Elimination and Addition Reactions. Part 43.[1] Eliminative Fission of Cyclobutanes and the Relationship between Strain and Reactivity in Cyclobutanes and Cyclopropanes

Harold A. Earl and Charles J. M. Stirling*
Department of Chemistry, University College of North Wales, Bangor, Gwynedd LL57 2UW

Eliminative fission of cyclobutanes has been compared with that of analogous cyclopropanes; reactivity differences of $10^{3.7}$—$10^{4.8}$ have been determined. In both sets of compounds, mechanisms have been shown to involve rate-determining ring fission. The possibilities that the large reactivity differences between the comparably strained systems are due either to peculiarity in the cyclobutane structures or to their abnormally slow deprotonation are rejected. Analysis of strain in the two systems suggests that as ring fission occurs, dispersal of the excess of enthalpy of the cyclobutanes is a less sensitive function of extension of a bond in the ring than for the cyclopropanes. The behaviour of these systems is compared with cleavage of cyclopropanes and cyclobutanes in other reactions; the results are remarkably similar. Calculations using the MINDO3 programme have been carried out for eliminative fissions of cyclopropylmethyl and cyclobutylmethyl carbanions. These reproduce remarkably closely the difference between the heats of formation of the species at the energy maxima for fission of each ring size; the maximum for fission of the cyclobutane is considerably displaced along the reaction co-ordinate towards product.
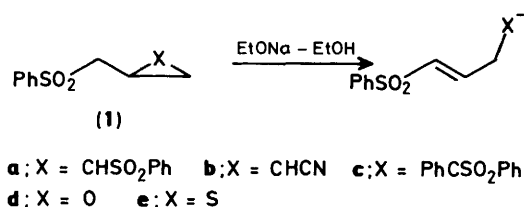
In previous papers in this series[1–3] we reported on investigations of the relationship between strain and reactivity in eliminative fission (Scheme 1) of oxa- and thia-cycloalkanes and cyclopropanes. In all cases there was a very large effect of strain on reactivity and we found, in those cases for which the mechanism of the reaction permitted, that in cleavage of cyclopropanes (1a—c) about 46% of the ring strain was expressed in reduction of the free energy of activation. The comparison with unstrained systems was not ideal because of the need to use systems modified to give sufficient reactivity to be measurable.

The comparisons are to be regarded as approximate, but nevertheless accelerations in the region of 10^9 by strain in three-membered rings were found.
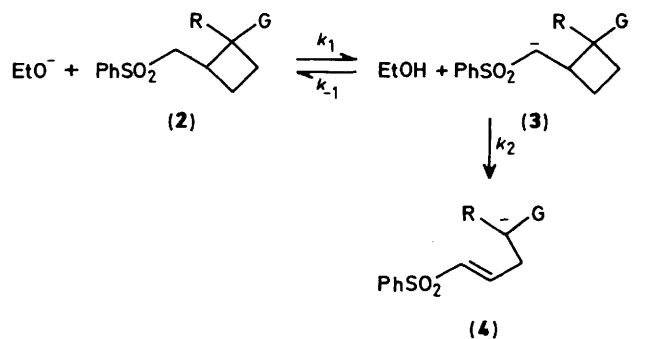
The advantage of using ring systems to examine the relationship between strain and reactivity lay in the fact that strain energies are very large (larger than for any acyclic system) and are accurately known from both experimental data and calculations. In most of the systems for which relationships between strain and reactivity have been derived, strain energies are calculated values without experimental verification.

Irrespective of constitution, four-membered rings are very nearly as strained as three-membered rings provided that all the atoms of the ring are singly bonded.[4–6] Considerable differences emerge, however, if a carbon atom in the ring is doubly bonded. The strain energies of methylenecyclopropane[6] and of cyclopropane are 171.4 and 115.4 kJ mol^{-1}, respectively, but those for methylenecyclobutane[7] and cyclobutane are 112.8 and 109.5 kJ mol^{-1}, respectively. Similarly, cyclobutene[8] (strain energy 124.6 kJ mol^{-1}) is only moderately more strained than cyclobutane whilst the strain energy of cyclopropene (222.0 kJ mol^{-1})[9] is close to double that for cyclopropane. Cyclobutanone[10] is actually less strained than cyclobutanol.

It was of considerable importance, therefore, to compare the behaviour of four-membered rings with those of three-membered rings to discover whether the effect of strain on reactivity in such systems was simply related to overall thermodynamic differences or whether other considerations needed to be taken into account. A qualitative precedent for the eliminative fission of four-membered rings under basic conditions activated by sulphonyl groups has been reported by
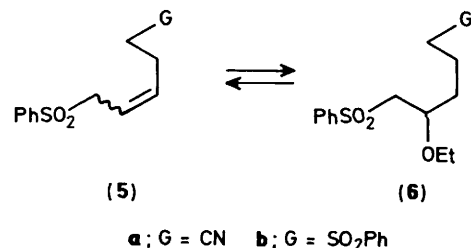

a: X = CHSO$_2$Ph   **b**: X = CHCN   **c**: X = PhCSO$_2$Ph
d: X = O   **e**: X = S

Scheme 1.

a: R = H, G = SO$_2$Ph (*trans*)   **b**: R = H, G = SO$_2$Ph (*cis*)
c: R = H, G = CN (*trans*)   **d**: R = Ph, G = SO$_2$Ph   **e**: R = Ph, G = CN
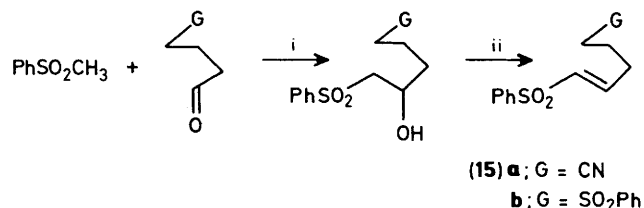
Scheme 2.

Kametani and his co-workers,[11] who have shown that 3-alkylsulphonylmethylcyclobutenes readily undergo ring fission giving dienes on treatment with n-butyl-lithium in tetrahydrofuran (THF). Throughout these papers we define 'strain energy' in thermodynamic terms; it is the excess of *enthalpy* derived from the comparison of heats of combustion of the cyclic systems with those calculated by summation of group equivalents derived from acyclic (unstrained) systems.[12]

Synthesis of Substrates.—Our targets were the cyclobutanes **(2a—d)** (Scheme 2). Syntheses proved troublesome and

Scheme 3. *Reagents:* i, KCN–MeOH; ii, NaCl–Me$_2$SO–H$_2$O; iii, LiBH$_4$–(MeO[CH$_2$]$_2$)$_2$O; iv, SOCl$_2$–pyridine; v, PhSNa–EtOH; vi, H$_2$O$_2$–NH$_4$MoO$_7$; vii, KOH–PhCH$_3$; viii, PhSH; ix, B$_2$H$_6$–THF; x, *m*-ClC$_6$-H$_4$CO$_3$H; xi, SOCl$_2$–pyridine

a ; G = CN   b ; G = SO$_2$Ph

Scheme 4.

Scheme 5. *Reagents:* i, BuLi–THF; ii, TsCl–pyridine

attempts to obtain the α-phenyl substrates (**2d** and **e**) were abandoned after many failures. Substrates (**2a**—**c**) were obtained as in Scheme 3.

Reduction of the *cis*-sulphide acid (**11a**) gave a *cis*–*trans* mixture of the alcohols (**12**) and hence a *cis*–*trans* mixture of the chlorides (**13**). On treatment with sodium benzenethiolate the chlorides showed an interesting difference in reactivity. The *cis*-isomer reacted substantially more slowly than the *trans*-isomer, probably for steric reasons, and at this point the isomerically pure *cis*- and *trans*-bis-sulphides (**14a** and **b**) could be obtained separately. Neighbouring group participation by sulphur, which would require an intermediate with a four-membered ring, can be discounted; earlier work[13] had shown that 3-bromopropyl *p*-tolyl sulphide is at least 16 times as reactive as 1-bromobutane towards ethoxide ion in ethanol.

Oxidation of the sulphide mixture (**14**) gave a low yield of bis-sulphone (**2b**), which was obtained in high yield from the pure bis-sulphide (**14b**). Pure *trans*-bis-sulphone (**2a**) could not be obtained.

Sulphones (**2a**—**c**) were treated with sodium ethoxide in anhydrous ethanol under the standard conditions used previously.[3] The product, in each case, was shown by [1]H n.m.r. to be a mixture of the non-conjugated alkene (**5**), which undoubtedly arises from its conjugated isomer (**15**) (see later), and the ethoxy-adduct (**6**). High-field (400 MHz) [1]H n.m.r. spectra showed that for the *cis*-bis-sulphone (**2b**), the first, rapid, step was isomerisation to the *trans*-isomer (**2a**). Loss of the *cis*-isomer signal was monitored, giving the rate of *cis* ⟶ *trans* conversion. The rate constants and activation parameters for

this process (Table 4) were inserted in our preliminary communication[1b] by an oversight in place of the values for ring fission. Rates of ring fission (Table 1) are for the *trans*-isomer (**2a**). Kinetic data for the (**2b**) ⇌ (**2a**) isomerisation are in Table 4.

Because of the small amounts of material available we have authenticated the origin of the product mixtures by synthesizing the *conjugated* alkenes (**15**) (Scheme 5) separately and subjecting them to the reaction conditions. The high-field [1]H n.m.r. spectra of the products from (**2**) and from (**15**) were identical for each series.

Formation of the non-conjugated alkenes (**5**) is expected for α,β-unsaturated sulphones under basic conditions,[14] and equilibration by re-elimination of ethoxide ion is expected on the basis of earlier work.[15,16]

In the cyclobutane series, the processes which followed the ring fission in the cyclopropyl series cannot occur; reactions are, therefore, simpler.

Kinetics.—Because the products of the reactions are mainly the alkoxy adducts (**6**), there was insufficient difference between the u.v. spectra of products and starting materials to provide an accurate spectrophotometric procedure for following the reactions. The [1]H n.m.r. spectra of the product mixtures were complicated by the presence of more than one product. Because the slowness of reactions gave time for equilibration between alkene and ethoxy adduct, however, rates of reaction were followed by using individual reaction mixtures, with measurement by high-field (400 MHz) [1]H n.m.r. of the changes of concentrations of starting material. Results are in Table 1, in which results for the cyclopropane analogues are included for comparison. Kinetic data are in Table 2.

Results and Discussion

The rate constants (Table 1) determined at several temperatures allow evaluation of the activation parameters for the reactions, and permit comparison with values obtained previously for cyclopropanes.

Mechanisms of the Reactions.—For the cyclopropanes studied earlier, assignment of mechanism required careful examination of the intermediates on the multi-stage pathways.
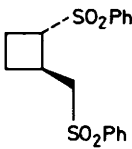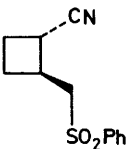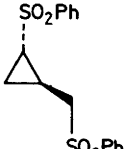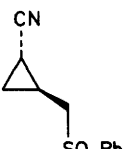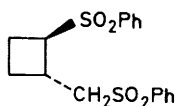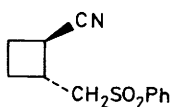
Table 1. Rate constants, activation parameters, and ranks for eliminative ring fission

	$k_{obs.}$ [a,b]	$\Delta H^{\ddagger}$ [c]	$\Delta S^{\ddagger}$ [d]	Rank [e]
(2a)	8.2×10^{-8}	125.0 [f]	37 [f]	4.3
(2c)	4.1×10^{-7}	130.8	71	4.9
(1a)	4.7×10^{-3} [g]	74.0 [g]	-42 [g]	8.8 [g]
(1b)	1.9×10^{-3} [g]	104.8 [g]	50 [g]	8.3 [g]

[a] Reactions in EtONa–EtOH; units $dm^3 mol^{-1} s^{-1}$; results for cyclopropanes at 25.0 °C. [b] Results for cyclobutanes at 25 °C from reactions at higher temperatures. [c] $kJ mol^{-1}$. [d] $J K^{-1} mol^{-1}$. [e] $\log k_{obs.} - \log k_1 + 11$. [f] These values replace those inadvertently inserted in the preliminary communication which referred to the isomerisation of (2b) to (2a) (see text). [g] Results from ref. 3.

Table 2. Kinetic data for eliminative ring fission of cyclobutanes

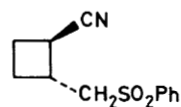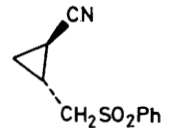|	$t/°C$	$k/dm^3 mol^{-1} s^{-1}$
(2a)	50.0	4.4×10^{-6}
	60.0	1.8×10^{-5}
	67.0	5.1×10^{-5}
	70.0	7.0×10^{-5}
(2c)	50.0	2.5×10^{-5}
	55.0	5.0×10^{-5}
	60.0	1.37×10^{-4}
	65.0	2.6×10^{-4}
	70.0	4.1×10^{-4}

For the cyclobutanes, assignment is straightforward; ring fission is slow and estimation of deprotonation rates under the reaction conditions is possible by measurements previously described.[17] The estimated value for (2a) (Table 3) is *ca.* 10^4 times greater than $k_{obs.}$ values and it is clear that deprotonation is not involved in the rate-determining step. This conclusion is strengthened by

determination of the rate of detritiation of the sulphone (2c). The value[17] of the primary kinetic tritium isotope effect for this process is *ca.* 7.1. There can be no question, therefore, when the known very rapid reprotonation of sulphonyl-stabilised carbanions is taken into account,[18] that ring fission of the carbanions (3) (Scheme 2) follows slowly upon rapid equilibration with the conjugate acids (2). In addition, the sulphone (2b) was recovered from partial reactions in EtOD with complete deuteriation at the exocyclic methylene group.

Results.—Ring opening of the cyclobutanes (2a and c) is 5.7×10^4 and 4.8×10^3 times slower than that for their cyclopropane analogues (1a and b). It was to be expected that the less strained cyclobutanes should be slightly less reactive than the cyclobutanes; if the extent of expression of ring strain energy found for cyclopropanes[3] at 46% were to be maintained in the cyclobutanes, rate ratios of about 5:1 at 25 °C would be expected. The observed ratios suggest a discrepancy between free energies of activation for fission of cyclopropanes *versus* cyclobutanes of about 21 $kJ mol^{-1}$.

As mentioned earlier, the mechanism of elimination in both series is $(E_1cB)_R$. The detritiation rates show that differentials between the pre-equilibrium constants are not responsible for the large reactivity differences observed. The ratio of the deprotonation rate constants for the cyclopropane (1b) and the cyclobutyl analogue (2c) is 1.7:1 (Table 3). The difference in

Table 3. Rates of detritiation of sulphones

Sulphone		$k_{detrit.}$ [a,b]
(2c)	CN / CH$_2$SO$_2$Ph	$6.9 \pm 0.04 \times 10^{-2}$ [c]
(1b)	CN / CH$_2$SO$_2$Ph	12.0×10^{-2} [d]
	PhSO$_2$ — SO$_2$Ph	6.6×10^{-2} [e]

[a] In sodium ethoxide–ethanol at 25 °C. [b] Units dm^3 mol^{-1} s^{-1}. [c] This work. [d] Ref. 3. [e] Ref. 17.

behaviour lies, therefore, in the different propensities of the rings to undergo fission.

Activation Parameters.—Table 1 shows that the differentials in the enthalpies of activation for ring fission between cyclopropanes and cyclobutanes greatly exceed the overall ring strain energy differences. The entropies are partly compensatory. We have no direct evidence that extents of ring fission in the transition structure are the same in each series but all the information that we have so far collected on activated eliminations suggests that extents of cleavage of the bond to the leaving group are small in both cyclic[3] and acyclic[19,20] systems. Also, the fact that leaving-group ranks are so insensitive to activating group and medium[21] speaks of a small and consistent amount of leaving-group bond cleavage. We suggest (see later) that release of excess of enthalpy in cyclobutanes lags behind that in cyclopropanes for all but very small extents of ring cleavage. It is not too surprising that entropies of activation are more favourable for cyclobutanes; the constraint of a larger number of atoms is being partially lifted in the transition structure.

Sources and Symptoms of Strain in Small Rings.—For cyclopropanes, the chief source of strain is the distortion of the C–C–C angle caused by incorporation in a ring. This has been estimated[22,23] to be responsible for about 75% of the total excess of enthalpy; the remainder is contributed by the eclipsing interactions (torsional strain).

For cyclobutane however, the angle distortion is much less severe and together with the torsional interaction probably accounts for 40–50% of the excess of enthalpy.[22a,23] The estimates of the balance between torsional and angle strain vary according to the conformation adopted by the ring. In the puckered conformation, torsional interactions are reduced at the expense of a slight increase in angle strain. The remainder of the excess of enthalpy results from 1,3 and 2,4 repulsive interactions.[22,23] The opposite carbon atoms of the ring are well within the sum of the van der Waals radii. The 1,3 and 2,4 internuclear distances for (2c) are 213 and 215 pm, respectively from the X-ray crystal structure[24] (calculated directly from Figure 2) and the sum of the Van der Waals radii for carbon is about 280 pm.[25]

Excess of Enthalpy and Bond Extension in Strained Rings.—When three- and four-membered rings open, all the factors
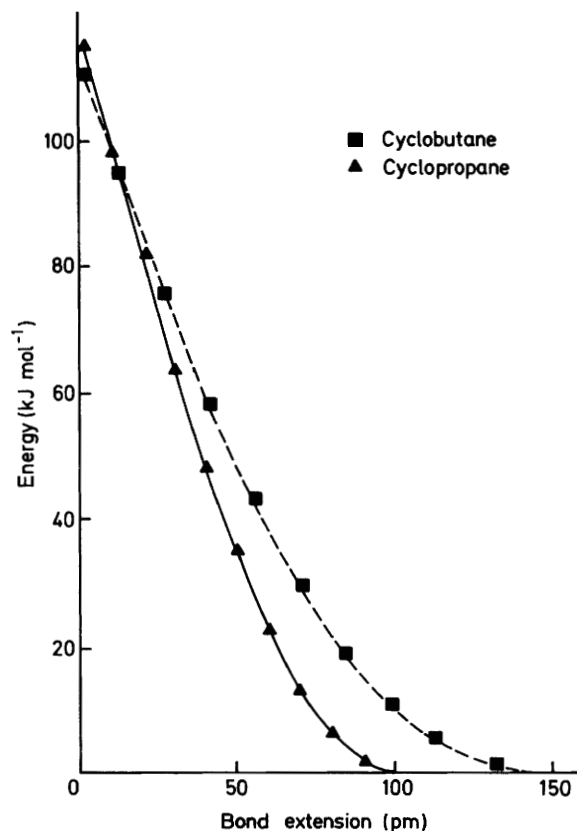

Figure 1. Excess of enthalpies of cyclopropane and cyclobutane as a function of extension of one carbon–carbon bond

responsible for the excess of enthalpy diminish. The ring angles widen, rotation around the carbon–carbon bond(s) becomes possible so as to reduce torsional strain and, for the cyclobutane, the 1,3 and 2,4 carbon–carbon distances increase. The change in excess of enthalpy as a function of the extension of one bond for cyclopropane and for cylobutane has been estimated by the approach pioneered by Dunitz and Schomaker,[23] with modification according to recent calculations by Page.[26]

It was assumed (i) that as one bond of the ring is extended, the change in the other carbon–carbon bond and carbon–hydrogen distances towards the acyclic norms of 154 and 109 pm, respectively, is linear with extension of the breaking bond, and (ii) that variation of torsion angles towards 60° is linear with bond extension. The energy of the structure with normal (60°) torsion and bond (109.5°) angles is set to zero, and for cyclopropane the final carbon–carbon distance for the breaking bond is 251 pm, or a 100 pm extension from that in the intact ring. The torsional and stretching constants used for cyclopropane were those given by Page.[27a] These allow derivation of the torsional strain, E_T, as 25.41 kJ mol^{-1} when the torsion angle $\varphi = 0$, and the extensional strain E_S[27a] as 4.43 kJ mol^{-1} in intact cyclopropane. The total (thermodynamic) strain for cyclopropane is 115.4 kJ mol^{-1}; hence the total angle strain E_A by difference is 85.5 kJ mol^{-1} and the angular constant $k_A = 1.16 \times 10^{-2}$ kJ mol^{-1} K^{-1}.

Similarly for *planar* cyclobutane, from the same torsional and extensional constants together with the angular constant derived for cyclopropane, $E_T = 33.9$ kJ mol^{-1}; $E_S = 3.26$ kJ mol^{-1}; and $E_A = 17.7$ kJ mol^{-1}. Subtraction of the total of these terms from the total thermodynamic excess of enthalpy of 110.4 kJ mol^{-1} gives the value for the 1,3 interaction $E_{1,3} = 55.6$ kJ mol^{-1}, in agreement with the Dunitz estimate.[23] If the puckered conformation is considered, the values become $E_A = 17.8$;
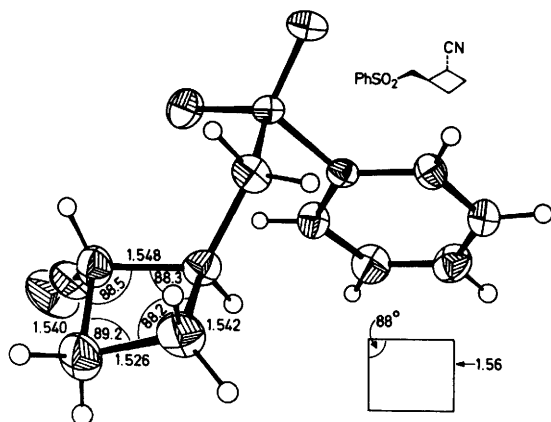
Figure 2. ORTEP representaton of the crystal structure of (E)-2-phenylsulphonylmethylcyclobutanecarbonitrile
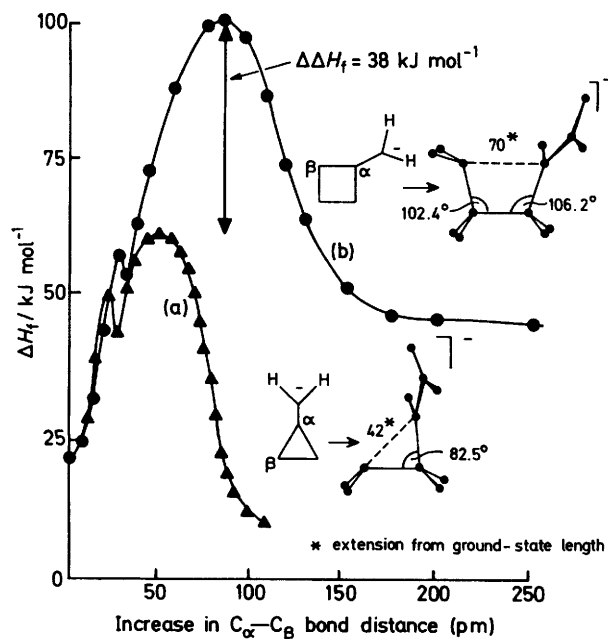

Figure 3. ΔH_f Values for (a) cyclopropylmethyl and (b) cyclobutylmethyl carbanions as a function of increase in the C_α–C_β carbon–carbon bond length calculated using MINDO3; inserts give shape and extension at the ΔH_f maxima

$E_T = 22.0$; $E_S = 3.26$; and $E_{1,3} = 67.6$ kJ mol⁻¹. The bond extension to $\theta_{CCC} = 109.5$ and $\theta_{torsion} = 60°$ is 139 pm. Intermediate values for each system give the curves in Figure 1.

The Figure shows that at very small extensions of one bond in a cycloalkane, the excess of enthalpy of cyclopropane remains higher than that of cyclobutane. As bond extension increases, however, the curves cross, and at other than very small extensions, the excess of enthalpy of cyclobutane decreases less sensitively as a function of bond extension than does that of cyclopropane. This is true of all of the components of this enthalpy. For dispersion of all of the excess of enthalpy, extension of a single bond in cyclobutane of 139 pm is required, whereas for cyclopropane the value is 100 pm. An *ab initio* study of the eliminative fission of cyclopropylcarbinyl and cyclobutylcarbinyl anions has recently been completed.[27b]

Rank Change as an Indication of Transition State Structure.— What, then, is the relationship of these conclusions to our results? The change of reactivity in an elimination reaction which is produced by constraining the bond to the leaving group
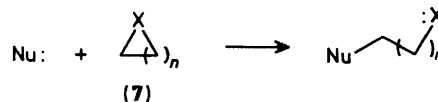
within a strained ring has been put on a quantitative basis by *ranking* the strained leaving group as before[3] (Table 1). Ranks can also be assigned to the cyclobutanes by the same procedure. Such ranking then quantitatively denotes the effect of strain on nucleofugality. The values of Table 1 in fact largely parallel the rate differences between the substrates; there is little differential to be taken into account in the deprotonation rates[17] of the two series.

The ranks for the cyclopropanes compared with that of the unstrained comparator suggest that about 46% of the strain energy is released in the transition structure.[3] Reference to Figure 1 suggests that about 46% of the strain energy is released at a C–C bond extension of about 32 pm. For cyclobutanes, the same comparison suggests a release of only about 26% of the excess of enthalpy of the ring at the transition structure and a C–C bond extension at the transition structure of about 25 pm. These conclusions for the cyclobutanes are not, however, supported by the more positive $\Delta S^‡$ values for four-membered-ring fission (Table 1) or molecular orbital calculations (Figure 3). On this basis the different reactivities turn out to be due to the lesser sensitivity of strain in the cyclobutane series to the extension of a ring bond.

Because we were unable to adduce other information on the natures of the transition structures, as a basis for discussion of these reactivities, we felt it important to attempt to eliminate other factors that might contribute to differential reactivities. A particularly difficult assumption that we have been compelled to adopt throughout our strain work is that ring strain is insensitive to ring substituents. Again, there is little direct evidence that bears upon this assumption and thermochemical evidence is not forthcoming for the particular substrates that we have used. In the comparison of 1,2-dimethylcyclopropanes with 1,2-dimethylcyclopentanes there is an 18.4 kJ mol⁻¹ differential between Z- and E-isomers for the former against 24.7 kJ mol⁻¹ for the latter. *Calculated* strain energies of (Z)- and (E)-dimethylcyclopropanes are, however, 24 and 13 kJ mol⁻¹, respectively, *higher* than for cyclopropane itself.[6] We considered that actual geometries of our substrates might reveal any particular factors that could have a bearing on strain energies. X-Ray structures could not be obtained for our cyclopropyl substrates[3] but the X-ray crystal structure[24] of (2c) (Figure 2) shows clearly that the normal puckered conformation of the ring is maintained and that bond lengths and angles are close to normal. On the basis of evidence at present to hand, therefore, we do not consider that any special factors which do not apply to the parent ring systems need to be taken into account.

It should be emphasised at this stage that the 'anomalous' behaviour of four-membered rings when compared with three-membered rings is not confined to this particular system, nor indeed to nucleophilic eliminative ring fission.[28,29] In nucleophilic substitutive ring cleavage (Scheme 6) we have shown[30] that for substrates (7) the three-membered ring ($n = 1$) to four-membered ring ($n = 2$) ratio varies from $10^4:1$ (X = O) to $10^5:1$ (X = S). The comparison is particularly striking for the thiacycloalkanes because the strain energies for the system $n = 1$ and $n = 2$ are almost exactly the same.
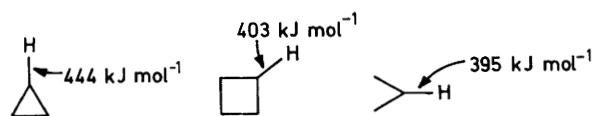
In eliminative ring fission of oxacycloalkanes (Scheme 7), the three-membered-ring[2] to four-membered-ring[31] ratio is *ca.* $6 \times 10^5:1$, and in homolytic eliminative ring fission (Scheme 8) the three-membered-ring[32] to four-membered-ring[33] ratio is $10^{3.7}:1$. Ingold[32] considered that if the enthalpies of the ring
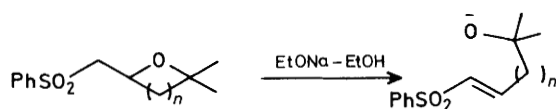
Scheme 6.
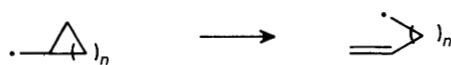
Scheme 7.

Scheme 8.

Scheme 9.

systems are broken down into the individual contributions of the bond strengths (Scheme 9) the results for homolytic fission can be accounted for.

Thus the total enthalpies are known from combustion data and the C–H bond strengths from halogenation kinetics. The conclusion follows that because of the high C–H bond strengths in cyclopropane, the C–C bonds must be correspondingly weaker.[34] If this factor is taken into account along with the strain energies of the rings, the plot of $\log k_{rel}$ vs. ring strain plus ΔD(C–H) is rectilinear.[33] Although this analysis contains the arbitrary choice of the C–H differential for a single bond, it does work remarkably well for homolytic ring fission. Such processes for non-polar substrates are well known to respond directly to differentials in bond dissociation energies.[35] Such is not the case for heterolytic cleavage and we must hesitate to extend this analysis to our results for heterolytic fission. We have encountered the same large differences between the behaviours of three- and four-membered-ring systems in eliminative cleavage of cycloalkanols.[36,37] This problem is, in principle, susceptible to semiempirical calculations. We report on preliminary calculations in this here (see later), and in the following paper.[37] It is also striking that, in comparison with their more strained three-membered-ring counterparts, *closure* of four-membered rings, especially carbocyclic, by intramolecular nucleophilic substitution is a much slower process.[38–41]

Molecular Orbital Calculations.—We have carried out calculations, using MINDO3, on the heats of formation of species generated by elongation of a ring bond adjacent to the substituent in the cyclopropylmethyl carbanion and in the cyclobutylmethyl carbanion. At each increment of extension the geometry is fully optimised; plots of heats of formation vs. bond extension are in Figure 3.

The results confirm our initial conclusions reached using the simple molecular mechanics approach. The energy maximum for the cyclopropane is reached at a lesser extent of bond extension than for the cyclobutane and the maximum for the cyclobutane is 38 kJ mol⁻¹ greater than for the cyclopropane. The $\Delta\Delta H_f$ value is in fair agreement with the mean enthalpy of activation difference measured kinetically (Table 1).

The opening cycloalkylmethyl carbanions undergo considerable contortion, as evidenced by the geometries derived at each increment of bond extension. The shapes of the bond-extended species are shown in Figure 3. We emphasise, of course, that these calculations are for (unsolvated) carbanions in the gas phase and, moreover, for carbanions lacking the stabilising cyano or phenylsulphonyl groups attached to the carbanion in the solution reactions.

The $\Delta\Delta H_f$ profiles of Figure 3 have been arbitrarily super-imposed at the zero of bond extension for ease of comparison. The divergence between the profiles at large bond extensions, e.g. 110 pm, is at least 40 kJ mol⁻¹. It is tempting to ascribe this relative stabilisation of the cyclopropylmethyl/but-3-enyl carbanion to homoconjugation. The profiles show for each system a small minimum corresponding to rotation of the methylene group about the bond to the ring.

Ab initio calculations on eliminative fission in cyclopropyl-methyl and cyclobutylmethyl carbanions have been carried out and will be reported on shortly in this journal.[27b]

Experimental

For general directions see Part 41.[3]

trans-*Methyl* 2-*Cyanocyclobutanecarboxylate* (**8**).—Dimethyl 1-cyanocyclobutane-1,2-dicarboxylate[42] (25 g) was added to a mixture of sodium chloride (14.8 g) and water (5.7 cm³) in dimethyl sulphoxide (125 cm³). After 4 h at 150 °C, addition to brine and extraction with ether gave an oil (14.4 g) which on distillation gave the *ester* (13.6 g), m.p. 76 °C at 0.5 mmHg (bath 109 °C), n_D^{20} 1.4530 (Found: C, 60.4; H, 6.3; N, 10.3. $C_7H_9NO_2$ requires C, 60.4; H, 6.5; N, 10.1%).

The ester was shown by ¹H and ¹³C n.m.r. to be a mixture of cis- and trans-isomers. Flash chromatography on silica gel in 3:2 light petroleum–ether gave first the trans-isomer [δ_H(CDCl₃) 3.75 (s, 3 H), 3.45 (m, br, 2 H), and 2.35 (m, br, 4 H); δ_C 23.13, 23.26, 24.27, 41.58, 52.11, 120.20, and 171.92]; and then the cis-isomer [δ_H(CDCl₃) 3.80 (s, 3 H), 3.45 (m, 2 H), and 2.45 (m, 4 H); δ_C 22.20, 23.91, 25.34, 40.28, 52.11, 119.55, and 171.40]. The esters (0.5 g) were separately subjected to acid hydrolysis (aqueous 10% hydrochloric acid at reflux for 16 h). The ester of higher R_f on saponification gave trans-cyclobutane-1,2-dicarboxylic acid, m.p. 130 °C (lit.,[43] 129—130 °C), and the ester of lower R_f the cis-diacid, m.p. 137 °C (lit.,[44] 136—137 °C). Each diacid (0.2 g) was treated with an excess of acetyl chloride at reflux. In the case of the lower melting acid this gave an oil showing a broad i.r. absorption centred at 3 000 cm⁻¹ and a strong band at 1 680 cm⁻¹. The higher melting acid gave the anhydride of the cis-diacid (m.p. 71 °C) (lit.,[45] 77—78 °C) ($\nu_{C=O\ str.}$ 1 820 and 1 750 cm⁻¹).

1-*Cyano*-2-*phenylsulphonylmethylcyclobutane* (**2c**).—The preceding trans-ester (10 g) in dry bis-(2-methoxyethyl) ether (100 cm³) was treated with lithium bromide (6.9 g) and sodium borohydride (3.0 g).[46] The mixture was boiled under reflux with stirring until t.l.c. showed no further change. Dichloromethane (200 cm³) was added to the cold mixture, which was neutralised (HCl) and dried. Distillation gave the *alcohol* (**9a**), b.p. 77 °C at 0.1 mmHg (5.9 g); $\nu_{max.}$ 3 400 (s) and 2 220 cm⁻¹ (s) (Found: C, 65.1; H, 8.2; N, 12.9. C_6H_9NO requires C, 64.9; H, 8.1; N, 12.6%). Treatment of the alcohol (2 g) with thionyl chloride (4.6 g) in chloroform (20 cm³) gave, on evaporation, a residue of the *chloride* (**9a**; Cl for OH) (2.88 g), b.p. 57 °C at 0.1 mmHg (1.72 g), $\nu_{max.}$ 2 220 cm⁻¹ (s) (Found: C, 55.8; H, 6.0; N, 10.8. C_6H_8ClN requires C, 55.6; H, 6.2; N, 10.8%). This (1.2 g) was treated with a methanolic solution of sodium benzenethiolate prepared from benzenethiol (1.12 g) and sodium (0.23 g) in methanol (10 cm³). After refluxing for 2 h, addition of water and extraction gave the *sulphide* (**10a**) (100%), b.p. 135 °C at 0.25 mmHg, $\nu_{max.}$ 2 220 cm⁻¹ (Found: C, 71.3; H, 6.0; N, 6.7. $C_{12}H_{13}NS$ requires C, 70.9; H, 6.4; N, 6.9%). Oxidation of the sulphide (1 g) in methanol (30 cm³) with hydrogen peroxide (30%; 3 cm³) and ammonium molybdate (0.3 g) in water (3 cm³) gave, on extraction after 6 h, the *sulphone* (**2c**) (86%), m.p. 104 °C (from toluene) (Found: C, 61.2; H, 5.8; N, 6.3. $C_{12}H_{13}NO_2S$ requires C, 61.2; H, 5.5; N, 6.0%); δ_H(CDCl₃) 2.25 (4 H, m), 3.0—3.3 (4 H, m), and 7.8 (5 H,

m); δ_C 24.43, 25.99, 27.42, 34.7, 60.04, 120.46, 128.26, 129.69, 134.24, and 138.65.

cis-2-Phenylthiocyclobutanecarboxylic Acid (**11**).—Benzene-thiol (0.52 g) was added to cyclobutenecarboxylic acid[47] (0.46 g). After 1 h, the mixture was cooled to 0 °C, precipitating the cis-*acid* (200 mg), m.p. 104.5 °C (from ether–light petroleum) (Found: C, 63.7; H, 5.5. $C_{11}H_{12}O_2S$ requires C, 63.5; H, 5.3%); n.O.e. at 400 MHz confirmed the assignment.

2-Phenylthiocyclobutylmethanol (**12**).—The preceding acid (200 mg) in dry THF under N_2 at -20 °C was slowly treated with borane–THF complex[48] (1M; 1.05 cm³). There was slight effervescence and after 2 h t.l.c. showed starting material to be still present. More borane–THF (1.05 cm³) was added and the mixture was warmed to -15 °C. Thereafter evaporation at 20 °C gave a residue (150 mg) which on flash chromatography gave the mixed cis- and trans-*sulphide alcohol* (64%) as an oil (Found: C, 68.3; H, 7.2. $C_{11}H_{14}OS$ requires C, 68.1; H, 7.2%).

1-Chloromethyl-2-phenylthiocyclobutane (**13**).—The sulphide alcohol (4.3 g) in chloroform (80 cm³) at 0 °C was treated with thionyl chloride (3.2 g) and a few drops of pyridine. After refluxing for 2 h, more thionyl chloride (2.6 g) was added and refluxing was continued until there was no further change (t.l.c.). Distillation gave the mixture of *cis-* and *trans*-chloride (72%), b.p. 100 °C at 0.1 mmHg (bath 130 °C).

cis-1-*Phenylsulphonyl-2-phenylsulphonylmethylcyclobutane* (**2b**).—The mixture of chloro sulphide isomers (3.3 g) was added to a solution of sodium benzenethiolate prepared from benzenethiol (1.9 g) and sodium (0.35 g) in dry ethanol (100 cm³). After 3 h at reflux, dilution with water and extraction gave a residue (4.05 g) which, on distillation, gave first unchanged cis-*chloride* (0.94 g), b.p. 114 °C at 0.1 mmHg (bath 144 °C) (Found: C, 62.3; H, 6.2. $C_{11}H_{13}ClS$ requires C, 62.1; H, 6.1%) [δ_H (CDCl₃) 2.10 (m, 4 H), 3.00 (m, 1 H), 3.70 (m, 2 H), 4.10 (d, 1 H), and 7.25 (m, 5 H); δ_C 23.26, 26.25, 41.45, 42.23, 46.00, 125.66, 128.00, 128.91, and 136.84]; and then a *cis–trans* mixture of the bis-sulphides (**14**), b.p. 179 °C at 0.1 mmHg (bath 200 °C) (59%) (Found: C, 70.9; H, 6.2. $C_{17}H_{18}S_2$ requires C, 71.3; H, 6.3%), the ¹³C n.m.r. spectrum of which showed peak doubling. The cis-chloride (2.1 g) was kept with a solution of benzenethiol (1.2 g) and sodium (0.25 g) in t-butyl alcohol (50 cm³) at reflux for 3 days. Work-up as before and distillation gave first unchanged chloride (1.37 g), b.p. 122 at 0.25 mmHg, and then cis-1-*phenylthio-2-phenylthiomethylcyclobutane* (1.91 g, 67%), b.p. 180 °C at 0.15 mmHg, n_D^{20} 1.6288 (Found: C, 71.6; H, 6.3. $C_{17}H_{18}S_2$ requires C, 71.3; H, 6.3%); δ_H(CDCl₃) 2.1 (m, 4 H), 2.92 (m, 1 H), 3.17 (d, 2 H), 4.13 (m, 1 H), and 7.25 (m, 10 H); δ_C 24.56, 26.38, 35.22, 38.33, 43.14, 126.96, 127.22, 131.12, and 135.28.

Oxidation of the bis-sulphide mixture containing mainly *trans*-isomer (2 g) with *m*-chloroperbenzoic acid (6.2 g) in dichloromethane at 0 °C gave, on work-up after 4 days, a residue (3.7 g) which on crystallisation gave the cis-*bis-sulphone* (**2b**) (31%), m.p. 131 °C (from ethanol) (Found: C, 58.0; H, 5.3. $C_{17}H_{18}O_4S_2$ requires C, 58.3; H, 5.1%); δ_H(CDCl₃) 7.6—8.0 (10 H, m), 2.5—3.9 (4 H, m), and 2.3 (m, 4 H); δ_C 21.96, 25.60, 31.45, 57.05, 60.17, 128.13, 129.43, 133.98, 138.37, and 139.7; configuration confirmed by n.O.e. at 400 MHz. The mother liquors showed the presence of the *trans*-isomer but attempts at crystallisation failed.

Oxidation of the pure *cis*-bis-sulphide (0.13 g) with 30% hydrogen peroxide (0.2 ml) in acetic acid (5 cm³) at 100 °C for 4 h gave the *cis*-bis-sulphone (0.16 g), m.p. 131 °C alone or mixed with the material obtained from the *cis–trans* mixture.

Products.—Because of the small amounts of material available we were unable to characterise directly the components of the product mixtures. We therefore synthesized the alkenes (**15**) and subjected them to the reaction conditions. In each case the mixtures of products were identical (t.l.c., i.r., and ¹H and ¹³C n.m.r.) with those obtained by eliminative ring fission of the cyclobutylmethyl sulphones.

4-*Cyanobutanol*—4-Chlorobutyl benzoate (3.2 g) and potassium cyanide (1.1 g) were kept at 100—110 °C for 1.5 h in Me_2SO (30 cm³). Addition to water and extraction with ether gave the ester (2.31 g), b.p. 141 °C at 0.4 mmHg.[48] Saponification of the ester with an equimolecular amount of sodium hydroxide in 1:1 v/v ethanol–water (15 min at 100 °C) and extraction with ether gave the alcohol (0.68 g), b.p. 129 °C at 10 mmHg (Found: C, 59.7; H, 8.9; N, 13.9. Calc. for C_5H_9NO: C, 60.0; H, 9.0; N, 14.1%).

5-*Cyano-1-phenylsulphonylpent-1-ene* (**15a**).—4-Cyanobutan-1-ol (1.56 g) and pyridinium dichromate (8.7 g) were stirred for 20 h in dichloromethane (20 cm³). Addition of ether (100 cm³) and filtration through 'Hy-flo' filter gave, after evaporation, a dark oil (1.0 g), $v_{max.}$ 2 720, 2 200, and 1 720 cm⁻¹. The crude aldehyde (1.0 g) was added to a solution at -80 °C prepared from methyl phenyl sulphone (1.6 g) and a solution of butyl-lithium in hexane (1.5M; 6.8 ml) in dry tetrahydrofuran (40 ml). The mixture was kept at -15 °C for 4 h, adjusted to pH 1, and then extracted with dichloromethane. The crude alcohol (2.1 g), $v_{max.}$ 3 400, 2 240, 1 300, and 1 150 cm⁻¹, was treated with tosyl chloride (3.5 g) in pyridine (50 ml). The mixture was stirred at 40 °C for 16 h, poured into dilute hydrochloric acid, and extracted. Flash chromatography gave unchanged methyl phenyl sulphone (0.85 g), m.p. and mixed m.p. 85 °C, and the *alkene* (0.23 g) as an oily semi-solid (Found: C, 61.0; H, 5.5, N, 6.1. $C_{12}H_{13}NO_2S$ requires C, 61.3; H, 5.5; N, 6.0%); δ_H(CDCl₃) 1.9 (m, 2 H), 2.5 (m, 4 H), 6.6—7.1 (m, 2 H), and 7.8 (m, 5 H); δ_C 16.63, 23.37, 30.02, 118.64, 127.61, 129.30, 132.29, 133.46, 140.08, and 143.59.

1,5-*Bisphenylsulphonylbut-1-ene* (**15b**).—Methyl phenyl sulphone (1.56 g) in dry THF (50 cm³) at -80 °C was treated with butyl-lithium (7.3 cm³ of a 1.5M-solution). To the mixture was added 4-phenylthiobutanal[36,37] and after 4 h at -60 °C the mixture was adjusted to pH 1. Extraction gave the crude alcohol (3.05 g), $v_{max.}$ 3 500, 1 300, and 1 150 cm⁻¹, which was directly treated with toluene-*p*-sulphonyl chloride (3.6 g) in pyridine (50 cm³). After 16 h at 40 °C the mixture was diluted with hydrochloric acid; extraction gave an oil (2.26 g), a mixture of several components (t.l.c.), which, on flash chromatography, gave unchanged methyl phenyl sulphone (0.95 g), m.p. and mixed m.p. 85 °C, and then the *alkene* (0.42 g) as an oil (Found: C, 63.9; H, 6.0. $C_{17}H_{18}O_2S_2$ requires C, 64.1; H, 5.7%), $v_{max.}$ 1 300 and 1 150 cm⁻¹; δ_H(CDCl₃) 1.80 (m, 2 H), 2.40 (m, 2 H), 2.95 (t, 2 H), 6.4—6.9 (m, 2 H), and 7.7 (m, 10 H); δ_C 27.03, 30.28, 33.14, 126.31, 127.61, 129.04, 129.30, 129.69, 131.25, 133.33, 135.79, 140.60, and 145.67.

The sulphone sulphide (0.36 g) in methanol (20 ml) was treated with 30% aqueous hydrogen peroxide (2 cm³) and a solution of ammonium molybdate (0.1 g) in water (1 cm³). After 18 h, extraction gave the *bis-sulphone alkene* (0.36 g), m.p. 167 °C (from ethanol) (Found: C, 58.1; H, 5.0. $C_{17}H_{18}O_4S_2$ requires C, 58.3; H, 5.1%); δ_H 2.0 (m, 2 H), 2.4 (m, 2 H), 3.2 (t, 2 H), 6.4—7.4 (m, 2 H), and 7.8 (m, 10 H); δ_C 20.79, 29.63, 54.97, 127.61, 127.87, 129.30, 129.43, 132.03, 133.46, 133.85, 138.78, 140.08, and 143.85.

Kinetics.—Rates of ring fission of (**2a**) were determined by removal of samples of reaction mixtures containing the

Table 4. cis-to-trans-Isomerisation of 1-phenylsulphonyl-2-phenyl-sulphonylmethylcyclopropane (2b) ⟶ (2a)

$10^5 k^a$	$t/°C$	$\Delta H^{\ddagger\,b}$	$\Delta S^{\ddagger\,c}$
16	40.0		
42	46.0	98	−4
55	50.0		
210	62.0		

^{a} Units dm^3 mol^{-1} s^{-1} in ethanolic sodium ethoxide. ^{b} kJ mol^{-1}. ^{c} J K^{-1} mol^{-1}.

substrates in ethanolic sodium ethoxide, quenching in acidified brine, and extracting with dichloromethane. Identical conditions were used for each sample. To each extract was added a known amount of bisphenylsulphonylmethane as internal standard and the extract was evaporated. Multiple individual reactions were also used. Examination of the residues by ^{1}H n.m.r. at 400 MHz allowed accurate integration of the methylene protons of the cyclobutane ring of (2a) at δ 3.13 against those of the standard at δ 4.80. For (2b) the same procedures were used as well as examination of samples by ^{13}C n.m.r. For (2c), low-field ^{13}C spectra (C-2 signal at 34.7 p.p.m.) versus the internal standard (tetramethylthiourea; δ 43.7) were used on individual reactions. For the isomerisation reactions (Table 4) reactions were followed by the loss of the signal at δ 3.86 due to the cis-isomer.

Detritiation Experiments.—Sulphone (2c). The sulphone (0.5 g) in dioxane (10 cm^3) and water (7 cm^3) was treated with aqueous 0.1M-sodium hydroxide (2.5 cm^3) and tritiated water (0.25 cm^3). The mixture was kept at 40 °C for 14 h. Dilution and extraction gave labelled sulphone (0.5 g), m.p. 104 °C alone or mixed with an authentic specimen. Longer reaction times gave amide.

The labelled sulphone (50 mg) was kept in ethanolic 0.1M-sodium ethoxide at 25 °C. Samples (1 cm^3) of the solution were injected into acetic acid (5 cm^3) and the solutions were evaporated. The residues were taken into toluene (9 cm^3) containing the scintillating agent t-butyl PBD (5 g l^{-1}) and counted in a Phillips liquid scintillation counter. The results are in Table 3.

Acknowledgements

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