Elimination and Addition Reactions. Part 42.[1,2] Structural Effects on Reactivity and Mechanism in Eliminative Fission of Three-membered Rings

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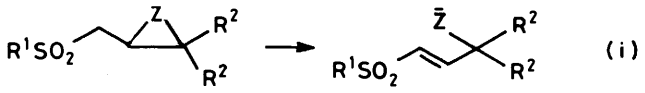
Three aspects of eliminative fission reactions of the type (i) have been studied. First, the effects of stabilisation of the carbon leaving group, Z, by nitro and by sulphonyl groups have been compared. The results show that stabilisation by nitro produces a 10^4-fold increase in reactivity over sulphonyl, which is modest when the stabilities of the discrete carbanions are considered. The enhanced stabilisation also produces a change in mechanism from $(E1cB)_R$ to *E*2.



(i)

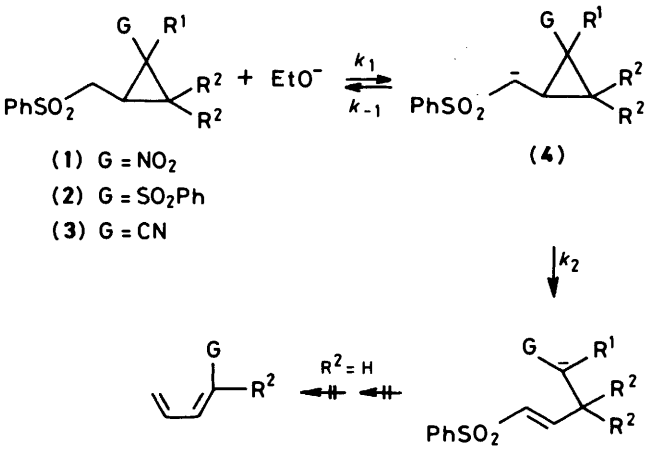
Secondly, the effect of *gem*-dimethyl substitution on reactivity has been compared for cyclopropanes with nitro- and with sulphonyl-stabilised leaving groups, and for oxiranes. When elimination involves rate-determining ring fission, the *gem*-dimethyl (Thorpe–Ingold) effect is substantial and clearly revealed in the activation parameters. When the processes of deprotonation and ring fission are concerted, the Thorpe–Ingold effect is small.

Thirdly, eliminative fission of a thiirane has been compared with that of oxiranes and with that of an unstrained analogue possessing an ethylthio leaving group. The thiirane is somewhat less reactive than the oxirane, but like the oxirane, undergoes fission *via* a concerted mechanism $10^{5.9}$ times faster than the unstrained analogue. The unstrained analogue undergoes elimination of the ethylthio group *via* the stepwise $(E1cB)_R$ mechanism, and ranking (≡ nucleofugality) for the EtS leaving group gives a rank value of 7.3. Detailed comparisons of the balance between nucleofugality and ring strain in such systems are vitiated by the different mechanisms followed by the strained and unstrained systems.

In the preceding paper,[1] the first evaluation of the effect of strain on nucleofugality was outlined, by use of the system (**2a**) of Scheme 1. The main significance of the findings was that incorporation of a very poor carbon nucleofuge in a strained three-membered ring could produce, in a reaction of constant mechanism, an enhancement of rank value (≡ nucleofugality) of the order of 9 (log) units. This figure can broadly be equated with a subtraction of 46% of the thermodynamic ring strain energy from the free energy of activation for leaving-group expulsion. The purpose of the present study was to seek answers to three questions related to earlier investigations: (*a*) what is the effect of greater stabilisation of the carbon nucleofuge in a strained system? (*b*) does *gem*-dimethyl substitution on the ring, well known to enhance ring closure (the Thorpe–Ingold effect), restrain eliminative ring fission? (*c*) how does the reactivity of thiiranes in eliminative fission compare with that of oxiranes studied[3] earlier?

Eliminative Fission of Nitrocyclopropanes.—To obtain information on the first of these questions, we have examined the reactivities of the nitrocyclopropanes (**1**) with ethanolic sodium ethoxide in ethanol. In these systems, the 'stability' of the leaving group is very much greater than in those [(**2a**) and (**3a**)] studied previously[1] (Table 1) (the Bordwell[4] pK_a values for the conjugate acids measured in Me_2SO are used as the basis for comparison). The nitrocyclopropane (**1b**) was obtained by the route of Scheme 2, following the literature route[5] to the ketone (**8**).

The reaction of (**1b**) in the base–solvent system was monitored by following the increase in absorbance which we attribute to the nitronate ion (**5**) (Scheme 1); the rapid isomerisation–elimination sequence demonstrated earlier[1] for (**2**) and (**3**) does not occur. Results are in Table 1, together with comparative data from the earlier study, which include that for the acyclic (unstrained) analogue (**11**).

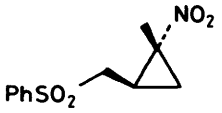
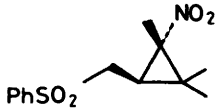
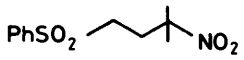
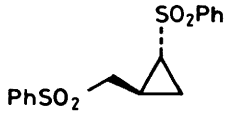
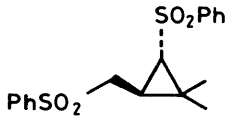
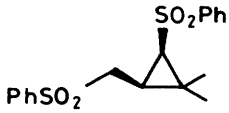
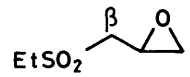
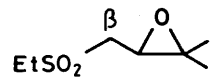
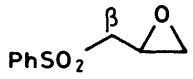
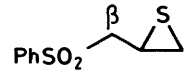
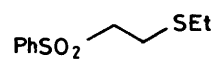


(1) G = NO_2
(2) G = SO_2Ph
(3) G = CN

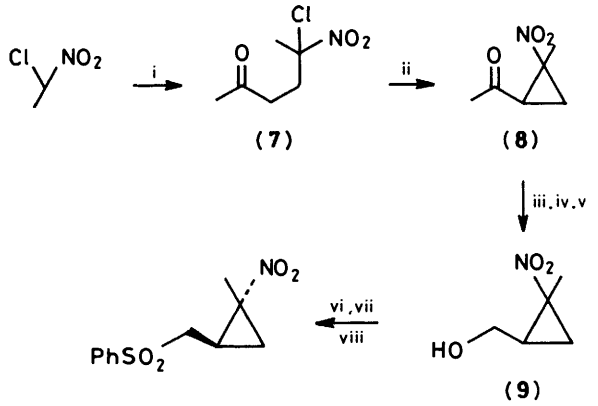
a; $R^1 = R^2 = H$
b; $R^1 = Me, R^2 = H$
c; $R^1 = Ph, R^2 = H$
d; $R^1 = H, R^2 = Me$
e; $R^1 = R^2 = Me$

Scheme 1.

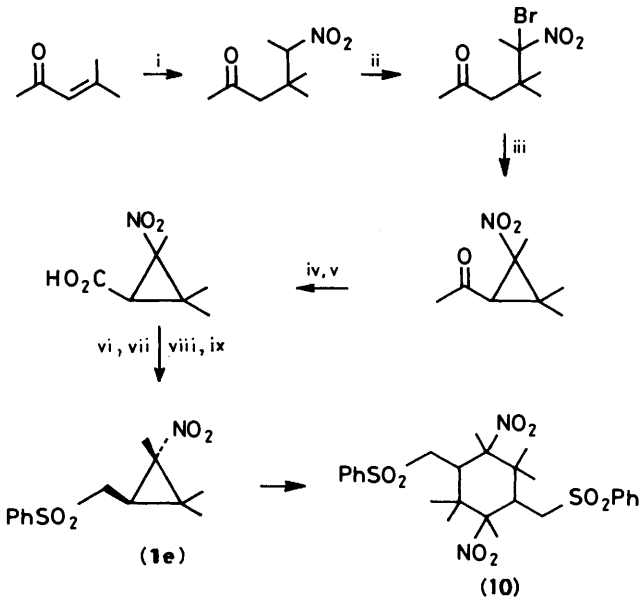
Table 1. Rate constants for eliminative ring fission

		$k_{obs.}$[a]	k_1[a]	Leaving group pK_a[b]	Leaving group rank[c]	$\Delta H^{\ddagger}$[d]	$\Delta S^{\ddagger}$[e]
	**(1b)**	61.7[r]	3.5[j]	16.2[w]	+12.2	77.4	+49
	**(1e)**	5.3	1.6[j]	16.2[h,w]	+11.5	75.8	+24
	**(11)**[f]	1.6×10^{-6}	1.1×10^{-2}[j]	16.2[w]	+5.6		
	**(2a)**[f]	4.8×10^{-3}	8.5×10^{-1}	31.3[u]	+8.8	74.0	−42
	(*E*)-(**2d**)	2.7×10^{-3}[s]	3.8×10^{-1}[j]	31.5[v]	+8.9	95.3	+29
	(*Z*)-(**2d**)	2.4×10^{-3}[s]	3.8×10^{-1}[j]	31.5[v]	+8.8	106.6	+63
	**(14a)**	185[i]	2.5×10^{-1}[j,k]	29.8[g]	+13.9		
	**(14b)**	184[p]	1.1×10^{-1}[j,k]	30.3[g,x]	+14.2		
	**(15)**	4 170[q]	2.5×10^{-1}[j]	29.8[g]	15.2		
	**(16)**	350[t]	1.7×10^{-1}[n]	17.05[t]	+14.3		
	**(18a)**[o]	3.6×10^{-4}	5.3×10^{-2}[m]	17.05[t]	+7.3	92.0	−2

[a] Units $dm^3\ mol^{-1}\ s^{-1}$ for reactions in ethanolic sodium ethoxide at 25.0 °C. [b] Estimated for Me_2SO solutions from the data of Bordwell *et al.* for conjugate acids of the leaving groups. [c] $\log k_{obs.} - \log k_{deprot.} + 11$ (see ref. 6). *N.B.* value ⩾ 11 indicates *E*2 mechanism from which no nucleofugality comparison can be drawn. [d] kJ mol^{-1}. [e] J K^{-1} mol^{-1}. [f] Data from preceding paper. [g] For ethanol, W. N. Olmstead, Z. Margolin, and F. G. Bordwell, *J. Org. Chem.*, 1980, **45**, 3295. [h] No correction. [i] Ref. 9. [j] Calculated from ρ*σ* plots (ref. 9). [k] Assuming that $k_{deprot.}$ ($EtSO_2C$–H) = $k_{deprot.}$ ($PhSO_2C$–H). [l] $k_{H/D} = 3.2$. [m] Calculated using σ* for $EtSCH_2 = 0.27$, derived from σ_I for $MeSCH_2$ from M. Charton (*Prog. Phys. Org. Chem.*, 1981, **13**, 119). [n] Reactions followed by increase of absorption at 232 nm. [o] Reactions followed by increase of absorption at 240 nm. [p] Reactions followed by increase of absorption at 220 nm. [q] Reactions followed by increase of absorption at 225 nm. [r] Reactions followed by increase of absorption at 230 nm. [s] Reactions followed by increase of absorption at 235 nm. [t] Value for PrSH: F. G. Bordwell and D. L. Hughes, *J. Org. Chem.*, 1982, **47**, 3225. [u] Value for $PhSO_2Et$: F. G. Bordwell, M. Van der Puy, and N. R. Vanier, *J. Org. Chem.*, 1976, **41**, 1885. [v] Value for (**2a**) modified on assumption that the effect of β-methyl substitution on $k_{deprot.}$ is the same as that on pK_a. [w] Value by extrapolation from values for $MeNO_2$, 17.2; $EtNO_2$ 16.7 (given in ref. 4). Value for Me_2CHNO_2 in 50% MeOH–H_2O is 8.85. F. G. Bordwell, J. E. Bartmess, and J. Hautala, *J. Org. Chem.*, 1978, **43**, 3107. [x] For Pr^iOH. Value in ref. of footnote *g*.



Scheme 2. *Reagents:* i, CH_2=CH–COMe–Et_3N; ii, NaH–Me_2NCHO; iii, Br_2–NaOH; iv, EtOH–H_2SO_4; v, $LiAlH_4$–Et_2O; vi, TsCl–pyridine; vii, PhSNa–EtOH; viii, H_2O_2–NH_4MoO_7–MeOH



Scheme 3. *Reagents:* i, $EtNO_2$–Et_3N; ii, NaOMe–MeOH–Br_2; iii, KOAc–EtOH; iv, Br_2–KOH–H_2O; v, EtOH–H_2SO_4; vi, $LiAlH_4$–Et_2O; vii, TsCl–pyridine; viii, PhSH–EtONa–EtOH; ix, H_2O_2–MeOH–NH_4MoO_7

It can be seen first that incorporation of the bond whose cleavage releases a nitronate leaving group in a strained ring produces rate enhancement of $10^{7.6}$. This enhancement is somewhat less than that (10^9) found for the much less reactive sulphonyl-stabilised system[1] (**2**) (Scheme 1), although in that case the difference between strained and unstrained systems had to be derived by a series of comparisons. Mechanistically, however, there is a significant difference between the strained nitronate system (**1b**) and the strained sulphonyl system (**2a**). In the former case, the calculated deprotonation rate constant is greater by a factor of nearly twenty than the observed rate constant for ring fission, giving a nucleofugality (≡ rank value; rank = $\log k_{obs.} - \log k_{deprot.} + 11$)[6] greater than 11. In such a case[7] therefore the mechanism moves across the spectrum from the clearly defined $(E1cB)_R$ mechanism for (**2a**) to that in which either ring fission occurs faster than deprotonation $[(E1cB)_I]$ or the processes of deprotonation and ring fission become concerted (*E*2). The effect of straining the leaving group connection in this system is to raise the nucleofugality of a very sluggish leaving group[8] to that of a very good leaving group such as tosylate, prone to take part in *E*2 or $(E1cB)_I$ processes. We have previously shown that such behaviour is typical of halogen or acyloxy groups, and it has also been seen[1] in eliminations of the nitrile (**3c**) in which increased stabilisation of the leaving group, for example with respect to that in (**3a**), pushed the mechanisms from $(E1cB)_R$ to the borderline of an irreversible or a concerted process.[9] In our earlier investigations of oxacycloalkanes,[3] we showed that strain similarly raised the nucleofugality of an indifferent nucleofuge such as methoxy over the *E*1cB borderline to the *E*2 mechanism.

In our earlier study[1] it was found that reactivity in eliminative ring fission was rather insensitive to leaving-group stabilisation. This characteristic was attributed to a small extent of ring cleavage in the transition structure and hence a small extent of charge development on the departing carbon atom. The lesser enhancement by strain in the nitrocyclopropane system found here is also consistent with a small degree of charge development on the leaving carbon atom; the carbanion-stabilising effect of nitro groups has a large resonance rather than an inductive component[10] and this is best exerted when electron density in the developing nitronate ion is high.

Thorpe–Ingold Restraint of Ring Fission.—It is an extremely familiar although not well understood finding that *gem*-dimethyl substitution affects ring cleavage and formation. This phenomenon is generally termed the Thorpe–Ingold effect.[11]

Closure of (especially small) rings for example is assisted by *gem*-dimethyl substitution on the chain of atoms which will comprise the ring. Discussion of the accelerative effect of *gem*-dimethyl substitution on ring formation has a long history, much of it controversial, and there is little kinetic information relating to the phenomenon.[12] Its operation has been noted chiefly in the beneficial effect on yields in conversions of acyclic into cyclic structures, especially when the ring formed is small.[12] The ground-state effects of *gem*-dimethyl substitution are, however, quite clear; Kirby[13] has emphasised that the angle between carboxy groups in malonic acid is substantially reduced by *gem*-dimethyl substitution and therefore that a cyclisation reaction should benefit both enthalpically from a smaller angle deformation on proceeding from ground structure to transition structure, and entropically from a greater degree of approximation of reactive chain end-groups. Controversy has centred on the relative importance of these general considerations and it seems reasonable to suggest that both contribute to the overall effect. The structural factors which encourage ring closure would also be expected to *restrain* ring fission; particularly striking examples are seen in the reactivity of anhydrides. Tetramethylsuccinic anhydride is distillable in steam, so great is the equilibrium constant in favour of the cyclic structure.[14] So far as *closure* of small rings is concerned, we have recently evaluated for the first time the Thorpe–Ingold effect on formation of cyclopropanes from γ-halogenoalkyl carbanions.[15]

Having at our disposal substrates undergoing ring fission by both concerted and reversible $(E1cB)_R$ mechanisms, we have examined quantitatively the effect of *gem*-dimethyl substitution, with the objective of evaluating any restraint of ring fission in such systems. With this in mind, we have measured rates of ring fission in the substrates (Table 1) (**1e**), (**2d**) (both diastereoisomers), and (**14b**). Substrate (**1e**) was obtained by the sequence of Scheme 3.

As the results of Table 1 show, the effect of *gem*-dimethyl substitution [(**1b**) compared with (**1e**)] is to reduce overall reactivity by slightly more than a power of ten. We can calculate that the *electronic* effect of *gem*-dimethyl substitution is to

Table 2. Rate constants for eliminative ring fission

Substrate	T/°C	k/dm^3 mol^{-1} s^{-1} [a]
(1b)	25.0	62.2
	29.5	99.7
	35.5	191.9
	39.0	260.9
(1e)	23.0	4.29
	27.0	6.46
	32.0	10.5
	38.0	20.2
(*E*)-(**2d**)	26.0	2.4×10^{-3}
(m.p. 193 °C)	30.5	5.2×10^{-3}
	34.7	9.4×10^{-3}
	39.1	17.0×10^{-3}
	42.9	25.6×10^{-3}
	44.7	29.6×10^{-3}
(*Z*)-(**2d**)	31.5	3.1×10^{-3}
(m.p. 169 °C)	35.4	5.3×10^{-3}
	40.0	10.5×10^{-3}
	44.1	17.8×10^{-3}
(17a)	25.0	3.6×10^{-4}
	35.1	1.3×10^{-3}
	45.0	4.2×10^{-3}
	54.9	1.2×10^{-2}

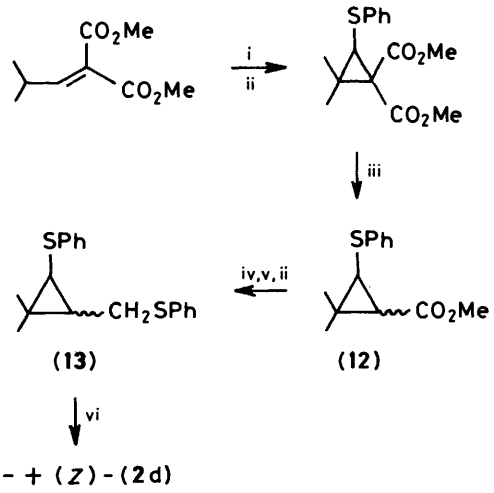
[a] Mean of 2—4 determinations.

reduce the rate of deprotonation by a factor of just over two; and so there appears to be a slight, but definite restraint on ring fission amounting to a factor of about 8. We have to recognise, however, that in neither case is ring fission the sole rate-determining step. For (**1b**) the mechanism is most probably the removal of β-proton concerted with ring fission (*E*2); $k_{obs.} = 20 \times k_1$. For (**1e**), however $k_{obs.}$ and k_1 are closely similar and the $(E1cB)_I$ mechanism seems the most probable. In the latter case, *gem*-dimethyl substitution is of no consequence apart from the small electronically depressive factor already mentioned; for the former it is hard to judge the importance of a structural effect on a concerted process. There will be a small destabilising effect on the nitronate leaving group and this may be part of the apparent *E*2 to $(E1cB)_I$ change on passing from (**1b**) to (**1e**). Because of this probable difference in mechanism and because of the deprotonation-driven reaction of (**1b**), we hesitate to interpret the activation parameters. The trend in enthalpies of activation for (**1b**) and (**1e**) is, however, in the expected direction.

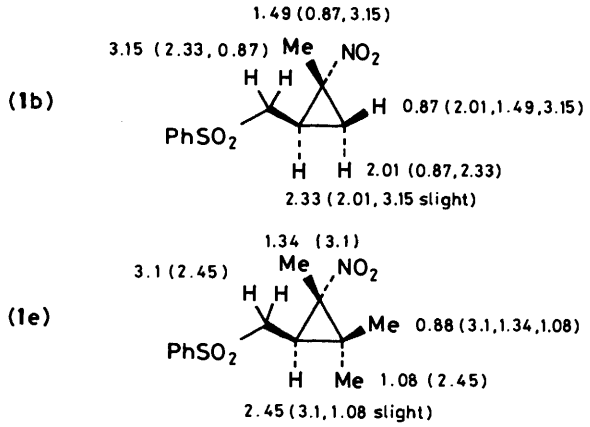
The observation of a distinct, albeit modest, difference in reactivity between substrates (**1b**) and (**1e**) prompted us to examine the *Z*- and *E*-isomer of the *gem*-dimethyl substrate (**2d**) and to compare their reactivity with (**2a**) examined previously.[1] These substrates were synthesized as shown in Scheme 4. The ring fission reactivities of substrates (*Z*)- and (*E*)-(**2d**) were not only very similar to each other but also to the nor-substrate (**2a**) (Table 2).

This time there is no ambiguity about mechanism. The k_1 values are well above $k_{obs.}$ values for these substrates and clearly both substrates react by the $(E1cB)_R$ mechanism with ring fission the rate-determining step.

However, the activation parameters (Table 1) show substantial effects on both enthalpy and entropy terms when compared with those for (**2a**). In each case $\Delta H^{\ddagger}$ is substantially greater. This is in direct agreement with the concept of restraint of angle widening as fission of the ring occurs. The $\Delta H^{\ddagger}$ value is somewhat greater for the *cis*- than for the *trans*-isomer; this is contrary to expectation on the basis of eclipsing interactions in the *cis*-isomer which might be expected to assist ring fission. The *cis*-isomer of the nor-substrate was not available and so a direct comparison cannot be made.



Scheme 4. *Reagents:* i, *N*-bromosuccinimide–CCl_4–$(PhCO_2)_2$; ii, PhSNa–MeOH; iii, NaCl–H_2O–Me_2SO, 160 °C, 2 h; iv, $LiAlH_4$–Et_2O; v, *p*-$MeC_6H_4SO_2Cl$–pyridine; vi, MeOH–H_2O_2–NH_4MoO_7



Scheme 5. Assignments of configurations to cyclopropanes by nuclear Overhauser enhancements (signals enhanced in parentheses)

The entropies of activation are substantially *more* favourable to ring cleavage in each case. These values suggest that a greater degree of ring fission is attained in the transition structure and hence loss of rigidity with it.

So far as we are aware, this is the first dissection of $\Delta G^{\ddagger}$ values for ring fission, or, for that matter, ring closure, in relation to the Thorpe–Ingold effect. The operation of these subtle structural effects deserves further attention.

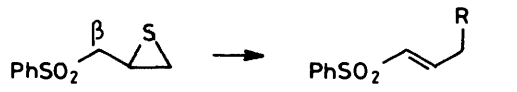
The gem*-Dimethyl Effect in Eliminative Fission of Oxiranes.*— The substrates already discussed all undergo strain-activated elimination of a carbon leaving group. Our first quantitative studies on eliminative ring fission were concerned with oxacycloalkanes, and for the oxirane (**14a**) we found that rates of eliminative ring fission were much greater than calculated deprotonation rates, indicating the concerted (*E*2) mechanism. Furthermore, reaction of (**14a**) (Table 1) showed a primary kinetic deuterium isotope effect of 2.5 (no secondary deuterium isotope correction). Evidently, strain so accentuates the nucleofugality of the alkoxide leaving group as to raise it from a medium-ranked group to one comparable in nucleofugality with halide, a situation comparable in many respects with that shown by the nitrocyclopropanes (**1b** and **e**).

In connection with the effects of ring substituents on rates, we have examined the *gem*-dimethyl substrate (**14b**) and find,

in contrast to the nitrocyclopropyl systems, and to the bis-sulphones, no restraint of ring cleavage. Rate constants are identical with those of the nor-substrate within experimental error and are considerably in excess (about 10^3 times) of calculated deprotonation rates. This evidence points to a concerted mechanism for (**14b**) as for (**14a**).

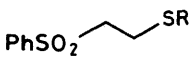
In an extension of our earlier study of the mechanisms of eliminative fission of oxacycloalkanes, the rate constant for the phenylsulphonyloxirane (**15**) has also been determined (Table 1). The value is substantially larger than that for the ethyl analogue (**14a**), reflecting the greater activation by $PhSO_2$ than by $EtSO_2$ and the ratio $k_{obs.}:k_{deprot.}$ ($1.7 \times 10^4:1$) is strong evidence for the operation of a concerted mechanism.

Eliminative Fission of a Thiirane.—In this general connection we have also determined the rate constant for fission of the thiirane (**16**), obtained from the oxirane (**15**) on treatment with thiourea,[16] together with that of its β,β-dideuterio analogue. The primary kinetic deuterium isotope effect (3.2) again shows that partial removal of the β-proton is involved in the rate-determining transition structure and, as shown in Table 1, the rate constant for ring fission is well in excess of the calculated deprotonation rate constant with a $k_{obs.}:k_{deprot.}$ ratio of $2.1 \times 10^3:1$. The product of ring fission is the thiolate ion (**17a**), trapped as the *S*-methyl derivative (**17b**).



(**16**) (**17**) a; R = $\bar{S}$ b; R = SMe

It is notable that the rate constant for concerted fission of the thiirane (**16**) is substantially less than for the oxirane (**15**); the ring strain[17] of the thiirane is around 29 kJ mol^{-1} *less* than for the oxirane.



(**18**)

a; R = Et b; R = Ph

We have also determined the nucleofugality (rank) of EtS^- under activation by $PhSO_2$ in the sulphide (**18a**) (Table 1). The value, +7.3, may be compared with that of OMe (6.1)[6] and to the extent (which is both questionable and substrate-variable) that nucleofugality determines reactivity in a *concerted* process of this type, there appears to be some compensation between smaller ring strain in the thiirane (say 50%[1] of 29 kJ $mol^{-1} \equiv 10^{2.5}$) and higher nucleofugality of EtS *vs.* OMe (say 50% of 1.2 rank units $\equiv 10^{0.6}$). The reactions of the small rings are concerted in both cases, however, and any further detailed consideration of this comparison is not justified.

The rank of the ethylthio group (+7.3) is also to be compared with that of PhS^- (= 8.7),[6] giving a β^{LG} value of *ca.* 0.35. There is considerable variation in the values of σ_I for alkylthio substituents required for ranking. We have used the value[18] $\sigma_I(EtS) = 0.26$ with the factor of 0.45 for conversion to σ^*_{EtS}. A value of σ_I as low as 0.23 is given for MeS.[19]

Conclusions.—Eliminative fission of three-membered rings occurs readily with carbon, oxygen, and sulphur leaving groups. The effect of ring strain is to raise the nucleofugality of the strained leaving group so much that stepwise processes, seen in the unstrained analogues, become, except for sulphonyl-stabilised carbon leaving groups, concerted ones.

The rates of the concerted processes are little affected by *gem*-dimethyl substitution but in the stepwise process $(E1cB)_R$ seen for the systems involving sulphonyl-stabilised carbanion leaving groups, there is substantial enthalpic restraint of ring fission.

Experimental

For general directions see Part 41.[1]

(E)-1-*Methyl*-1-*nitro*-2-*phenylsulphonylmethylcyclopropane* (**1b**).—(*E*)-2-Acetyl-1-methyl-1-nitrocyclopropane[5] (**8**) (1 g, 7 mmol) was added to a solution of bromine (3.36 g, 21 mmol) in aqueous 20% sodium hydroxide (14 ml) at 0 °C. After 2 h, the bromoform produced was separated and the excess of bromine was destroyed with sodium disulphite. Acidification (HCl) and extraction gave (E)-2-*methyl*-2-*nitrocyclopropanecarboxylic acid* (0.8 g, 80%), m.p. 109 °C (from toluene–light petroleum) (Found: C, 42.0; H, 4.8; N, 9.5. $C_5H_7NO_3$ requires C, 41.4; H, 4.8; N, 9.6%). The acid (3 g) in ethanol (4.6 ml) was refluxed with sulphuric acid (20 mg) for 7 h. Extraction gave the ester (87%), n_D^{20} 1.454 (lit.,[3] n_D^{25} 1.4522) which (1 g) was reduced with lithium aluminium hydride (0.1 g) in anhydrous ether (50 ml). The usual work-up gave the *alcohol* (**9**) (0.5 g), b.p. 105 °C at 2 mmHg, n_D^{25} 1.4760 (Found: C, 45.5; H, 7.1; N, 10.5. $C_5H_9NO_3$ requires C, 45.8; H, 6.9; N, 10.7%). Treatment of the alcohol (1 g) in dry pyridine (5 ml) with toluene-*p*-sulphonyl chloride gave the *tosylate* (1.5 g), m.p. 81 °C (from methanol) (Found: C, 50.2; H, 5.55; N, 5.1. $C_{12}H_{15}NO_5S$ requires C, 50.5; H, 5.3; N, 4.9%). The tosylate (1.5 g) in ethanol (50 ml) was added to a solution prepared from sodium (0.13 g), benzenethiol (0.61 g), and ethanol (50 ml). After 20 h, dilution with water and extraction gave the *sulphide* (1.2 g), n_D^{18} 1.572 after flash chromatography in ether on silica gel (Found: C, 59.0; H, 5.7; N, 6.1. $C_{11}H_{13}NO_2S$ requires C, 59.2; H, 5.9; H, 6.3%). The sulphide (1 g) in methanol (50 ml) was treated with 30% aqueous hydrogen peroxide (5.1 ml) and ammonium molybdate (0.4 g). After 15 h, dilution with water and extraction gave the *sulphone* (**1b**) (0.5 g), m.p. 114 °C (from methanol) (Found: C, 51.5; H, 5.1; N, 5.8. $C_{11}H_{13}NO_4S$ requires C, 51.8; H, 5.1; N, 5.5%).

The nitrocyclopropane (300 mg) was kept with ethanolic M-sodium ethoxide for 15 min at 20 °C. The mixture was quenched with M-acetate buffer (pH 4.5; 5 ml), diluted with brine, and extracted to give a residue (250 mg) consisting of several compounds (t.l.c.); the ^1H n.m.r. spectrum was consistent with the chief component being the conjugate acid of (**5a**, G = NO_2).

1,1,2-*Trimethyl*-2-*nitro*-3-*phenylsulphonylmethylcyclopropane* (**1e**).—4,4-Dimethyl-5-nitrohexan-2-one, obtained by addition of nitroethane to 4-methylpent-3-en-2-one, had b.p. 82 °C at 0.3 mmHg, n_D^{19} 1.4530 (lit.,[20] b.p. 67 °C at 0.2 mmHg, n_D^{25} 1.4498) (Found: C, 55.6; H, 8.4; N, 8.1. Calc. for $C_8H_{15}NO_3$: C, 55.5; H, 8.7; N, 8.1%). The ketone (15 g, 86 mmol) was added to a solution prepared from sodium (2.3 g) and methanol (30 ml). Bromine (5 ml, 0.1 mol equiv.) in chloroform (30 ml) was added to the solution at −10 °C over 1.5 h. Dilution with water and extraction gave the bromo ketone (21.4 g, 98%), n_D^{17} 1.4860; *semicarbazone*, m.p. 208 °C (from ethanol) (Found: C, 35.1; H, 5.5; N, 17.9. $C_{10}H_{17}BrN_4O_4$ requires C, 35.0; H, 5.5; N, 18.1%).

The bromide (5 g, 20 mmol) and potassium acetate (5.9 g, 60 mmol) were refluxed in ethanol for 15 h. Dilution with water and extraction gave 3-*acetyl*-1,1,2-*trimethyl*-2-*nitrocyclopropane* (72%), b.p. 91 °C at 15 mmHg, n_D^{21} 1.4630 (Found: C, 56.0; H, 7.5; N, 8.3. $C_8H_{13}NO_3$ requires C, 56.1; H, 7.65; N, 8.2%). The ketone (3 g, 17 mmol) was added dropwise with stirring to a solution of bromine (51 mmol) in aqueous 30% potassium hydroxide (35 ml) at 0 °C. After 2 h, the bromoform which

separated was removed and excess of bromine was destroyed by addition of sodium disulphite. Acidification (HCl) and extraction of the aqueous solution gave the *acid* (2 g), m.p. 100 °C (from light petroleum) (Found: C, 48.3; H, 6.3; N, 7.9. $C_7H_{11}NO_4$ requires C, 48.6; H, 6.4; N, 8.1%).

Esterification of the acid with ethanol–sulphuric acid as before gave the *ethyl ester* (74%), b.p. 65 °C at 1 mmHg, n_D^{27} 1.4540 (Found: C, 53.5; H, 7.4; N, 6.8. $C_9H_{15}NO_4$ requires C, 53.7; H, 7.5; N, 7.0%).

Reduction of the ester (1.5 g) with lithium aluminium hydride as before gave the *alcohol* (78%), b.p. 77 °C at 2 mmHg, n_D^{20} 1.4720 (Found: C, 52.7; H, 8.5; N, 8.7. $C_7H_{13}NO_3$ requires C, 52.8; H, 8.2; N, 8.8%).

Treatment of the alcohol (1 g) with toluene-*p*-sulphonyl chloride (1.22 g) in pyridine as before gave a crude tosylate which (0.7 g) was treated directly with a solution of benzenethiol (0.44 g) and sodium (80 mg) in ethanol (30 ml). After 10 h at 25 °C, dilution with water, and extraction gave the *cyclopropyl sulphide* (0.5 g), which, after flash chromatography, had n_D^{20} 1.5470 (Found: C, 62.1; H, 7.0; N, 5.3. $C_{13}H_{17}NO_2S$ requires C, 62.1; H, 6.8; N, 5.6%).

Oxidation of the sulphide as before with hydrogen peroxide–ammonium molybdate gave the *sulphone* (**1e**) (92%), m.p. 145 °C (from methanol) (Found: C, 55.4; H, 6.1; N, 5.2. $C_{13}H_{17}NO_4S$ requires C, 55.1; H, 6.05; N, 5.0%).

The sulphone was treated with a 5 molar excess of ethanolic 0.1M-sodium ethoxide. After 10 min at 25 °C addition to water and extraction gave (on trituration of the residue with ether) the *nitrosulphone* (**10**) (90%), m.p. 139—141 °C (Found: C, 55.3; H, 6.1; N, 4.9. $C_{26}H_{34}N_2O_8S_2$ requires C, 55.1; H, 6.0; N, 5.0%), $\delta_H(CDCl_3)$ 8.2—7.7 (m, 5 H), 4,83 (t, 1 H), 3.75 (d + s, 2 H), 2.0 (s, 3 H), 1.45 (s, 4 H), 1.25 (s, 4 H); $\delta_C(CDCl_3)$ 8.84, 18.97, 23.26, 48.34, 55.62, 78.62, 128.39, 129.43, 134.37, and 138.92.

(*Z*)- *and* (E)-1,1-*Dimethyl*-2-*phenylsulphonyl*-3-*phenylsulphonylmethylcyclopropane* (**2d**).—Dimethyl 2,2-dimethyl-3-phenylthiocyclopropane-1,1-dicarboxylate[21] (2 g, 7 mmol) was heated under reflux with sodium chloride (0.4 g) and water (0.15 g) in dimethyl sulphoxide (25 ml). Dilution with water and extraction gave the *monoester* (1.5 g), b.p. 117 °C at 0.2 mmHg, n_D^{20} 1.5490 (Found: C, 65.8; H, 6.5. $C_{13}H_{16}O_2S$ requires C, 66.1; H, 6.8%). The ester (8.3 g, 34 mmol) in dry ether (35 ml) was treated with lithium aluminium hydride (0.7 g). When reaction was complete, addition of methanol (5 ml) and then water gave, after extraction in the usual way, the *alcohol* (97%), b.p. 128 °C at 0.4 mmHg, n_D^{19} 1.5650 (Found: C, 69.6; H, 7.3. $C_{12}H_{16}OS$ requires C, 69.2; H, 7.7%). The alcohol (1 g) was treated with toluene-*p*-sulphonyl chloride (1.05 g) in pyridine (8 ml) below 0 °C. After 2 h at 0 °C slow addition of water and extraction gave (after washing with dilute hydrochloric acid) the crude toluene-*p*-sulphonate, which was treated with a solution of benzenethiol (0.3 g) and sodium (60 mg) in ethanol (20 ml). After 2 h, dilution with water and extraction gave the *bis-sulphide* (75%), b.p. 121 °C at 0.2 mmHg, n_D^{19} 1.5875 (Found: C, 72.4; H, 6.9. $C_{17}H_{19}S_2$ requires C, 72.0; H, 6.7%). The *bis-sulphide* (3 g, 10 mmol) (a mixture of isomers) in methanol (50 ml) was treated with 30% hydrogen peroxide (12 ml, 0.2 mol) and ammonium molybdate (0.8 g). After 15 h, dilution with water and extraction gave a residue which on tituration with methanol gave the (E)-*bis-sulphone* (30%), m.p. 195 °C (from methanol) (Found: C, 59.5; H, 5.8. $C_{18}H_{20}O_4S_2$ requires C, 59.3; H, 5.5%). Flash chromatography (in ethyl acetate on silica) of the residue from evaporation of the combined filtrates gave the (*Z*)-*bis-sulphone*, m.p. 169 °C (from methanol) (Found: C, 59.1; H, 5.5. $C_{18}H_{20}O_4S_2$ requires C, 59.3; H, 5.5%).

Each bis-sulphone (200 mg) was kept in ethanolic 0.05M-sodium ethoxide for 3 h at 35 °C. Dilution with acidified brine and extraction gave 1,4-*bisphenylsulphonyl*-3,3-*dimethylbut*-1-*ene* (150 mg, 75%), m.p. 105—107 °C (from toluene–light petroleum) (Found: C, 58.9; H, 5.6. $C_{18}H_{20}O_4S_2$ requires C, 59.3; H, 5.5%); $\delta_H(CDCl_3)$ 7.85 (m, 10 H), 7.4 (d, 1 H, *J* 15 Hz), 6.4 (d, 1 H, *J* 15 Hz), 3.35 (s, 2 H), and 1.5 (s, 6 H).

1-*Ethylsulphonylmethyl*-2,2-*dimethyloxirane* (**14b**).—1-Chloro-3-methylbut-2-ene[22] (10 g) was added to a solution prepared from sodium (2.3 g) and ethanethiol (6.1 g) in methanol (50 ml). After 30 min, addition to water and extraction with dichloromethane gave the crude sulphide (70%), b.p. 67 °C at 20 mmHg, n_D^{24} 1.4790, which (10 g) was oxidised with aqueous 30% hydrogen peroxide (54 ml) and ammonium molybdate (0.5 g) in methanol (80 ml) at 0 °C. After 16 h, dilution with brine and extraction gave 1-*ethylsulphonyl*-3-*methylbut*-2-*ene* (11.3 g, 90%), b.p. 119 °C at 0.1 mmHg, n_D^{18} 1.4810 (Found: C, 51.7; H, 8.8. $C_7H_{14}O_2S$ requires C, 51.9; H, 8.6%). The sulphone (7 g) in 1,2-dichloroethane (15 ml) at 0 °C was treated with *m*-chloroperbenzoic acid (16.6 g) in 1,2-dichloroethane (100 ml). After 24 h at 20 °C, the solution was filtered and the filtrate was washed with aqueous sodium hydrogencarbonate and evaporated to give the *oxirane* (6.5 g), m.p. 42—43 °C (from toluene–light petroleum) (Found: C, 47.0; H, 7.9. $C_7H_{14}O_3S$ requires C, 47.1; H, 7.9%).

Treatment of the oxirane (900 mg, 0.56 mmol) with ethanolic 0.2M-sodium ethoxide gave (on acidification after 5 s and extraction) 4-*ethylsulphonyl*-2-*methylbut*-3-*en*-2-*ol* (300 mg, 33%), m.p. 52—53 °C (Found: C, 47.4; H, 7.6. $C_7H_{14}O_3S$ requires C, 47.2; H, 7.9%). When the reaction was repeated at reflux for 6 h, the product was 4-*ethylsulphonyl*-3-*ethoxy*-2-*methylbutan*-2-*ol*, obtained as an oil by flash chromatography in chloroform on silica gel (Found: C, 48.2; H, 8.9. $C_9H_{20}O_4S$ requires C, 48.0; H, 8.6%).

Phenylsulphonylmethyloxirane (**15**).—The oxirane (90%) was obtained[23] by reaction of allyl phenyl sulphone with *m*-chloroperbenzoic acid in 1,2-dichloroethane at reflux for 24 h. It had n_D^{23} 1.5490 after chromatography in ether on silica gel.

Treatment of the oxirane (1 g) with ethanolic 10^{-2}M-sodium ethoxide (30 ml), neutralisation after 5 s with dilute nitric acid, and extraction gave 3-phenylsulphonylbut-2-en-1-ol (900 mg), m.p. 139—140 °C (from toluene) (lit.,[23] 139—141 °C).

Phenylsulphonylmethylthiirane (**16**).—The oxirane (**15**) (3 g, 15 mmol) was added to a solution at 20 °C of thiourea (1.14 g, 15 mmol) and aqueous 10% sulphuric acid (15 ml). The temperature rose to 26 °C and a solid precipitated. Potassium carbonate (2.1 g) in water (8 ml) was added to take the pH to 7. Extraction gave the *thiirane* (62%), m.p. 53 °C (from toluene–light petroleum) (Found: C, 50.1; H, 4.8. $C_9H_{10}O_2S_2$ requires C, 50.5; H, 4.7%).

Treatment of the thiirane with sodium ethoxide in ethanol as for the oxirane gave a solution, which, when the initial u.v. spectral change was complete, was treated with an excess of methyl iodide. Dilution with water and extraction gave 1-*methylthio*-3-*phenylsulphonylprop*-2-*ene* (70%), m.p. 81 °C (from chloroform–light petroleum) (Found: C, 53.0; H, 5.5. $C_{10}H_{12}O_2S_2$ requires C, 52.6; H, 5.3%).

The β,β-dideuterio derivative was obtained from allyl phenyl sulphone by following the procedure for β,β-dideuterio-(**14a**).[3]

2-*Ethylthioethyl Phenyl Sulphone* (**18a**) (*with* **Dr. A. Bury**).—The *sulphone sulphide* was obtained (90%) as an oil, n_D^{18} 1.5611, by treatment of an equimolecular mixture of phenyl vinyl sulphone (10 mmol) and ethanethiol in ethanol (20 ml) with one drop of triethylamine and subsequent evaporation (Found: C, 52.6; H, 6.2. $C_{10}H_{14}O_2S_2$ requires C, 52.2; H, 6.1%).

Kinetics.—With ethanolic sodium ethoxide (1M) in the reference cell, substrate (0.1 ml of 10^{-2}M-solution) was injected into the sample cell containing ethanolic M-sodium ethoxide (2 ml). The cell was sealed with a septum cap under argon. Increase of absorbance at 240 nm corresponding to liberation of ethanethiolate ion was continuously recorded.

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