, n_D^{20} 1.5891. ^{1}H N.m.r. showed complete exchange.

Triethylamine (0.5 ml) was added to the deuteriated vinyl sulphone (10 mmol) and benzene[^{2}H]thiol (10 mmol) in benzene (40 ml). After 1 h, evaporation gave the sulphide

[78] 'Handbook of Chemistry and Physics,' 52nd edn., The Chemical Rubber Co., Cleveland, Ohio, 1971.

[79] L. E. Smith and H. R. Davies, *J. Org. Chem.*, 1950, **15**, 824.

[80] C. R. Johnson and J. E. Keiser, *Org. Synth.*, 1966, **46**, 78.

[81] R. P. Redman, Ph.D. Thesis, London, 1970.

(90%), m.p. and mixed m.p. (with an isotopically normal specimen) 70°.

1-*Phenylsulphonyl*-2-*phenylselenoethane*.—Diphenyl diselenide (8 mmol) in absolute ethanol (50 ml) was treated with sodium borohydride (16 mmol). After 0.5 h, triethylamine hydrochloride (20 mmol) and phenyl vinyl sulphone (16 mmol) in ethanol (90 ml) were added. After a further 0.5 h at 25 °C, extraction gave the *sulphone selenide* (96%), m.p. 64.7° (from methanol) (Found: C, 51.7; H, 4.3. $C_{14}H_{14}O_2SSe$ requires C, 51.7; H, 4.7%).

The selenide (5 mmol) was kept with sodium ethoxide (50 mmol) in ethanol (120 ml) at 25 °C for 2 h, and the mixture was poured into brine. Extraction gave 2-ethoxyethyl phenyl sulphone [26] (96%), b.p. 140° at 0.35 mmHg, n_D^{23} 1.5200. Neutralisation (HCl) of the aqueous layer, addition of hydrogen peroxide (15 ml; 100 vol.) and re-extraction gave diphenyl diselenide (79%), m.p. and mixed m.p. 63° (lit.,[78] 63—64°).

Hydrogen–deuterium exchange studies (6 h at 25 °C) showed complete exchange at C_β in both starting material and product but none at C_α.

1-Phenylsulphonyl-2-phenylseleno[1,1-$^2H_2$]ethane was recovered from the above reaction and purified [m.p. and mixed m.p. (with isotopically normal sulphone) 65°]. ^1H N.m.r. showed complete exchange at C_β.

Reactions were followed at 280 nm (appearance of $PhSe^-$).

Dimethylphenyl-(2-*phenylsulphonylethyl*)*ammonium Iodide*. Preparation and product analysis are reported elsewhere.[41]

Dimethylphenyl-(2-*phenylsulphonyl*[2,2-$^2H_2$]*ethyl*)*ammonium Iodide*.—This was prepared by treatment of isotopically normal *N*-methyl-*N*-2-phenylsulphonylethylaniline (10 mmol) in dioxan (3.5 ml) with sodium deuteroxide (1 mmol) in deuterium oxide (7 ml) at reflux for 56 h. Extraction and evaporation gave the amine, m.p. 71° alone or mixed with isotopically normal material. This amine was converted into the ammonium salt with methyl iodide as described elsewhere: [41] m.p. 145° alone or mixed with isotopically normal salt. ^1H N.m.r. showed complete exchange adjacent to the sulphonyl group.

N-*Methyl*-N-2-p-*tolylsulphonylethyltoluene*-p-*sulphonamide*.—*p*-Tolyl vinyl sulphone (20 mmol) in methanol (100 ml) was treated with an excess of aqueous 25% w/v methylamine. After 2 h at 25 °C, extraction gave crude 2-methylaminoethyl *p*-tolyl sulphone, which was kept with toluene-*p*-sulphonyl chloride (20 mmol) in ethanol (100 ml) at 80 °C for 24 h. Extraction gave the *sulphone sulphonamide* (42%), m.p. 114.4° (from methanol) (Found: C, 55.7; H, 5.9; N, 3.8. $C_{17}H_{21}NO_4S_2$ requires C, 55.6; H, 5.7; N, 3.8%).

The sulphonamide (5 mmol) was kept with sodium ethoxide (50 mmol) in ethanol (150 ml) at 20 °C for 4 days, and the mixture was poured into brine. Extraction gave 2-ethoxyethyl *p*-tolyl sulphone (94%), b.p. 138° at 0.15 mmHg, n_D^{19} 1.5217. Neutralisation (HCl) of the aqueous layers and re-extraction gave *N*-methyltoluene-*p*-sulphonamide (80%), m.p. and mixed m.p. 74.6° (lit.,[78] 74—75°).

Hydrogen–deuterium exchange studies (2 days at 25 °C) showed complete exchange adjacent to the sulphonyl group.

N-*Methyl*-N-2-*phenylsulphonylethylacetamide*.— Phenyl vinyl sulphone (20 mmol) in methanol (100 ml) was treated with an excess of aqueous 25% w/v methylamine. After 3 h at 25 °C, extraction gave crude 2-methylaminoethyl phenyl sulphone which was refluxed with acetic anhydride (30 mmol) in dry toluene (40 ml) for 2 h. Extraction gave the *sulphone amide* (97%), m.p. 53.1° (from di-isopropyl ether) (Found: C, 54.8; H, 6.1; N, 5.9. $C_{11}H_{15}NO_3S$ requires C, 54.8; H, 6.2; N, 5.8%). The amide (5 mmol) was kept with sodium ethoxide (50 mmol) in ethanol (150 ml) for 9 days at 20 °C. Extraction gave 2-ethoxyethyl phenyl sulphone (85%), b.p. 140—142° at 0.3 mmHg, n_D^{23} 1.5200.

Hydrogen–deuterium exchange studies (4 days at 25 °C) showed complete deuterium incorporation in the methylene group adjacent to the sulphonyl group.

NN-*Dimethyl*-N-2-*phenylsulphonylethylamine*.—The preparation is reported elsewhere.[41]

The amine (5 mmol) was refluxed with sodium ethoxide (50 mmol) for 2 days. Extraction gave unchanged amine (91%). The amine (10 mmol) in ethanol (75 ml) was treated with piperidine (50 mmol) in ethanol (50 ml). After 12 h, the mixture was extracted to give 2-piperidinoethyl phenyl sulphone (92%), b.p. 161° at 0.1 mmHg (lit.,[82] 163° at 0.15 mmHg).

The amine (10 mmol) in ethanol (75 ml) was treated with sodium ethoxide (10 mmol) and piperidine (50 mmol) in ethanol (75 ml). After 12 h extraction gave unchanged amine (96%).

2-(*N*-Methylanilino)ethyl phenyl sulphone [41] (5 mmol) in ethanol (75 ml) was treated with piperidine (50 mmol) in ethanol (50 ml). After 1 h, evaporation gave unchanged amine (99%).

2-*Cyanoethyltriphenylphosphonium Bromide*.—1-Bromo-2-cyanoethane (22 mmol) was treated with triphenylphosphine (22 mmol) in 1,4-dioxan (35 ml) containing 45% hydrobromic acid (4 ml). After 8 h at 20 °C, dropwise addition to dry ether gave the *cyanophosphonium salt* (91%), decomposing at 128° (from ethanol–ether) (Found: C, 63.9; H, 5.0; N, 3.7. $C_{21}H_{19}BrNP$ requires C, 63.6; H, 4.8; N, 3.5%).

The phosphonium salt (15 mmol) was kept with sodium ethoxide (150 mmol) in ethanol (100 ml) for 0.5 h at 20 °C. Extraction gave 3-ethoxypropiononitrile (89%), b.p. 60° at 11 mmHg, n_D^{20} 1.4068 (lit.,[78] b.p. 65° at 15 mmHg, n_D^{20} 1.4068).

Hydrogen–deuterium exchange studies (5 min at 25 °C) showed complete exchange adjacent to the cyano-group.

Diethyl 2-*Benzoylethylphosphonate*.—3-Chloropropiophenone (10 mmol) was boiled under reflux with triethyl phosphite (20 mmol) in bis-(2-methoxyethyl) ether (25 ml) for 15 h under nitrogen. The mixture was evaporated; distillation of the residue gave the ester (73%), b.p. 172° at 0.1 mmHg, n_D^{19} 1.5078 (lit.,[83] b.p. 162° at 0.04 mmHg, n_D^{20} 1.5060).

The ester (5 mmol) was kept with sodium ethoxide (50 mmol) in ethanol (175 ml) for 3 h at 25 °C. Extraction as before gave 1-benzoyl-2-ethoxyethane (93%), b.p. 121° at 12 mmHg, n_D^{20} 1.5392 (lit.,[84] b.p. 135° at 18 mmHg).

Succinonitrile.—The dinitrile [m.p. 57° (from ether)] (25 mmol) was kept with sodium ethoxide (100 mmol) in ethanol (50 ml) at 25 °C for 8 days. Extraction gave quantitatively the starting dinitrile. When the mixture was heated under reflux and when potassium t-butoxide in t-butyl alcohol was used, g.l.c. showed that no acrylonitrile or β-alkoxy-nitrile was formed.

[82] S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc.* (*B*), 1967, 343.

[83] P. Friedlander, *Annalen*, 1907, **351**, 402.

[84] E. P. Kohler, *J. Amer. Chem. Soc.*, 1920, **42**, 388.

In hydrogen–deuterium exchange studies, perdeuteriation was complete after 13 h at 25 °C.

3-Benzoylpropiononitrile.—3-Chloropropiophenone (10 mmol) was stirred with sodium cyanide (12 mmol) in 4 : 1 water–methanol (60 ml) at 25 °C. After 3 h, extraction gave the nitrile (94%), m.p. 75.7° (from di-isopropyl ether) (lit.,[85] 76°).

The nitrile (5 mmol) was kept with sodium ethoxide (10 mmol) in ethanol (100 ml) for 7 days at 25 °C. Extraction gave quantitatively the starting material. When the mixture was heated decomposition occurred and no ethoxy-ketone was detected (g.l.c.).

2-Methyl-2-nitrobutyl p-Tolyl Sulphone.—*p*-Tolyl vinyl sulphone (3.64 g, 20 mmol) in methanol (50 ml) was added with stirring to 2-nitropropane (20 mmol) and potassium hydroxide (20 mmol) in methanol (100 ml). The mixture was kept for 1 h at 60 °C, neutralised (H_2SO_4), and extracted to give the *nitro-sulphone* (4.05 g, 75%), m.p. 101.7° (from di-isopropyl ether) (Found: C, 53.1; H, 6.3; N, 5.1. $C_{12}H_{17}NO_4S$ requires C, 53.1; H, 6.3; N, 5.2%).

The sulphone (5 mmol) was kept at 80 °C for 84 h with sodium ethoxide (50 mmol) in ethanol (175 ml). Extraction gave starting material (98%), m.p. and mixed m.p. 101.5°.

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