Elimination and Addition Reactions. Part 41.[1,2] Nucleophilic Eliminative Fission of Cyclopropanes: the Coiled Spring Effect of Ring Strain on Nucleofugality and its Evaluation

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Rates have been measured of sulphonyl-activated eliminative ring fissions of a series of six cyclopropanes in which the leaving group is stabilised by alkoxycarbonyl, cyano, or sulphonyl groups. The measurements allow assignment of ranks (nucleofugalities) to carbon leaving groups in systems in which the connection to the leaving group is strained by incorporation in a cyclopropane ring. The values obtained are compared with those obtained for a unstrained (acyclic) analogues. Rank enhancements of about 9 (log) units are obtained; these enhancements suggest that free energies of activation for leaving-group expulsion are reduced by about 53 kJ mol^{-1}, or about 46% of the excess of enthalpy of the strained ring, notwithstanding the small degree of ring fission in the transition structure. The effect of phenyl substitution at the leaving group suggests that cleavage of the ring is very little advanced in the transition structure, although this is variable with the nature of the leaving-group stabilisation. This is the first direct determination of the effect of strain on nucleofugality.

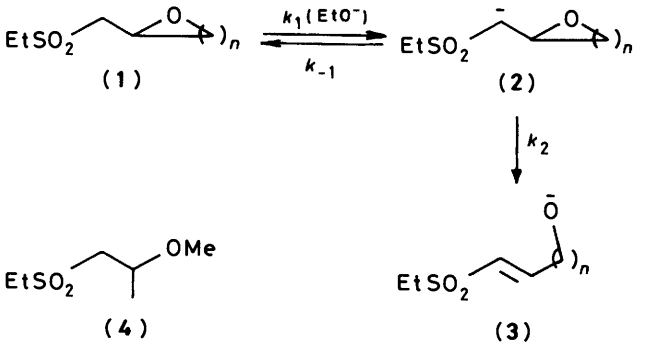
During the past decade, a number of groups have been concerned with the important but difficult question of evaluating the nucleofugality of functional groups.[3–5] Elimination is undoubtedly the reaction of choice for such an investigation; the range of leaving groups is exceptionally wide, in contrast, for example, with S_N2 processes, and for alkene-forming elimination from carbanions rate-determining loss of leaving group can readily be identified.[3]

An aspect of elimination reactions and their leaving groups that has received little attention in the past is the role of strain in assisting the cleavage of the bond to the leaving group. Much consideration has been given to the role of strain in determining the regiospecificity of alkene-forming eliminations in simple halides and 'onium salts, but strain differentials were not quantified, reactivity differences were small, and from the controversial discussion of such reactions no very clear generalisations have emerged.[6]

Some time ago we intiated the first work on the effect of strain in elimination reactions of known mechanism for which the nucleofugality of the leaving group has been determined.[7] The system employed is shown in Scheme 1. The overall reaction (**1**) ⟶ (**2**) ⟶ (**3**) is an eliminative ring fission.[8] The objective was to compare reactivities of substrates (**1**) with that of an unstrained comparator (**4**). Clearly, the process with rate constant k_2 was required to be rate-determining [$(E_1cB)_R$] if information relating to strain effects on nucleofugality was to be obtained. The observed rate constant for much the most strained substrate, the epoxide (**1a**), showed a primary kinetic deuterium isotope effect of 2.5; thus an E_2 or possibly $(E_1cB)_I$ but certainly not an $(E_1cB)_R$ mechanism was operating. The direct comparison with (**1**) was thus obviated. The (**1a**):(**4**) rate ratio of 2.46 × 10^6:1 demonstrated, however, the considerable potential for acceleration in these systems.

Carbon Leaving Groups in Strain-accelerated Eliminations.— The results with oxacycloalkanes pointed to the need to select an even lower ranked leaving group[3] than alkoxy for evaluation of strain effects. A carbon leaving group was chosen. Our earlier work[9–11] had shown that leaving groups such as cyano could not be expelled in alkene-forming elimination in protic solvents, and dimethylnitronate ion[11] had also been found to depart very reluctantly when sited β to a carbonyl-stabilised carbanion.

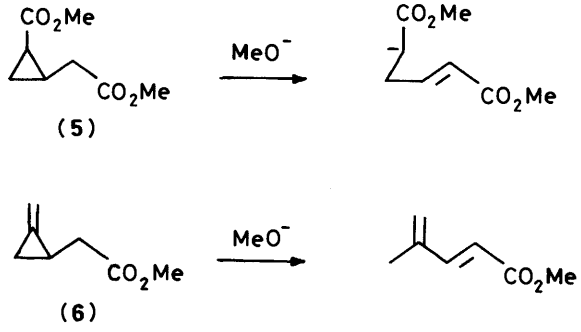
The objective of the work described in this paper was to examine a system involving elimination of a carbon leaving group and to compare the reactivity of the system with an analogue in which the bond to the leaving group is strained by incorporation in a small ring of known strain energy.

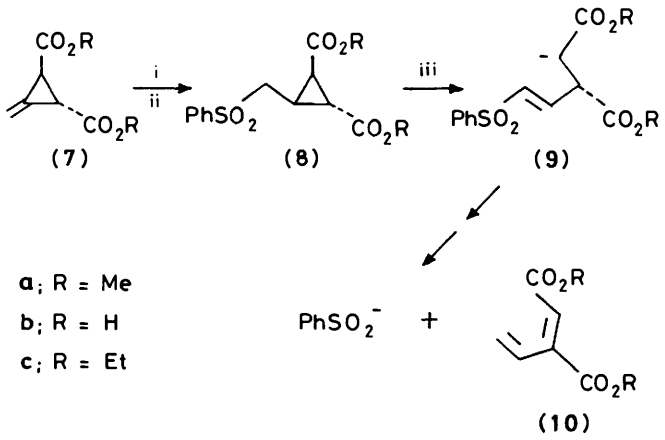


a; n = 1
b; n = 3
c; n = 4

Scheme 1.

Eliminative ring fission has been reviewed[8] and several systems which involve activated elimination of a stabilised carbon leaving group have been studied qualitatively. Typical examples are the esters (**5**)[12] and (**6**),[13] both of which have been shown to undergo ring fission easily. Against the background of





Scheme 2. *Reagents:* i, PhSH–Bu^{t}OOBu^t; ii, H_2O_2–NH_4MoO_7; iii, EtONa–EtOH

our earlier work on nucleofugality, we decided to study such systems quantitatively.

Choice of System.—Our initial experiments were with the diester (**8**) (Scheme 2), readily obtained from Feist's ester (**7**) following earlier work of Rees and his group.[14]

In product analysis studies, problems were encountered with the very rapid hydrolysis by traces of water in the base–solvent system (ethanolic sodium ethoxide). Such abnormal reactivity had been encountered previously[15] and the product (**8b**) (as the anion) was then inert to the eliminative fission. The methyl ester also underwent transesterification very rapidly ($t_{\frac{1}{2}} < 10$ s) in molar ethanolic sodium ethoxide.

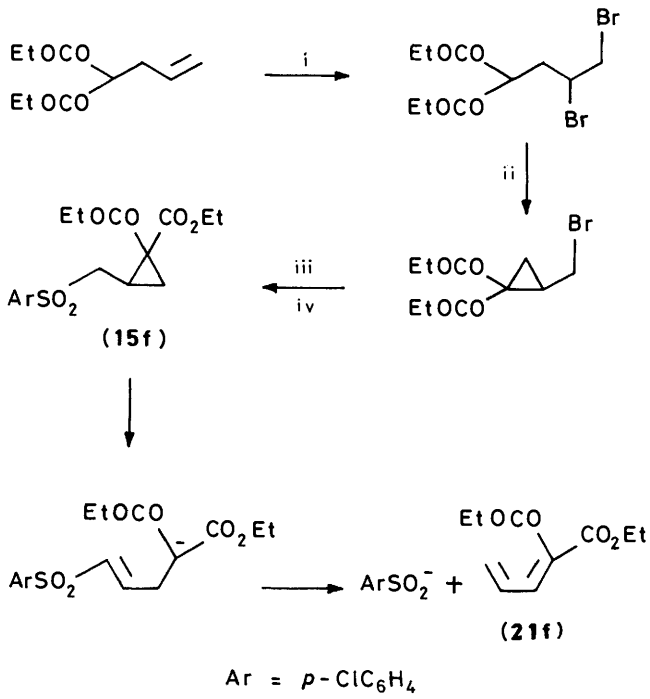
Treatment of (**8c**) with sodium ethoxide in carefully dried ethanol caused rapid ring fission with generation of benzenesulphinic acid and formation of tarry products into which incorporation of ethoxy groups, presumably by nucleophilic addition, was clearly discernible by n.m.r. Attempts to trap the diene (**10c**) with nucleophiles more reactive than ethoxide, such as piperidine,[16] failed to give characterisable products.

An attempt was also made to use the related system (**15f**) (Schemes 3 and 4). Treatment of the diester sulphone with ethanolic sodium ethoxide caused elimination of *p*-chlorobenzenesulphinic acid (85%) presumably *via* (**17f**) and (**19f**) (Scheme 4). Discrete products derived from the putative intermediate (**21**) (Scheme 4) could not, however, be obtained.

Rough rate constants for eliminative ring fission were obtained by following the supposed formation of diene (see later).

Cyclopropanes with Sulphonyl and Cyano-stabilised Leaving Groups.—The quantitative work reported in this paper was carried out with the systems (**15a—e**). Syntheses were accomplished by the general route established for conversions of compounds (**11**) into (**14**) by Durst[17] (Scheme 4) with simple subsequent steps to the substrates (**15**).

Our preliminary results[1] for the bis-sulphone (**15c**) were obtained with very insoluble material which was later shown by high-field proton n.m.r. measurements to be an approximately 50:50 mixture of *Z*- and *E*-stereoisomers. In later work, we have been able to separate the isomeric chlorides obtained by treatment of the mixed alcohols (**14**) with thionyl chloride and these were taken through the further steps to give the separate *Z*- and *E*-isomer of (**15c**). Assignment of configuration was made by n.O.e. measurements on the sulphones at 400 MHz. Details are in Table 9. The configurations of the chlorides (Table 6) and the sulphides (Table 7) follow from assignments for the sulphones.

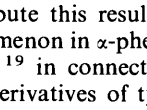


Scheme 3. *Reagents:* i, Br_2–$CHCl_3$; ii, EtONa–EtOH; iii, *p*-ClC_6H_4SNa–EtOH; iv, H_2O_2–MeOH–NH_4MoO_7

Products of Eliminative Ring Fission.—The bis-sulphone (**15a**) gave as stable end-product the diethoxy sulphone (**22a**) resulting from bis-addition of ethoxide to the diene (**21a**). U.v. spectroscopic examination of solutions of (**15a**) in ethanolic sodium ethoxide showed development of absorption at 260 nm attributed to the diene (**21a**) which slowly decreased as (**22a**) was formed.

For the cyano sulphone (**15b**), formation of the cyano diene (**21b**) was followed at 260 nm and again absorption decreased as the diethoxy compound (**22b**) was formed.

The bis-sulphone (**15c**) gave the diene (**20**) directly and this did not undergo addition of ethoxide under preparative conditions. The orientation of elimination of benzenesulphinate from the intermediate bis-sulphone (**19c**) is of considerable interest. The product, the diene (**20**), must be derived from deprotonation at C_α and not C_δ despite the fact that C_δ bears a phenyl group and the pK_a at this site is some 5.7 units *lower* than at C_α.[18] We attribute this result to steric inhibition of deprotonation, a phenomenon in α-phenyl sulphones which we first called attention to[19] in connection with orientation of elimination in simple derivatives of type (**27**) in which G = $PhSO_2$, PhS, or $(EtO)_2P(O)$. In all cases, except for G = $PhSO_2$, deprotonation was α to the phenyl group.



(**27**)

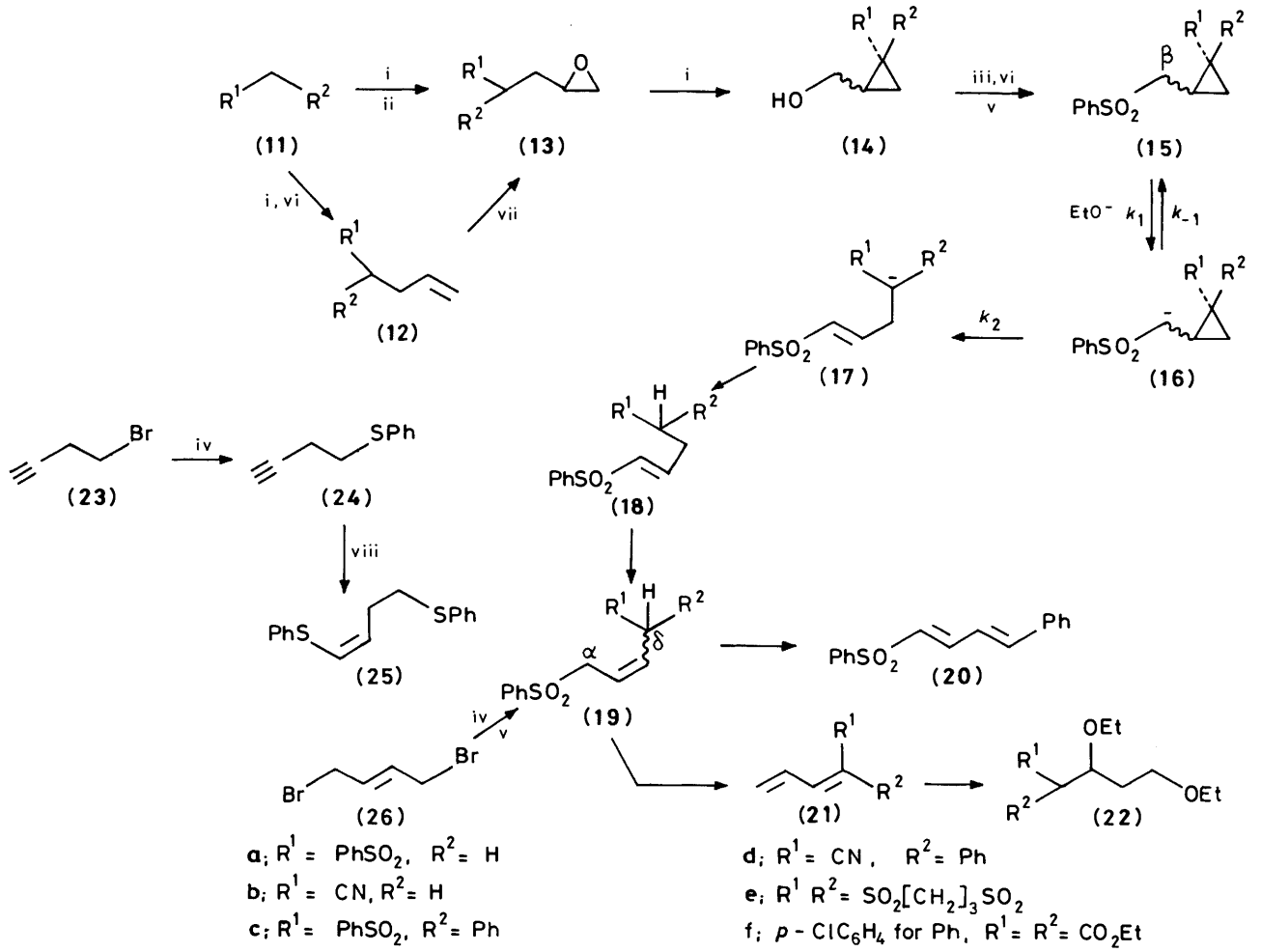
For the cyano sulphone (**15d**) the stable end product was the diethoxy adduct (**22d**) and similarly, from the tris-sulphone (**15e**), the product was (**22e**). Details are in Table 1.

The suggested route from substrates (**15**) to products (**20**), (**21**), and (**22**) is a sequence of deprotonation, ring fission, prototropy, and elimination. In connection with the kinetic work it was necessary to establish that the behaviour of

Table 1. Products of eliminative ring fission reactions

Substrate	Product	Yield (%)	Yield of $PhSO_2H$[a] (%)	Found (%) C	H	N	Formula	Required (%) C	H	N	B.p./mmHg	n_D
(15a)	**(22a)**	66	80	59.0	7.6		$C_{14}H_{22}O_4S$	58.7	7.6		160/0.1	1.4380
(15b)	**(22b)**	84	85	63.2	9.6	8.2	$C_9H_{17}NO_2$	63.1	9.9	8.2	65/0.1	1.4280
(15c)	**(20)**	94	83	71.3	4.8		$C_{16}H_{14}O_2S$	71.1	5.1		97[b]	
(15d)	**(22d)**	79	81	72.7	8.5	5.5	$C_{15}H_{21}NO_2$	72.8	8.5	5.7	88/0.1	1.4465
(15e)	**(22e)**	89	88	42.2	7.2		$C_{11}H_{22}O_6S$	42.0	7.0		*c*	
(18a)	**(22a)**	96	88									
(19c)	**(22a)**	97	90									

[a] Additionally characterised as benzyl phenyl sulphone, m.p. and mixed m.p. 149 °C. [b] M.p. from MeOH. [c] Isolated by flash chromatography.



Scheme 4. *Reagents:* i, BuLi–THF; ii, 1-bromo-2,3-epoxypropane; iii, $SOCl_2$; iv, PhSNa–EtOH; v, H_2O_2–MeOH–NH_4MoO_7; vi, $BrCH_2CH{=}CH_2$; vii, *m*-$ClC_6H_4CO_3H$; viii, PhSH, *hν*

conjugated and non-conjugated sulphones (**18**) and (**19**) was consistent with their being intermediates in these reactions.

The *trans*-bis-sulphone (**19a**) was obtained from the dibromide (**26**), and the bis-sulphone (**18a**) from 4-bromobut-1-yne (**23**) *via* bis-sulphide (**25**) (Scheme 4). Both sulphones gave products identical with those obtained from the cyclopropane (**15a**) and, as Table 2 shows, much more rapidly.

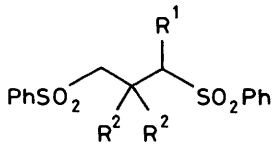
Comparison with Acyclic (Unstrained) Analogues.—A simple acyclic unstrained analogue of cyclopropane (**15a**) is (**28c**) (Scheme 5). This is stable under the reaction conditions[16a,20] for (**15a**). The *gem*-dimethyl compound (**28b**) undergoes 1,3-elimination under forcing conditions.[21] Bis-stabilisation of the leaving group, as in (**29**), still did not give a substrate in which eliminative fission of a carbon–carbon bond occurred; instead, benzenesulphinate ion (86%) was eliminated. Presumably the bis-sulphone (**30**) is also obtained in this reaction, but we were unable to obtain recognisable complementary products.

To obtain comparison of elimination in an unstrained (acyclic) analogue with the eliminative fission of cyclopropanes we have followed two rather extended series of analogies. First, the tris-sulphone (**29b**) smoothly undergoes elimination of

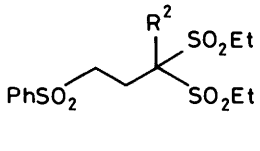
Table 2. Rate constants and activation parameters for eliminative ring fission

Substrate	$k_{obs.}$[a]	$k_{add.}$[a,b]	k_H/k_D	$k_{detrit.}$[a,c]	pK_a-(Me_2SO)[d,e] of $MeCHR^1R^2$	$\Delta H^{\ddagger}$[f]	$\Delta S^{\ddagger}$[g]	Rank[h]
(*E*)-(**15a**)	4.7×10^{-3}[i]	7.8×10^{-4}[i]	0.97	1.2×10^{-1}	31.1	73.9	−42	8.8
(*Z*)-(**15c**)	8.5×10^{-3}[j]				25.4	89.9	+17	8.8
(*E*)-(**15c**)	5.7×10^{-2}				25.4	76.7	−12	9.6
(*E*)-(**15b**)	1.94×10^{-3}[i]	3.7×10^{-4}	1.02	1.1×10^{-1}	32.6	104.1	+50	8.4
(*Z*)-(**15d**)	2.42[k]		1.03[l]	*m*	23.0	71.1	0	10.9
(**15e**)	11.0				16.7	61.9	−17	9.0
(**8a**)	8×10^{-3}[n]							8.2[n]
(**15f**)	7×10^{-1}[n]							10[n]
(**18a**)	12.7[i]							
(**19a**)	12.7[i]							

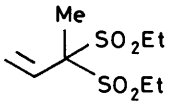
[a] Units $dm^3\ mol^{-1}\ s^{-1}$ for reactions in ethanolic sodium ethoxide at 25 ± 0.1 °C. [b] Rate constant for disappearance of diene. [c] Rate constant for detritiation. [d] Data from ref. 18. [e] R^1 and R^2 as in Scheme 3. [f] kJ mol^{-1}. [g] J $mol^{-1}\ K^{-1}$. [h] = log $k_{obs.}$ − log k_1 + 11. [i] Followed at 260 mm. [j] Followed at 310 nm. [k] Followed at 280 nm. [l] Values uncertain as only partially deuteriated material could be obtained. [m] Detritiation too rapid for accurate determination. [n] Approximate value (see text).



(**28**)



(**29**)



(**30**)

a; R^1 = Me, R^2 = H b; R^1 = H, R^2 = Me c; R^1 = R^2 = H

Scheme 5.

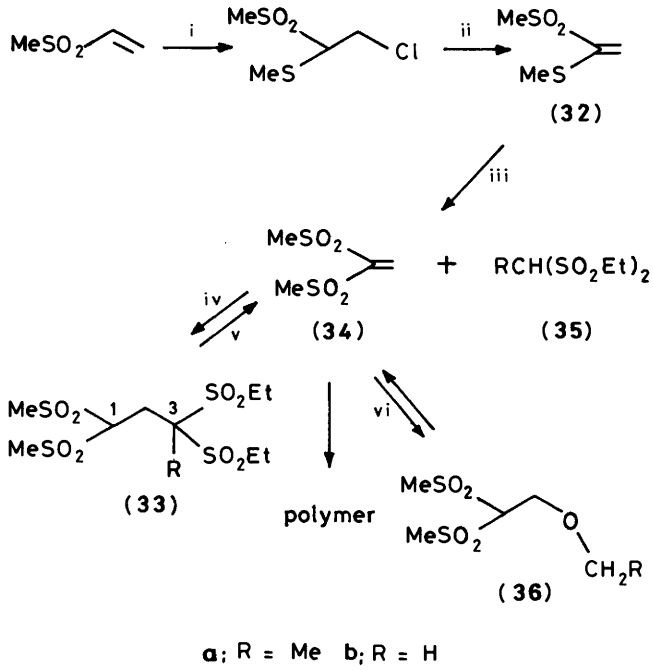
1,1-bisethylsulphonylethane (**35a**) in the base–solvent system potassium t-butoxide in t-butyl alcohol.

The rate of reaction can readily be followed by observing the appearance of this product by g.l.c. To calibrate the effect of the solvent–base system upon the kinetics, we have measured the rate of elimination of 2-nitropropane from the nitro compound (**31**) (Table 3) under the same conditions. The reactivity of the same compound in our standard base–solvent system, ethoxide–ethanol (Table 3) then gives a ratio which we apply to obtain the elimination rate for the acyclic substrate (**29b**) which differs from the strained analogue (**15a**) in possessing a leaving group stabilised by two alkylsulphonyl groups but destablised by a methyl group. For $(E1cB)_R$ eliminations such as these, the observed rate constant is the product Kk_2 of the equilibrium constant for deprotonation and the rate constant for loss of the leaving group from the carbanion. We can allow for the effect of bis-sulphonyl stabilisation of the leaving group on k_2 of (**29b**) by applying the lowest β_{LG} value (0.4) obtained in any of our nucleofugality studies.[22] This value was measured for β-aryloxyethyl sulphones. If this figure is applied to the leaving group ΔpK_a value obtained by comparison of (**29b**) [$pK_a(Me_2SO)$ of leaving group conjugate acid = 16.4 (ref. 23*b*) allowing 2 pK_a units for replacement of α-H by α-Me[23*c*]], the ratio obtained is $10^{5.8}$:1. The difference in the value of *K* between (**29b**) and (**28a**) is estimated from the differential inductive effects of two ethylsulphonyl groups *versus* one phenylsulphonyl group. Allowing a σ* differential of 0.1 between $PhSO_2CH_2$ and $EtSO_2CH_2$ (precise values are difficult to estimate) and the ρ* value (4.89) for β-substituents in sulphones[20] (attenuated by a factor of 2.8 for β *vs.* γ substitution as in this case) gives an additional rate factor of $10^{2.1}$. This value is included in Table 3. We recognise, of course, that these are very long extrapolations necessitated by the widely divergent reactivities of the strained and unstrained substrates. The reactivity of the nitro compound (**31**) is substantially greater

Table 3. Rate constants for elimination in acylic (unstrained) analogues

Substrate	$k_{obs.}$[a]	Rank[b]
$4\text{-}MeC_6H_4SO_2CH_2CH_2CMe_2NO_2$ (**31**)	1.6×10^{-6}[c] (EtONa–EtOH)	+5.6
	6.2×10^{-3}[d] (Bu^{t}OK–Bu^{t}OH)	
$PhSO_2CH_2CH_2CMe(SO_2Et)_2$ (**29a**)	6.2×10^{-3}[e] (Bu^{t}OK–Bu^{t}OH)	
	1.6×10^{-6}[f] (EtONa–EtOH)	+3.4
	5.3×10^{-5}[g] (EtONa–EtOH)	(+5.9)
$PhSO_2CH_2CH_2CHMeSO_2Ph$ (**28a**)	2.5×10^{-12}[f,h] (EtONa–EtOH)	−0.1
	2.0×10^{-14}[i] (EtONa–EtOH)	−2.2
	8.3×10^{-11}[h] (EtONa–EtOH)	(+1.4)
	6.6×10^{-13}[j] (EtONa–EtOH)	(−0.7)
$(MeSO_2)_2CHCH_2CMe_2NO_2$ (**37**)	7.5×10^{-4} (EtONa–EtOH)	
$(MeSO_2)_2CHCH_2CMe(SO_2Et)_2$ (**33a**)	2.5×10^{-2} (EtONa–EtOH)	

[a] Units $dm^3\ mol^{-1}\ s^{-1}$ at 25 °C. [b] Log $k_{obs.}$ − log k_1 + 11. [c] Derived from determinations at 60.0, 70.0, and 79.0 °C; reactions followed by appearance of 2-ethoxyethyl phenyl sulphone and by appearance of 2-nitropropane. [d] Derived from determinations at 50.0, 40.0, and 30.0 °C; reactions followed by appearance of 2-nitropropane. [e] Derived from determinations at 30.0, 40.0, and 50.0 °C; reactions followed by appearance of 1,1-bisethylsulphonylethane. [f] Derived by multiplying EtONa:Bu^{t}OK rate constant ratio for (**31**) by Bu^{t}OK rate constant for (**29b**). [g] Derived by dividing the rate constant for (**33a**) by the ratio of the rate constants for (**37**):(**31**). [h] Derived by dividing the rate constant derived from (**29b**) by $10^{5.8}$, this factor being derived from ΔpK_a-(Me_2SO) [$PhSO_2CH_2CH_3$–$(EtSO_2)_2CHMe$] × β_{LG} = 0.4. [i] Value in *f*,*h* corrected for equilibrium (see text). [j] Value of *g*,*h* corrected for equilibrium deprotonation (see text).



Scheme 6. *Reagents:* i, MeSCl; ii, Et_3N–$PhCH_3$; iii, $PhCO_3H$; iv, $RCH(SO_2Et)_2$–EtONa–EtOH; v, EtONa–EtOH; vi, RCH_2OH

than that given in our preliminary report; on the basis of other subsequent measurements we became dubious about the procedures used earlier and have recently redetermined this value. It is used only as a linking substrate in this work and the change of value does not affect the conclusions.

In our preliminary work, we had obtained data for an unstrained system by using a doubly activated substrate with a bis-stabilised leaving group to surmount the problem of the very low nucleofugality of carbon leaving groups. The system employed is shown in Scheme 6. The substrate (**33a**) incorporates a methyl group to block deprotonation at C-3 and bis-activation at C-1 to raise the equilibrium concentrations of C-1 carbanion. Reaction of this tetrakis-sulphone with ethanolic sodium ethoxide was, however, very slow. This low reactivity was surprising and we concluded that, in ethanolic sodium ethoxide, equilibration to a small standing concentration of the ethoxy adduct (**36a**) occurred and that loss of substrate was essentially due to formation of polymer from the alkene (**34**).

Treatment of the tetrakis-sulphone (**33a**) with the bis-sulphone (**35a**) enriched with ^{13}C in the methyl group (R) showed that exchange occurred quite rapidly, confirming our conclusion that this was an equilibrating system.

It was impossible to assign a rate constant to the initial elimination but the problem was circumvented by the device of adding the bis-sulphone (**35b**) to the reaction mixture. The anion derived from this sulphone competes, in readdition, with the anion of (**35a**) ejected from (**33a**). Because in (**33b**) the leaving group ionises and is not re-eliminated, appearance of (**35a**) in the reaction mixture monitors the elimination rate. The equilibration observed in this system is a striking consequence of the high nucleophilicity of the sulphonyl-stabilised carbanion from (**35**), coupled with its low nucleofugality. By comparison, the competing ethoxide ion from the solvent is rapidly eliminated and is only moderately nucleophilic. For the linking nitro substrate (**31**) (Table 3) used to monitor the effect of having to use t-butoxide–t-butyl alcohol as the base–solvent system, competition of the anion of 2-nitropropane and ethoxide ion for phenyl vinyl sulphone under the reaction conditions gives only β-ethoxy sulphone.

In order to allow for the effect of double activation and double leaving-group stabilisation on the reactivity of the tetrakis-sulphone (**33a**) and hence derive the reactivity of (**28a**), we have taken the ratio of the reactivities of nitro compounds (**37**) (Table 3) and (**31**), and then divided this factor into the rate constant for (**29b**) to give a value of 5.3×10^{-5}; this figure is then further divided by a factor of $10^{5.8}$ as before to take account to the effect of double stabilisation of the leaving group. It should be noted that the nitro compound (**37**) is 33 times less reactive than the bis-sulphone (**33a**) with the same activating groups, in contrast to the identical reactivities of the monoactivated systems (**31**) and (**29**) (Table 3). We have no satisfactory explanation for this anomaly. In work carried out since our preliminary publication we also became suspicious of our value for the rate constant for (**37**). That included in Table 3 is much lower than our original figure.

In view of the uncertainties of assessing the reactivity of the unstrained systems, we are using *maximum* values for their reactivity so as to avoid any exaggeration of conclusions. Use of the lower values in Table 3 simply increases the estimates of the proportions of the strain energies of the cyclic systems reflected in the energies of the transition structures.

These two different attempts to assess the reactivity of (**28a**) under the reaction conditions give markedly different results. In terms, however, of the proportion of the strain energy of the cyclopropane released at the transition structure, the difference is not very considerable.

We have had considerable difficulty in obtaining accurate data for the very unreactive carbon leaving-group system, and the large disparity between the rank values obtained in the two comparisons reflects this problem. The lower value modified as a result of later comparisons is 2.6 units greater than that included in our preliminary communication; the disparity has centred on obtaining accurate data for the nitronate leaving-group system. The lower rank value for the acyclic system (**28a**) gives a proportion of cyclopropane strain energy harnessed to acceleration (see later) of about 46%.

Results and Discussion

The data from the systems described allows direct comparison of strained and unstrained systems in activated alkene-forming elimination reactions; reservations about precise quantitation of the acyclic unstrained systems are recognised but these do not affect our general conclusions.

Rate-determining Step.—For the cyclopropyl systems, rates were followed by observing the appearance of diene; this is either the final or the penultimate product of a series of two prototropic shifts coupled with two eliminations. It was essential, therefore, to determine for one typical system whether the rate constants of any of these intervening steps were comparable with the observed rate constants for production of diene (**20**) or (**21**). The bis-sulphonylbutadienes (**18a**) and (**19a**) were substantially more reactive than the cyclopropane (**15a**) and the possibility that eliminations in the open-chain structures might be rate-determining is rejected. The fact that rates of formation of diene from (**18a**) and (**19a**) are identical also points to prototropic interconversions occurring faster than eliminative ring fission. It was clear, therefore, that reactions subsequent to ring fission were rapid; the question remained as to which step in the sequence (**15**)—(**17**) was rate-determining. Cyclopropanes (**15a**—**c**) all showed primary kinetic deuterium isotope effects close to unity and we conclude that for these systems the mechanism is $(E_1cB)_R$, with a rapidly established equilibrium concentration of carbanion (**16**) (Scheme 4) which undergoes rate-determining ring fission. This conclusion is strengthened by the detritiation rate constants for cyclopropanes (**15a** and **c**),

which exceed the observed rate constants for eliminative ring fission by factors of 26 and 57, respectively. The primary kinetic tritium isotope effect for deprotonation α to a phenylsulphonyl group[20] is about 7.1 thus *deprotonation* of the cyclopropanes occurs 180—400 times more rapidly than ring fission. Deprotonation of the cyano cyclopropane (**15d**) is clearly very rapid. Introduction of tritium was accompanied by considerable ring fission and we cannot be certain of the rate-determining step in reactions of this substrate. The rate constant derived from a Taft plot for sulphone detritiation[20] suggests a value close to that observed for ring fission (see later); for this substrate the mechanism is evidently a borderline one.

Effect of Leaving Group on Reactivity in Ring Fission.—Table 2 shows striking variations of leaving group effects. Comparison of sulphone (**15a**) and nitrile (**15b**) shows the slightly higher rank (≡ nucleofugality) of the sulphonyl-stabilised leaving group. The sulphonyl group is a somewhat better carbanion stabiliser than the cyano group as shown by the pK_a data obtained by Bordwell[18] for solutions in Me_2SO, but stabilisation by cyano has a greater component of p–π stabilisation and a lower inductive component than for phenylsulphonyl. The activation parameters reveal the substantial difference between these carbanions; for the sulphone, the entropy of activation is much less favourable than for the nitrile, suggesting that there is a much smaller degree of ring cleavage in the transition state for the former than for the latter. The lesser extent of ring cleavage is also suggested by the *lower* enthalpy of activation. This pattern of behaviour is consistent with different compromises being established between ring opening and rigidity in the transition state. For the nitrile, stabilisation of the leaving group requires a larger extent of delocalisation of the charge on the leaving group and hence a larger degree of charge transfer to it. This is achieved by a greater degree of ring cleavage in the transition state. Compensation for the enthalpic cost of a greater degree of ring fission arises from the greater degree of flexibility in the part-opened ring. This is reflected in the entropy of activation.

The situation is thrown into sharper focus by the effect of α-phenyl substitution at the leaving group. For the sulphone (**15c**) only a small acceleration is observed. The rank of the leaving group is unaffected and the rate difference can be attributed to the effect of α-phenyl substitution on k_1 (Scheme 4) alone. The difference in stabilities of the leaving groups in the sulphones (**15a** and **c**) as reflected in the conjugate acid pK_a values[18] ($\Delta pK_a = 5.7$) therefore suggests that there is only a small degree of ring fission at the transition state.

A rather similar situation applies for the bis-sulphone (**15e**). The leaving-group stabilisation (ΔpK_a) is now 14.4 and yet the rank differential is only 0.2. The effect of the second sulphonyl group on $k_{obs.}$ is almost entirely on the pre-equilibrium. Comparison of the nitriles (**15b** and **d**), however, shows a very different picture. α-Phenyl substitution causes a rate enhancement approaching 10^4 against a leaving-group ΔpK_a value of 9.6. The nitrile system is thus much more sensitive to acceleration by α-phenyl substitution. This is consistent with a greater degree of transfer of charge to the ring carbon atom and its effective delocalisation by the phenyl group. The enthalpy of activation is substantially decreased but the entropy of activation becomes less favourable, perhaps because a slightly different compromise involving a lower degree of ring fission can be achieved.

Effect of Strain on Nucleofugality.—The rank data of Tables 2 and 3 show a comparison of leaving-group nucleofugality for the strained and unstrained systems, and, within the strained systems, the effect of leaving-group stabilisation. Comparison of the rank of the unstrained leaving group [substrate (**28a**)] (Table 3) with that of the strained analogue (**15a**) (Table 2) shows a gross difference of about 9 units. This difference, translated into an energy of activation difference, amounts to about 53 kJ mol^{-1}. This corresponds to about 46% of the strain energy of the cyclopropane ring,[23] defined in thermodynamic terms as the excess of enthalpy.[24] In this connection, it is assumed in this and the following papers that the strain energies of small rings are not affected by single substituents on one or more of the ring atoms. Ring strain energies of cycloalkanes with alkyl or amino groups are close to those of the parent cycloalkanes.[25] Crystallographic evidence suggests normal structures for a polysubstituted cyclobutane[26a] and (*Z*)- and (*E*)-1,2-diethylcyclopropane differ little in stability.[26b]

Stereochemistry.—Subsequently to our preliminary report[1] our finding that both isomers are obtained in the preparation of the bis-sulphone (**15c**) has enabled us to investigate the reactivity difference between them. The rather modest difference in relative rates disguises considerable differences in activation parameters, which are mutually compensating. We found[26c] the same pattern of reactivity for the *gem*-dimethyl analogues of (**15a**). In these cases, the *Z*-isomer again has a substantially greater enthalpy of activation than the *E*-isomer, a difference somewhat compensated by a more positive entropy of activation. The origin of these differences in behaviour is not clear.

Conclusions.—This is the first example of a direct measurement of the effect of strain on nucleofugality. The remarkable conclusion to be drawn from the data is that the strain energy of the cyclopropane system decreases very considerably in the early stages of bond extension. For the bis-sulphones, the lack of effect of α-phenyl substitution at the leaving group betokens a very small extent of charge localisation on the leaving group. Simple molecular mechanics calculations[26a] support this conclusion. As has been mentioned, when the leaving carbanion is cyano-stabilised, a greater degree of ring opening appears to apply. In the case of the α-phenyl-substituted nitrile (**15d**), acceleration is so great that the mechanism approaches the borderline between rate-determining ring fission $(E_1cB)_R$ and rate-determining deprotonation $(E_1cB)_I$.

The systems selected for this study have enabled direct evaluation of the effect of strain on nucleofugality. The results show that very large accelerations are achieved by incorporation of the bond to a leaving group in a strained ring and that the rank change of around 9 units, corresponding to about 46% of the excess of enthalpy of the ring, is achieved with only a small degree of ring cleavage. Results of quantum mechanical calculations using MINDO3[26a] are consistent with these conclusions.

Experimental

For general instructions, see Parts 30[9] and 39.[1] Light petroleum had b.p. 40—60 °C. 4-Phenylsulphonylbut-1-ene had n_D^{26} 1.5374 (lit.,[27], n_D^{20} 1.5404).

Pent-4-enenitrile was obtained by reaction of 4-bromobut-1-ene with sodium cyanide in dimethyl sulphoxide at 60 °C. It had n_D^{20} 1.4175 (lit.,[28] n_D^{20} 1.4189). 2-Phenylpent-4-enenitrile had b.p. 66 °C at 0.1 mmHg, n_D^{20} 1.5224 (lit.,[27] b.p. 130 °C at 0.9 mmHg, n_D^{20} 1.5221).

Oxidation of sulphones was performed with hydrogen peroxide in methanol catalysed by ammonium molybdate. For hydroxy sulphones, sodium tungstate was used as catalyst.[29] Flash chromatography was carried out according to Stills' procedure.[30] Tetrahydrofuran (THF) was dried by distillation from benzophenone ketyl.

Table 4. Epoxides (**13**)

Epoxide	Yield (%)	M.p.	Found (%) C	H	N	Formula	Calc. (%) C	H	N
(**13a**)	83[a]	53[b]	56.3	5.4		$C_{10}H_{12}O_3S$	56.6	5.6	
(**13b**)	74[a]	*e*							
(**13c**)	90[c]	113[d]	66.4	5.2		$C_{16}H_{16}O_3S$	66.6	5.5	
(**13d**)	78[a]	(116 at 0.1 mmHg)[f] (n_D^{17} 1.5290)	76.0	6.1	8.1	$C_{11}H_{11}NO$	76.3	6.4	8.1
(**13e**)[g]	71[c]	(97 at 0.2 mmHg)[f] (n_D^{17} 1.5673)	47.4	6.5		$C_7H_{12}OS_2$	47.7	6.8	

[a] From alkene with *m*-$ClC_6H_4CO_3H$. [b] From di-isopropyl ether. [c] From 1-chloro-2,3-epoxypropane. [d] From methanol. [e] Decomposed on attempted distillation. [f] B.p. [g] S for SO_2.

Table 5. Hydroxymethylcyclopropanes (**14**)

Cyclopropane	Yield (%)	B.p./mmHg	Found (%) C	H	N	Formula	Calc. (%) C	H	N
(**14a**)	35, 40[a]	171/0.1 (n_D^{20} 1.5544)	56.5	5.6		$C_{10}H_{12}O_3S$	56.6	5.6	
(**14b**)	40	90/0.1 (n_D^{16} 1.4685)	61.0	7.1		C_5H_7NO	61.8	7.2	
(**14c**)	96	(225)[b]	66.7	5.6		$C_{16}H_{16}O_3S$	66.6	5.5	
(**14d**)	72	130/0.1 (n_D^{18} 1.5567)	76.1	6.4	7.8	$C_{11}H_{11}NO$	76.3	6.4	8.1
(**14e**)	67[c]								
(**14e**)[d]	75	122/0.1 (n_D^{20} 1.5832)	47.6	6.9		$C_7H_{12}OS_2$	47.7	6.8	

[a] One pot from $PhSO_2Me$. [b] M.p. from methanol. [c] From oxidation of bis-sulphide. [d] S for SO_2.

Table 6. Chloromethylcyclopropanes (**14**; Cl for OH)

Chloride from	Yield (%)	B.p./mmHg	Found (%) C	H	N	Formula	Calc. (%) C	H	N
(**14a**)	44	160/0.2 (n_D^{20} 1.5576)	52.0	4.6		$C_{10}H_{11}ClO_2S$	52.1	4.7	
(**14b**)	57	55/0.1 (n_D^{19} 1.4736)	51.4	4.8	12.0	C_5H_6ClN	51.9	5.2	12.1
(*E*)-(**14c**)	65[d]	(114)[a]	63.1	4.9		$C_{16}H_{15}ClO_2S$	62.7	4.9	
(*Z*)-(**14c**)	27[d]	(96)[a]	62.5	4.8					
(**14d**)	47	*c*	68.8	5.0	7.4	$C_{11}H_{10}ClN$	69.0	5.2	7.3
(**14e**)	98	(163)[b]	32.8	4.1		$C_7H_{11}ClO_4S_2$	32.5	4.3	

[a] M.p. from EtOH. [b] M.p. from di-isopropyl ether. [c] Column chromatography, not distilled. [d] Separated by flash chromatography in 3:1 light petroleum–diethyl ether on silica gel. Assignment of configuration from bis-sulphones (Table 9).

Table 7. Phenylthiomethylcyclopropanes (**14**)[a]

Sulphide	Yield (%)[b]	M.p.	Found (%) C	H	Formula	Calc. (%) C	H
(**14a**)	84	*c*		*d*			
(**14b**)	99	*c*	69.5	5.8	$C_{11}H_{11}NS$	69.8	5.8
(*Z*)-(**14c**)[g]	87	133[e]	69.1	5.3	$C_{22}H_{20}O_2S_2$	69.4	5.3
(*E*)-(**14c**)[g]	88	149[e]	69.0	5.2			
(**14d**)	97	114[e]	77.4	5.95[f]	$C_{16}H_{15}ClO_2S$	77.0	5.7
(**14e**)	97	148[e]	46.7	5.0	$C_{13}H_{16}O_4S_3$	47.0	4.8

[a] PhS for OH. [b] From chloride (Table 6). [c] Liquid from column chromatography. [d] Not further purified. [e] From di-isopropyl ether. [f] %N: Found: 4.8; Calc. 5.2. [g] Configurations derived from the sulphones (Table 9).

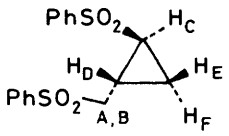
General Procedure for Preparation of Cyclopropanes (**15**).—*Epoxides* (**13**). The γ,δ-unsaturated sulphone or nitrile (**12**) was epoxidised by treatment with *m*-chloroperbenzoic acid (1.1 mol equiv.) in dry chloroform at 20 °C for 16 h. *m*-Chlorobenzoic acid was removed by washing with aqueous sodium hydrogen carbonate and the residue was crystallised or used directly. Details are in Table 4. Alternatively, the sulphone or nitrile (**11**) (1 mol equiv.) in dry THF at −30 °C was treated with n-butyl-

Table 8. Phenylsulphonylmethylcyclopropanes (**15**)

Sulphone (**15**)	Yield (%)	M.p.	Found (%) C	H	N	Formula	Calc. (%) C	H	N
(*E*)-(**15a**)	99	*a*	56.9	5.0		$C_{16}H_{16}O_4S_2$	57.1	4.7	
(*E*)-(**15b**)	99	109[b]	60.2	5.0	6.7	$C_{11}H_{11}NO_2S$	59.7	4.9	6.3
(*Z*)-(**15c**)[d]	74	203[c]	64.2	4.9		$C_{22}H_{20}O_4S_2$	64.1	4.9	
(*E*)-(**15c**)[d]	31	164[c]	63.8	4.9					
(*E*)-(**15d**)	98	114[c]	68.7	5.1	4.5	$C_{17}H_{15}NO_2S$	68.7	5.0	4.7
(**15e**)	98	216[c]	43.1	4.6		$C_{13}H_{16}O_6S_3$	42.8	4.4	

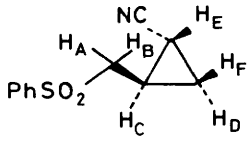
[a] Liquid from column chromatography. [b] From ethanol. [c] From methanol. [d] For assignments by n.O.e. measurements see Table 9.

Table 9. N.O.e. assignment of configuration to the cyclopropanes (**15**)[a]



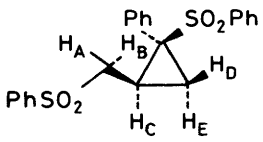
(*E*)-(**15a**)

$\delta(^1H)$ H_A 3.15, H_B 3.00, H_C 2.52, H_D 1.90, H_E 1.50, H_F 0.95; $\delta(^{13}C)$ 11.65, 13.04, 37.92, 57.61, and aromatics
Irradiate H_A, H_B → doublet enhanced; H_B, H_A → doublet; H_C, H_F and H_{AB} enhanced; H_D, H_{AB} and H_E enhanced; H_E, H_D and H_F enhanced; H_F, H_C and H_E enhanced



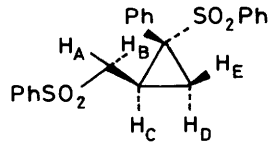
(*E*)-(**15b**)

$\delta(^1H)$ H_A 3.15, H_B 2.97, H_C 1.60, H_D 1.29, H_E 1.20, H_F 0.91
Irradiate H_A, H_B and H_C enhanced; H_C, H_D enhanced; H_D, H_E enhanced; H_E, H_F and H_A and H_B (enhanced slightly)



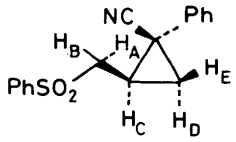
(*Z*)-(**15c**)

$\delta(^1H)$ H_E 1.50, H_D 1.74, H_C 2.04, H_B 3.97, H_A 4.11
Irradiate H_C, H_E, H_B, and α-Ph enhanced



(*E*)-(**15c**)

δ(1H) H_E 1.16, H_D 1.99, H_C 2.52, H_B 2.17, H_A 3.46
Irradiate H_E, H_D and α-Ph enhanced
Irradiate H_C, H_D and H_A or H_B enhanced



(*Z*)-(**15d**)

$\delta(^1H)$ H_A 3.61, H_B 3.35, H_C 1.99, H_D 1.74, H_E 1.59; $\delta(^{13}C)$ 19.91, 22.19, 22.83, 57.37, cyano, and aromatics
Irradiate H_A, H_B and H_C enhanced; H_B, H_A and H_C and H_E enhanced; H_D, H_E and highest-field phenyl proton enhanced

[a] ^1H Spectra at 400 MHz in $CDCl_3$.

lithium (1 mol equiv.) in hexane, and after 30 min 1-chloro-2,3-epoxypropane (1 mol equiv.) was added and the solution was allowed to attain room temperature. It was then boiled under reflux for 30 min. Dilution with saturated brine and extraction with dichloromethane gave the epoxide.

Hydroxymethylcyclopropanes (**14**). The epoxy sulphone or nitrile in dry THF at −30 °C was treated with n-butyl-lithium (1.1 mol equiv.) in hexane and the solution was kept at −30 °C for 1 h. Dilution with brine and extraction with dichloromethane gave the hydroxymethylcyclopropane (details in Table 5).

Choromethylcyclopropanes (**14**; Cl for OH). The hydroxymethylcyclopropane (1 g) in dichloromethane (10 ml) was treated with thionyl chloride (2 ml) and pyridine (0.1 ml). The mixture was refluxed for 2 h; dilution with water and extraction, followed by flash chromatography of the residue, gave the chloride (details are in Table 6).

Phenylthiomethylcyclopropanes (**15**; PhS for $PhSO_2$). The chloromethylcyclopropane in methanol was treated with a solution of sodium benzenethiolate (1.1 mol equiv.) in methanol, and the mixture was boiled under reflux for 16 h. Dilution with water and extraction as before gave the sulphide (details in Table 7). Oxidation of the sulphides with hydrogen peroxide and ammonium molybdate in methanol gave the sulphones (**15**) (details in Table 8).

(Z)-1,4-*Bisphenylsulphonylbut*-1-*ene* (**18a**).—3-Phenylthiobut-1-yne (**24**) (2.7 mmol) and thiophenol (2.7 mmol) were irradiated with a low-pressure mercury arc until the i.r. absorption band at 3 280 cm^{-1} had disappeared. Column chromatography (ether–light petroleum) gave a residue of crude sulphide (**25**) (57%) which, on oxidation with hydrogen peroxide and ammonium molybdate in methanol, gave the *sulphone* (93%), m.p. 127 °C (from methanol) (Found: C, 56.8; H, 4.9. $C_{16}H_{16}O_4S_2$ requires C, 57.1; H, 4.7%), δ($CDCl_3$) 7.7 (10 H, m), 7.0 (1 H, m), 6.5 (1 H, m), 3.3 (2 H, m), and 2.7 (2 H, m).

(*E*)-1,4-Bisphenylsulphonylbut-2-ene (**19a**), obtained by oxidation of the bis-sulphide,[31] had m.p. 161 °C.

Product Analysis.—General procedure. The cyclopropane (**15a**) (3.9 mmol) in ethanol (20 ml) was treated with M-ethanolic sodium ethoxide (20 ml) for 16 h at 20 °C. The mixture was poured into saturated brine; extraction with dichloromethane gave a residue which on distillation gave the product (alternatively, the residue was crystallised) (yields are in Table 1). The aqueous layer was acidified (H_2SO_4) and extraction gave a crystalline residue of crude benzenesulphinic acid (m.p. 75—78 °C), which was boiled under reflux in methanol with benzyl chloride (3 ml) and aqueous 5% sodium hydrogen carbonate (10 ml) for 16 h. Extraction gave benzyl phenyl sulphone (yields in Table 1), m.p. and mixed m.p. 149 °C.[32]

Kinetics.—Reactions were followed in dry ethanolic sodium ethoxide, solutions being prepared from ethanol dried by the magnesium–iodine method. For the cyclopropanes (**15**), reactions were followed by measuring the increase in absorbance of solutions due to the formation of the dienes (**20**) and (**21**) at the wavelengths given in Table 2. Typical substrate concentrations were 10^{-5}M and typical base concentrations 10^{-1}M. Rate constants for eliminative ring fission are the means of at least three determinations in which base concentration and substrate concentration were independently varied. Values are in Table 2 together with activation parameters. Rates of addition to the diene were measured at the same wavelengths and rate constants are also in Table 2. The same procedures were used for alkenes (**18a**) and (**19a**).

Isotope Exchange vs. *Elimination.*—In a typical experiment, the substrate (5 mmol) in ethan[^{2}H]ol (3 ml) was stirred with sodium ethoxide (2.5 mmol) in ethan[^{2}H]ol (1.5 ml) at 25 °C for 1 h. Solvent was removed *in vacuo* and ^{1}H n.m.r. spectroscopy showed that the methylene group at C_β (δ 3.1) had disappeared.

Preparation of Deuteriated Substrates (**15**).—The cyclopropane (5 mmol) in dioxane (5 ml) was treated with sodium hydroxide (0.05 g) in deuterium oxide (3 ml) for 1 h. Dilution with acidified saturated brine and extraction gave the deuteriated substrate. Exchange of the proton adjacent to the sulphonyl group on the ring did not occur under these conditions. This is in accord with the much lower acidity of the cyclopropyl sulphone.[33] Kinetics of eliminative ring fission were determined as before, giving the primary kinetic deuterium isotope effects listed in Table 2.

Detritiation of Phenylsulphonylmethylcyclopropanes (**15a** *and* **b**).—The cyclopropane (1.25 mmol) in dioxane (4 ml) was treated with sodium hydroxide (0.80 g) in water (3 ml) and tritiated water (0.25 ml; 1.25 mCi) at 25 °C. After 1 h, the mixture was poured into saturated acidified brine (20 ml); extraction gave the labelled cyclopropane. The product (0.25 mmol) in ethanol (20 ml) was treated with ethanolic sodium ethoxide (2.7×10^{-2}M; 80 ml) at 25 °C under nitrogen. Samples (10 ml) were removed at intervals, quenched with acidified saturated brine, and extracted with dichloromethane (3 × 50 ml). The dried extracts were evaporated and the residues were dissolved in scintillation fluid (9 ml) prepared by dissolving butyl P.B.D. (5 g) in Analar toluene (1 l). Counting was performed with a Philips liquid scintillation counter; rate constants were the means of three determinations.

Dimethyl 3-*Phenylsulphonylmethylcyclopropane*-trans-1,2-*dicarboxylate* (**8a**).—The *sulphone* (91%) was obtained by oxidation of the sulphide[14] with hydrogen peroxide and ammonium molybdate in methanol. It had m.p. 67 °C (from toluene–light petroleum) (Found: C, 54.3; H, 5.7. $C_{14}H_{16}O_6S$ requires C, 53.8; H, 5.2%). The sulphone (2 mmol) was kept in methanolic M-sodium methoxide (100 ml) for 10 min. Saturated brine (100 ml) was then added and the basic solution was extracted with dichloromethane (3 × 100 ml) to give a residue (280 mg). The aqueous layer was acidified and again extracted with dichloromethane (3 × 100 ml). The aqueous solution was resaturated with sodium chloride and re-extracted with chloroform (3 × 100 ml). T.l.c. of the first extract (0.26 g) showed several components and a complex ^{1}H n.m.r. spectrum was observed. The second extract (200 mg) probably contains the cyclopropane monoacid, as judged by the n.m.r. spectrum, and the third acidic extract gave the *dicarboxylic acid* (**8b**) (200 mg). This material had m.p. 221 °C (from toluene–light petroleum) alone or mixed with an authentic specimen (m.p. 222 °C) (from EtOAc) obtained by saponification of the ester (**8a**) with methanolic sodium hydroxide (Found: C, 50.9; H, 4.3. $C_{12}H_{12}O_6S$ requires C, 50.7; H, 4.2%). The extract from the basic solution clearly showed ethoxy groups in the spectrum and no phenyl group was present. The residue could not be crystallised and no distillation occurred up to 180 °C and 0.1 mmHg. In a separate experiment, the combined acidic extracts were evaporated to give a residue which, on treatment with benzyl chloride and aqueous sodium hydrogen carbonate in methanol as before, gave benzyl phenyl sulphone (70%), m.p. and mixed m.p. 149 °C.

Diethyl 2-p-*Chlorophenylsulphonylmethylcyclopropane*-1,1-*dicarboxylate* (**15f**).—Diethyl but-3-ene-1,1-dicarboxylate[34] (0.14 mol) in chloroform (150 ml) was treated with bromine (0.141 mol) at 0 °C. After 6 h, evaporation gave the *dibromide* (22%), b.p. 149 °C at 0.1 mmHg, n_D^{20} 1 4890 (Found: C, 33.1; H, 4.8. $C_{10}H_{16}Br_2O_4$ requires C, 33.1; H, 4.7%). The dibromide (0.11 mol) was treated with ethanolic sodium ethoxide prepared from sodium (0.12 g atom) in dry ethanol (200 ml). The mixture was kept at 20 °C for 16 h; dilution with water and extraction then gave *diethyl* 2-*bromomethylcyclopropane*-1,1-*dicarboxylate* (44%), b.p. 109 °C at 0.1 mmHg, n_D^{22} 1.4680 (Found: C, 42.8; H, 5.7. $C_{10}H_{15}BrO_4$ requires C, 42.9; H, 5.7%). The bromide (18 mmol) in ethanol (50 ml) was treated with a solution of *p*-chlorobenzenethiol (19 mmol) and sodium ethoxide (19 mmol) in ethanol (75 ml) at 20 °C. After 16 h, dilution with water and extraction gave the *sulphide* (99%), m.p. 38 °C (from

toluene–light petroleum) (Found: C, 56.1; H, 5.5. $C_{16}H_{19}ClO_4S$ requires C, 56.0; H, 5.5%). Oxidation of the sulphide with hydrogen peroxide and ammonium molybdate in ethanol as before gave the *sulphone* (**15f**) (95%), m.p. 56 °C (from methanol) (Found: C, 51.5; H, 4.9. $C_{16}H_{19}ClO_6S$ requires C, 51.3; H, 4.8%).

The ester (26 mmol) was kept with dry ethanolic 0.5M-sodium ethoxide (20 ml) for 16 h. Work-up as before gave a neutral residue (0.58 g) which showed no phenyl group in the n.m.r. spectrum, no vinylic protons, and strong signals for ethoxy-groups. Distillation and column chromatography both failed to yield identifiable products and the behaviour of the residue indicated polymerisation. The aqueous layer on acidification and work-up gave, on treatment of the residue with benzyl chloride as before, benzyl *p*-chlorophenyl sulphone (85%), m.p. and mixed m.p. 139 °C (lit.,[35] 142.5—143 °C).

Kinetics of Reactions with the Cyclopropanecarboxylates.—Reproducibility of the results was not satisfactory, probably owing to polymerisation. For the 1,2-diester (**8a**) values range from 4 to 13 × 10^{-3} and for the 1,1-diester (**15f**) from 0.6 to 0.8 $dm^3\ mol^{-1}\ s^{-1}$.

2-Methyl-2-nitro-4-phenylsulphonylbutane (**31**).—2-Nitropropane (3.6 mmol) was added to a solution of potassium hydroxide (3.6 mmol) in methanol (20 ml). Phenyl vinyl sulphone (3.6 mmol) in methanol (10 ml) was added dropwise and the mixture was kept at 60 °C until t.l.c. showed the absence of the vinyl sulphone. The mixture was neutralised (H_2SO_4); extraction gave the *nitro sulphone* (0.28 g), m.p. 93 °C (from methanol) (Found: C, 51.4; H, 5.8; N, 5.4. $C_{11}H_{15}NO_4S$ requires C, 51.7; H, 5.8; N, 5.4%).

The sulphone, in ethanolic M-sodium ethoxide, was kept for 1 h at 80 °C. Quenching with acetate buffer (pH 4.5) and extraction with dichloromethane gave 2-ethoxyethyl phenyl sulphone (81%).

Kinetics of Nitro Sulphone Reaction.—The nitro sulphone was treated with sodium ethoxide in sealed tubes under argon. At intervals the contents (1 ml) of the tubes were diluted with M-acetate buffer (2.5 ml) and extracted with h.p.l.c. grade chloroform (1 ml) containing, as internal standard, *trans*-stilbene (90 mg per 100 ml). Samples (4 μl) were injected onto a 10% Carbowax–Celite g.l.c. column (2 750 × 5 mm) at 237 °C (N_2 carrier gas). These conditions gave complete separation of product, 2-ethoxyethyl *p*-tolyl sulphone, and internal standard. The yield of sulphone at infinity (no increase in ratio to internal standard) was 95%. Additionally, production of nitronate ion was monitored by u.v. spectrometry at 250 nm. Infinity absorbances were *ca.* 95% of stoicheiometric.

Competition between Ethoxide Ion and Nitronate Ion in addition to Phenyl Vinyl Sulphone.—Phenyl vinyl sulphone (0.12 g, 0.71 mmol) in ethanol (0.2 ml) was treated with 2-nitropropane (0.72 mmol) dissolved in ethanolic M-sodium ethoxide (4.3 mmol). After 2 h at 20 °C, t.l.c. showed no residual vinyl sulphone, and after 16 h acidification to pH 4—5 (HCl) and extraction (CH_2Cl_2) gave a residue (0.129 g) of 2-ethoxyethyl phenyl sulphone[9] (95%) (i.r. and ^1H n.m.r.).

2,2-Bisethylsulphonyl-4-phenylsulphonylbutane (**29b**).—Phenyl vinyl sulphone (2.98 mmol) in ethanol (5 ml) was added to the bis-sulphone (**35a**) (3.28 mmol) in ethanolic M-sodium ethoxide (3.28 ml). After 20 min, t.l.c. showed no vinyl sulphone, and after 16 h the precipitate of *tris-sulphone* (0.58 g) was filtered off; m.p. 134 °C (from ethanol) (Found: C, 44.0; H, 6.0. $C_{14}H_{22}O_6S_3$ required C, 44.0; H, 5.8%). The filtrates were quenched with brine; extraction gave unchanged bis-sulphone (0.16 g), m.p. and mixed m.p. 77 °C.

1,1-Bisethylsulphonyl-3-phenylsulphonylpropane (**29c**).—The same procedure with (**35b**) gave the *tris-sulphone*, m.p. 124 °C (from methanol) (Found: C, 43.4; H, 5.6. $C_{13}H_{20}O_6S_3$ requires C, 43.4; H, 5.6%).

When competitive experiments involving treatment of an equimolecular mixture of phenyl vinyl sulphone and the sulphones (**35a** and **b**) in ethanolic sodium ethoxide were conducted, g.l.c. of the product mixture showed that the ratio of changed sulphones (**35a**):(**35b**) was 2:1, the remainder of the adduct being 2-ethoxyethyl phenyl sulphone.

Treatment of the sulphone (**29b**) (0.25 mmol) with an equimolecular amount of the sulphone (**35b**) in ethanolic M-sodium ethoxide (25 ml) at 90 °C for 5 days showned (g.l.c.) no appreciable formation of the sulphone (**35a**) nor of ethoxy sulphone.

The sulphone (**29b**) (0.4 g) was kept with ethanolic M-sodium ethoxide (50 ml) at 90 °C for 11 days. The usual work-up with separation of the acidic fraction gave benzenesulphinic acid (0.16 g, 86%, m.p. and mixed m.p. 63 °C.

1-Chloro-2-methylsulphonyl-2-methylthioethane (*Scheme 6*).—Methyl vinyl sulphone (0.114 mol) in dry dichloromethane (20 ml) at −30 °C was treated with methanesulphenyl chloride (0.125 mol) over 15 min. After 15 min, the temperature of the mixture was allowed to rise to 20 °C; evaporation gave the sulphone sulphide (13.6 g), m.p. 60 °C (from di-isopropyl ether) (lit.,[36] 61—62 °C).

1-Methylsulphonyl-1-methylthioethene (**32**).—The preceding sulphone (0.02 mol) in toluene (30 ml) at 20 °C was treated with triethylamine (0.0205 mol). The resulting suspension was shaken for 90 min; after 16 h, filtration, and evaporation of the filtrate gave the alkene (2.2 g), b.p. 84 °C at 0.1 mmHg, n_D^{14} 1.5340 (lit.,[36] b.p. 96 °C at 2 mmHg).

1,1-Bismethylsulphonylethene (**34**).—The preceding alkene (0.014 mol) in chloroform (10 ml) was treated with a standardised solution of perbenzoic acid (0.028 mol) in choroform (25 ml) over 1 h. After 16 h, the mixture was poured into an excess of saturated aqueous sodium hydrogencarbonate; extraction gave the alkenyl bis-sulphone (1.1 g), m.p. 173 °C, after trituration of the residue with dichloromethane (Found: C, 26.3; H, 4.4. Calc. for $C_4H_8O_4S_2$: C, 26.1; H, 4.4%) (lit.,[36] m.p. 167—168 °C).

1-Alkoxy-2,2-bismethylsulphonylethanes (**36a** *and* **b**).—Recrystallisation of the preceding alkene from methanol gave the *methyl ether* (**36b**) (90%), m.p. 109 °C (from methanol) (Found: C, 27.5; H, 5.5. $C_5H_{12}O_5S_2$ requires C, 27.5; H, 5.5%). Similar treatment with ethanol gave the *ethyl ether* (**36a**) (90%), m.p. 77 °C (from di-isopropyl ether) (Found: C, 31.0; H, 6.4. $C_6H_{14}O_5S_2$ requires C, 31.3; H, 6.1%).

In each case small amounts of material with m.p. *ca.* 165 °C were obtained. This material did not show alkoxy or vinyl proton signals in the n.m.r. and is probably a (low molecular weight) polymer of (**34**).

1,1-Bisethylsulphonylethane (**35a**).—Bisethanesulphonylmethane (2.5 g)[37] was treated with the solution obtained from dissolution of sodium (0.28 g) in ethanol (4 ml). Dry ether (5 ml) was added and the mixture was filtered at 0 °C to give the hygroscopic sodium salt (1.96 g), m.p. 146 °C. The salt (0.78 g) in dry dimethylformamide (0.8 ml) was treated with methyl iodide (0.5 g). The reaction was exothermic; the mixture became neutral after 30 min, and addition of water and extraction then gave the sulphone (59%), m.p. and mixed m.p. 74—76 °C (lit.,[38] 74—75 °C). This procedure was employed to obtain (**35a**) using 30% ^{13}C-enriched methyl iodide, in the same yield.

3,3-*Bisethylsulphonyl*-1,1-*bismethylsulphonylbutane* (**33a**).—The bis-sulphone (**34**) (20 mmol) in methanol (15 ml) was added to a mixture of 1,1-bisethylsulphonylethane (20 mmol) and triethylamine (21 mmol). After 16 h at 20 °C evaporation gave the tetrakis-sulphone (6.06 g), m.p. 200 °C (from chloroform–di-isopropyl ethyl) (Found: C, 30.3; H, 5.7. $C_{10}H_{22}O_8S_4$ requires C, 30.2; H, 5.5%).

Exchange Experiments.—(*a*) The ^{13}C n.m.r. spectrum of an equimolecular mixture of the tetrakis-sulphone (**33a**) (0.25 mmol), the bis-sulphone (^{13}C enriched) (**35a**), and M-sodium ethoxide in ethanol (3 ml) at 23 °C showed exchange of ^{13}C between bis- and tetrakis-sulphone ($t_{\frac{1}{2}}$ *ca.* 2 min).

(*b*) The methoxy bis-sulphone (**36b**) (0.5 mmol) and the bis-sulphone (**35a**) (0.5 mmol) in ethanol (5 ml) were treated with ethanolic M-sodium ethoxide (0.5 ml). After 30 min, t.l.c. showed the mixture to contain the tetrakis-sulphone (**33a**). After 1 h, quenching of the mixture with acetate buffer (pH 5) and extraction gave the tetrakis-sulphone (**33a**) (220 mg), m.p. and mixed m.p. 200 °C identical (i.r.) with an authentic specimen.

Kinetics of Reactions of the Tetrakis-sulphone (**33a**).—Two procedures were employed. (i) The rate of exchange between the tetrakis-sulphone (**33a**) and the ^{13}C-enriched bis-sulphone (**35a**) in ethanolic sodium ethoxide was determined by measurement at appropriate intervals of the (enchanced) ^{13}C n.m.r. absorptions at 9—11 (based concentration dependent) and 13.9 p.p.m.

(ii) The tetrakis-sulphone (**33a**) (*ca.* 4 mmol) was treated with the bis-sulphone (**35b**) (*ca.* 4 mmol) in ethanolic sodium ethoxide (typically 0.2M) in the presence of methyl phenyl sulphone (4 mmol) as internal standard. Samples (2 ml) were removed, neutralised (HCl) with brine, and extracted with chloroform (10 ml). Extracts were washed with water (2 ml) and evaporated and the residues in chloroform subjected to g.l.c. analysis (Carbowax at 210 °C; N_2 carrier gas; flame ionisation detector) for sulphones (**35a**) and (**35b**). The value given in Table 3 is the mean of determinations by the two procedures.

2-*Nitro*-2-*methyl*-4,4-*bismethylsulphonylbutane* (**37**) (*with* **Dr. P. J. Thomas**).—The alkene (**34**) (0.02 mol) was added to 2-nitropropane (0.02 mol) and potassium hydroxide (0.02 mol) in methanol (100 ml). After 2 h, t.l.c. showed complete reaction; the mixture was cooled to 0 °C, taken to pH 4—5 (H_2SO_4), poured into brine, and extracted with dichloromethane. Evaporation gave the *sulphone*, m.p. 183 °C (from methanol) (81%) (Found: C, 30.5; H. 5.3; N, 5.0. $C_7H_{15}NO_6S_2$ requires C, 30.8; H, 5.5; N, 5.1%). The compound was also obtained by oxidising the *sulphide* (**37**; MeS for one $MeSO_2$) obtained analogously by addition of 2-nitropropane to 1-methylsulphonyl-1-methylthioethene (**32**) (Scheme 6) (80%), m.p. 85 °C (from di-isopropyl ether) (Found: C, 35.0; H, 6.1; N, 5.7. $C_7H_{15}NO_4S_2$ requires C, 34.9; H, 6.2; N, 5.8%).

The sulphone (2.73 g) in ethanol (150 ml) was treated with ethanolic M-sodium ethoxide (100 ml) for 3 h; t.l.c. then showed complete reaction. Work-up as before gave the ether (**36a**) (2.1 g, 91%), m.p. and mixed m.p. 77 °C.

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