

Elimination and Addition Reactions. Part 44.¹ Eliminative Fission of Cycloalkanols

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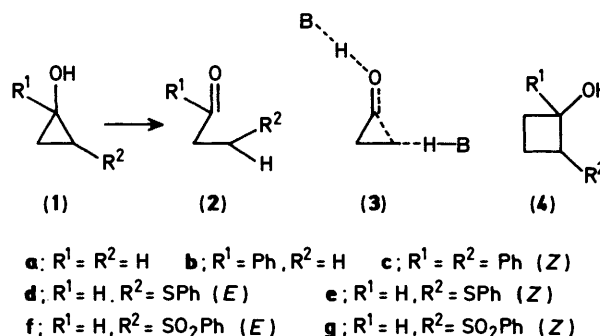
Activation parameters for the fission of cyclopropanols and cyclobutanols with phenyl groups α or phenylthio or phenylsulphonyl groups β to the hydroxy group have been obtained. The results show very large differences in reactivity between cyclopropanols and cyclobutanols; such differences are also found in energy profiles for the opening of cycloalkoxide ions obtained by using MINDO3. The results are entirely compatible with other three-membered/four-membered ring comparisons and the role of strain in these systems is discussed. Attempts to extend the well established enforced catalysis of cycloalkanol ring fission to electrophiles other than Brønsted acids have failed.

In preceding papers of this series, we reported on alkene-forming eliminations which involve rupture of a bond to a leaving group strained by its incorporation in a small ring. In this paper we describe an investigation of the rupture of carbocyclic rings involving carbonyl-forming elimination.

Because of their involvement in acyl-transfer processes, carbonyl-forming eliminations are the most widespread of all organic reactions. Notwithstanding this situation, however, these reactions have proved very poorly amenable to investigation of the details of the processes involved. They have the widest range of leaving groups seen in any organic reaction and for familiar leaving groups, such as halogen, onium, and so on, the individual stages of the process of elimination and leaving group protonation, as in amide hydrolysis, can all be very rapid processes.

Earlier papers in this series and information from other groups of workers have demonstrated that eliminations involving carbon leaving groups are invariably sluggish and that the pK_a value of the conjugate acid of the leaving group gives little insight into the propensity of the group for departure. Carbon leaving groups are, of course, familiar in carbonyl-forming eliminations such as retro-aldol and the reverse of cyanohydrin formation. In such examples, the leaving group is considerably stabilised. In the present work, we were concerned to compare the behaviour of carbon leaving groups in alkene- and in carbonyl-forming eliminations. For the former, considerable stabilisation of the leaving group is a pre-requisite for reaction and rates have been seen¹ to be greatly accelerated when the leaving-group connection is strained by incorporation into a small ring. Carbonyl-forming eliminations involving rupture of strained rings are the subject of this paper.

It has been known² for more than forty years that cyclopropanols (**1**) are unstable, undergoing rearrangement in basic conditions to aldehydes or ketones (**2**) (Scheme 1). Such compounds were studied particularly thoroughly by De Puy and his collaborators,³ who established that, in basic media, the regioselectivity of the reaction was entirely in accord with protonation on that carbon atom for which the pK_a value of the conjugate acid was the lower. For cyclopropanol itself some approximate kinetic data were obtained *via in situ* hydrolysis of the acetate. No evidence was sought in these studies as to the precise mechanisms of the reaction involved and this matter was taken up again later by Thibblin and Jencks⁴ in connection with enquiries as to the nature of concerted processes. It was concluded that for the cyclopropanol (**1b**), ring opening in basic, protic, media involved enforced general (pre-association) acid catalysis.⁵ Separation of the unstabilised carbon leaving group [as in (**3**)] required the proximity of an appropriate proton



Scheme 1.

donor, and strong evidence was adduced in favour of a process involving concerted formation of the carbonyl group, ring cleavage, and carbon protonation. Thibblin and Jencks⁴ also showed that the rate of cleavage of (**1c**) was enhanced 10⁵-fold by attachment to the leaving group of the additional phenyl group, and concluded that a considerable degree of negative charge resided on the departing carbon atom in the transition structure (**3**).

Eliminative ring fission of cyclobutanols has been extensively studied with respect to synthetic application.⁶ Ring cleavage is considerably assisted by the presence of β -arylthio or β -alkylthio groups.^{6b,c} For some spiro-systems, Trost and his collaborators⁷ have found that reactions are slow, a finding attributed to the operation of the Thorpe–Ingold (*gem*-dialkyl) effect.

Against the background of this considerable previous work on the reactivity of cycloalkanols, which had not, however, considered explicitly the role of strain in such reactions, we have compared the behaviour of cyclopropanols with that of cyclobutanols, addressing ourselves in particular to the following questions:

(i) What is the effect of strain in such reactions and, in particular, how does the reactivity of cyclobutanols compare with that of their nearly identically strained three-membered-ring counterparts?












(ii) What can be deduced about the nature of the transition structure on the basis of the response of reactivity to substituent effects?

(iii) What is the nature of the proton-transfer step?

(iv) How do calculations of energy surfaces match with experimental findings?

Our objective, therefore, was to make a general comparison

Table 1. Carbonyl-forming eliminative fission of cycloalkanols

	k_{rel}^a	ΔH^\ddagger^b	ΔS^\ddagger^c		k_{rel}^a	ΔH^\ddagger^b	ΔS^\ddagger^c
	(1a) $1.5 \times 10^{-1 d,o}$				(4e) $1 \times 10^{-4 k}$	117	12
	(1b) 1^e	72 (84) ⁿ	-50 (-17) ⁿ		(4f) 500^m		
	(1d) $1.1 \times 10^{2 f}$	83	+18		(4g) $500^{l,m}$		
	(4a) $(9.2 \times 10^{-10})^{g,h}$	(132) ⁿ	(-29) ⁿ		(2a) 5.8^o	51 ^o	-114 ^o
	(4b) $7.4 \times 10^{-10 h,i}$ $(7.8 \times 10^{-10})^n$	120 (125) ⁿ	-63 (-54) ^h		(2e) 9.28×10^3		
	(4d) $6.4 \times 10^{-5 j}$	97	-65				

^a Reactions in aqueous NaOH-dioxane (5:3 v/v) at 25 °C. Unless otherwise stated rate constants did not vary with base concentrations in the range 0.16–1.2M. ^b In kJ mol⁻¹. ^c In J K⁻¹ mol⁻¹. ^d Revised measurement; see text and ref. 3e. ^e k For 1M-NaOH-dioxane-H₂O, 3.1×10^{-3} ; k for 1M-NaOH 1.46×10^{-3} dm³ mol⁻¹ s⁻¹; for 0.1M-NaOH 2.09×10^{-3} dm³ mol⁻¹ s⁻¹. Value obtained in ref. 4; 1.45×10^{-3} dm³ mol⁻¹ s⁻¹. ^f k For reactions on 4-nitro- and 3,5-dinitro-benzoate (see text) in 0.32M-NaOH; changed from 1.5×10^{-1} to 1.9×10^{-1} over the range 0.16–0.60M-NaOH. In 3:1 v/v EtOH-H₂O, the rate constant was lower by a factor of 1.5. ^g Estimated from reactions at ca. 180 °C. ^h Reactions in stainless steel bombs pre-conditioned above 150 °C. ⁱ Estimated for reactions at 150–180 °C. ^j Estimated from reactions at 70, 75, 80, and 95 °C. ^k Estimated from reactions at 80, 89, 91, and 100 °C. ^l Minimum value; configuration determined from X-ray crystal structure and configuration of (4d) thereby derived. ^m Minimum value see text. ⁿ Values in parentheses in water. ^o Values for conversion into 2-methylprop-2-enal, which also slowly reacts under conditions used; rate constants and activation parameters are to be regarded as approximate.

of the reactivities of cyclopropanols (1) with that of cyclobutanols (4).

Eliminative fission of cyclopropanols and cyclobutanols has been reviewed,^{6a} and it is clear that the latter are much less reactive than the former. This has been commented upon by Trost.⁷

Substrates.—For cyclopropanol itself (1a), De Puy's reactivity data^{3e} have been revised (Table 1). In the original work on the base-catalysed cleavage of cyclopropanol,^{3e} the complexity of the reaction (to give 2-methylpent-2-enal) was recognised and reactions of prop-2-enal and cyclopropanol (or cyclopropyl acetate) were followed only to 1–4% of reaction.* In our work we have followed reactions to the maximum absorbance change and, in the case of cyclopropanol, find a considerable induction period corresponding to the build up of prop-2-enal, the precursor of 2-methylpent-2-enal. We suspect that this induction period may have given rise to the apparent underestimate of the reactivity of cyclopropyl derivatives reported earlier.^{3e} 1-Phenylcyclopropanol (1b) and (*E*)-2-

phenylthiocyclopropanol (1d) were obtained by the literature procedures. However in the preparation of (1d) it was found impossible to obtain a pure specimen because of partial ring cleavage to 3-phenylthiopropenal, the structure of which was confirmed by comparison with an authentic specimen obtained by base-catalysed addition of benzenethiol to propenal. Attempts to remove the aldehyde with Girard's reagent T or hydrogen sulphite were ineffective and the alcohol was converted into the crystalline 4-nitro- and 3,5-dinitro-benzoate. The former was also oxidised to the sulphone. Rates of reaction were followed by monitoring the release of benzenethiolate from the initial product (2e) of ring fission. This approach is valid only if transesterification of the 3,5-dinitrobenzoate and elimination of benzenethiolate from (2e) are both rapid in comparison with ring fission of (1d). In separate experiments we have measured the rates of elimination of benzenethiolate from (2e) [k (25 °C) = 13.50 ± 0.05 dm³ mol⁻¹ s⁻¹]. This is nearly 100 times faster than ring fission and we have shown that the 4-nitro- and 3,5-dinitro-benzoate of (1d) release benzenethiolate at the same rate. 3,5-Dinitrobenzoates are known to be much more reactive, however, in alkaline hydrolysis⁸ and these checks establish that ring fission is rate-determining. 1-Phenylcyclobutanol (4b) was obtained from cyclobutanone.⁹ The (*E*)- and (*Z*)-2-phenylthiocyclobutanol (4d and e) were obtained as a

* We thank Professor C. H. De Puy for access to the original data of Dr. Mahoney and for his encouragement in these redeterminations.

mixture by reduction of 2-phenylthiocyclobutanone¹⁰ with sulphurated borohydride.¹¹ The sulphone (4g) was obtained by oxidation of (4e). The configuration of (4g), and hence of (4d) and (4e), followed from the X-ray crystal structure (Figure 1).

The preparations of (1b and d) deserve special comment in view of the reactivity of these substrates; each is prepared in conditions in which the ions resulting from *O*-deprotonation of (1) are produced in high concentrations in aprotic media. The sulphide (1d), for example, is obtained by treatment of 1,3-bisphenylthioopropan-2-ol with two equivalents of *n*-butyllithium in tetrahydrofuran. This point will be returned to later.

Kinetics.—As Table 1 shows, there is a considerable spread of reactivity. The most reactive substrates, (1d) and (2e), required stopped-flow spectrometric methods. Conventional spectrophotometric procedures near room temperature sufficed for (1a and b) and higher temperatures for (4d and e). The cyclobutanols without leaving-group stabilisation, (4a and b), required extremely severe conditions. A period of days at 180 °C in aqueous *m*-sodium hydroxide was typical and, as Pyrex glass was more reactive than the cyclobutanols in such conditions, measurement on individual reactions had to be carried out in stainless steel tubes pre-heated for 1 week with aqueous *m*-sodium hydroxide; loss of cyclobutanol was followed by ¹H n.m.r. Activation parameters were evaluated to allow direct comparison of the systems of different reactivities.

Results and Discussion

The rate constants in Table 1 show the very large differences in reactivity between three- and four-membered-ring systems with the same substitution pattern. Variations of 10⁷ and 10⁹ between the systems at 25 °C are typical, and these ratios are very much (10³–10⁵) greater than those found for alkene-forming ring fission of cycloalkanes.¹

In the preceding paper,¹ we demonstrated that simple molecular mechanical considerations of the effect of extension of a single bond on the excess of enthalpy of a small-ring cycloalkane could account for the relatively modest difference in reactivity between the cyclopropanes and the cyclobutanes. For the present results, such considerations are clearly out of the question. The calculated (STO-3G) strain energy of cyclopropanol (117 kJ mol⁻¹)¹² is close to that of cyclobutanol (see later).¹³ To account for the observed differences, there would have to be a large difference between the transition structures for the two systems. Substituent effects on reactivity (see later) do not suggest that there are any gross differences between them.

Consideration of excess of enthalpy as a guide to reactivity is beset with two obvious difficulties; when substituents such as hydroxy are present, the excess of enthalpies may not be known and the tempting assumption that substituents do not affect the excess of enthalpies of rings has to be made. In the present cases, the strain energy of cyclobutanol is 105 (ref. 13) or 111 (ref. 14) kJ mol⁻¹, close to that for cyclobutane itself.¹⁵ For the other substrates, no direct information is available; in an attempt to detect any distortion occasioned by substituents, as well as to define its configuration, the crystal structure of (4f) has been determined (Figure 1).¹⁶ This shows that the 1,2 and 1,4 bond distances are close to those in cyclobutane (156 pm) but that the other two ring bonds, especially the 2,3, are very much shorter. So far as the comparison between cyclopropanes and cyclobutanes is concerned, it might be expected that substituents would stabilise cyclopropanes in preference to cyclobutanes.¹⁷ The Thorpe–Ingold effect¹⁸ of *gem*-dimethyl substitution is more pronounced for the smaller ring system, and in the comparison of the substrates (1b) and (4b) interaction of the phenyl group with the ring system would be expected to stabilise

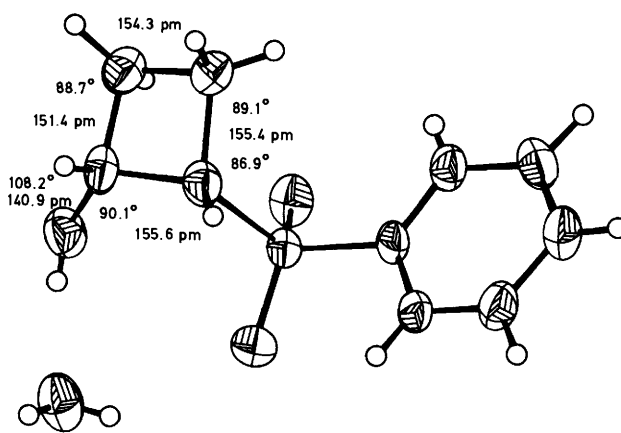
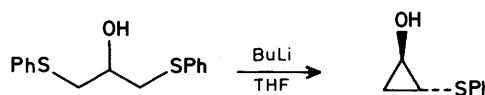


Figure 1. X-Ray crystal structure of *cis*-2-phenylsulphonylcyclobutanol



Scheme 2.

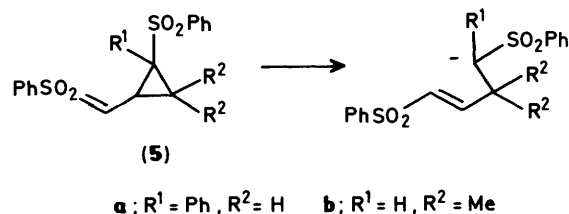
the cyclopropane rather than the cyclobutane. Nevertheless, a ratio of 10⁷:1 in favour of fission of the cyclopropane is found.

Stability of Cycloalkoxide Ions.—Thibblin and Jencks⁴ have clearly shown that carbonyl-forming eliminative fission of the cyclopropanols requires the availability of a proton donor. We have found that treatment of the cyclopropanol (1b) with butyllithium in tetrahydrofuran (THF) gives a solution from which the alcohol can be recovered, even after 24 h at 20 °C, when the solution is rapidly quenched with a large excess of dilute acid. If water is added slowly to the solution, no alcohol is recovered and the product is propiophenone. These observations are clearly consistent with the detailed earlier work and similar results were obtained for (4e). The reaction (Scheme 2) used for the preparation of (1d) is a striking example not only of the facility of 1,3-elimination even with such a moderately ranked nucleofuge¹⁹ as SPh, but of the stability of the product under severely basic conditions in the absence of the proton donor.

We have also investigated the stability of the oxyanion of 1-phenylcyclopropanol in THF in the presence of other electrophiles to find out whether 'enforced electrophilic catalysis' is restricted to protons. Treatment of 1-phenylcyclopropanol in THF successively with butyl-lithium and benzaldehyde, benzophenone, acetophenone, methyl phenyl sulphone, methyl vinyl ketone, or an excess of the cyclopropanol produced negligible amounts of ring fission at room temperature in periods of 2–60 h.

In view of the previous detailed studies of these carbonyl-forming eliminations we have concerned ourselves specifically with the response of reactivity to ring size and to the effects of substituents on both three- and four-membered systems.

Substituent Effects on the Reactivity of Cyclopropanols.—Comparison of the data for (1a) with those for (1b) shows the expected trend of product stabilisation, but differences are not large. The heats of formation of ketones are substantially more negative than those of their aldehyde isomers²⁰ (*cf.* CH₃CH₂CH₂CHO –241.2; CH₃CH₂COCH₃ –275.7 kJ mol⁻¹), and the heat of formation of an aryl-conjugated ketone is substantially greater than that of a non-conjugated isomer²⁰ (*cf.* PhCOCH₂CH₃ –167.2; PhCH₂COCH₃ –152.1). The sum



Scheme 3.

of these differences (*ca.* 45 kJ mol⁻¹) if fully expressed would produce a rate ratio at 25 °C of about 10^{3.6}:1, suggesting that ring opening is little advanced in the transition structures (3) for these reactions. This conclusion from substituent effects is supported by calculations (see later), but it must be remembered that the calculations refer to the situation in which proton addition (the enforced catalysis of Jencks) is *not* included.

We were also concerned to calibrate the leaving-group departure; attachment of a phenylthio group to the leaving carbon atom produces a rate enhancement of *ca.* 10³. This is a modest enhancement when the effect of a phenylthio group on carbanion stability is taken into account. Bordwell and his collaborators²¹ have shown that the p*K*_a values of carbon acids, the counter ions of which are poorly delocalised, are reduced by about 10 units on attachment of a phenylthio group. The effect is, as expected, dependent upon the nature of the carbanion. When the charge on carbon is extensively delocalised, as by nitro or carbonyl groups, the effect is much less than for more localised carbanions such as those stabilised by α-sulphonyl groups. In making the present comparison we have chosen the higher value, consistent with the lack of any stabilising group in the parent system. It has been shown clearly that a carbanion is *not* involved in the ring fission of cyclopropanols;⁴ in this connection, rearrangement of such a carbanion has been ruled out for (1d) or (1e) by labelling experiments.²¹ Nevertheless the modest effect of β-substitution suggests a modest extent of ring cleavage in the transition structure. The detailed mechanism for fission of the 2-phenylthiocyclopropanol (1d) may be different from that of cyclopropanol (1a) itself. It is significant, however, that both (1b) and (1d) are stable under strongly basic conditions in aprotic media.

Comparison of Cyclopropanols and Cyclobutanols.—The striking feature of the results in Table 1 is the very large difference in reactivity between the three- and four-membered-ring systems. For alkene-forming eliminative fission,¹ the three-membered- to four-membered-ring ratios were between 10³ and 10⁴:1. The activation parameters showed substantial differences between the enthalpy terms, which were partially compensated by more favourable entropies in the case of the cyclobutanols. In the present cases, however, both enthalpy and entropy terms disfavour the cyclobutanols with respect to cyclopropanols, and this is true whether or not the leaving group is stabilised by a phenylthio group.

In the previous paper¹ we suggested that the reluctant fission of cyclobutylmethyl carbanion was due to the fact that the strain energy declines less rapidly with the extension of the α,β-bond than for cyclopropane, and that a less favourable compromise between double-bond formation and ring bond cleavage with attendant strain release is struck in the case of cyclobutane. In the present cases, the balance is even less favourable. Calculations (see later) suggest that the α,β-bond extension in the transition structure is again greater for the cyclobutoxide ion, but the experimental entropy of activation is less favourable. This substantial difference between three- and four-membered rings, notwithstanding their closely similar

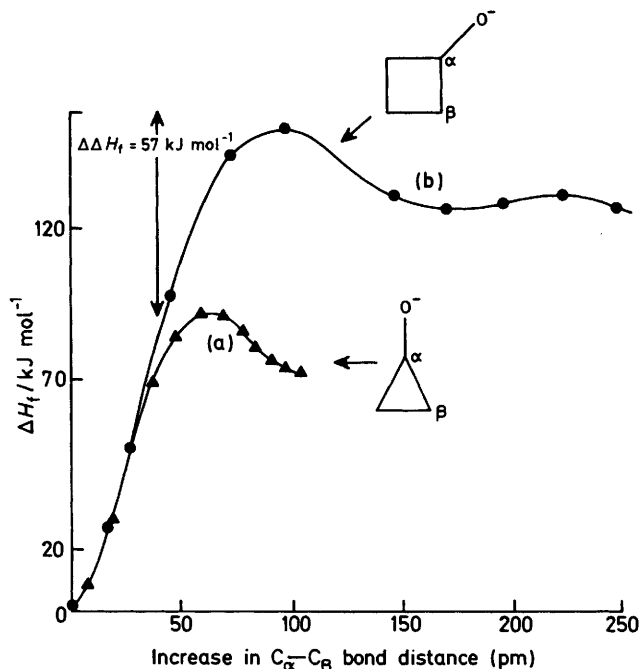


Figure 2. ΔH_{\ddagger} vs. α,β -bond extension for (a) cyclopropoxide and (b) cyclobutoxide ion; energies for both species are normalised to zero in the starting structure

strain energies, has been noted before in a number of other reaction types. These include nucleophilic substitutive fission of oxacycloalkanes,²² nucleophilic eliminative fission of carbocycles,¹ homolytic eliminative fission of carbocycles,²³ and, most recently, eliminative fission of oxacycloalkanes.²⁴

Stereochemical Effects.—There is a small difference between the rate constants for *cis*- and *trans*-isomers (4d and e). Similar small stereochemical effects have been seen in the *cis-trans* pairs (5a)²⁵ and (5b)²⁶ (Scheme 3). In all the data the small differences are disguised by cancellation of substantial differences in the activation parameters. In the present work on cyclobutanols, fission of the *E*-isomer (4d) has the lower enthalpy of activation; in the work on cyclopropanes, this was found for the *Z*-isomers.^{25,26}

Calculations.—In order to understand the process of ring cleavage better, we have carried out calculations, by MINDO3, of the heat of formation of the cyclopropoxide and cyclobutoxide ions as a function of the extension of one ring bond as the ring opens; *cf.* (3). The geometries are fully optimised and the energies at each fixed point of C–C bond extension are minimised. The results are in Figure 2. The plots obtained differ substantially from those obtained for the eliminative cleavage of cycloalkylmethyl carbanions. In this case, there is, unsurprisingly, a large difference between the heats of formation of the alkoxide ions and the open-chain ω-oxo carbanions. In the case of the four-membered ring in particular, little stabilisation is available by further α,β-C–C bond extension once the maximum has been passed. The calculated situation, of course, refers to energies of gas-phase species. Furthermore, the role of enforced acid catalysis in solution has been clearly demonstrated.⁴ Ring cleavage is concerted with carbon protonation and no account of this has been taken in the present calculations. The presence of solvent in the experimental situation emphasises the difference between the alkoxide ion and the carbanion. The former is much more solvated than the

latter. The curves are, nevertheless, strikingly consistent with the experimental data; the $\Delta\Delta H_f$ three-membered/four-membered ring value of 57 kJ mol⁻¹ at the maxima is close to the $\Delta\Delta G^\ddagger$ (25 °C) value for 1-phenylcyclopropanol versus 1-phenylcyclobutanol of 51 kJ mol⁻¹. The maximum for the four-membered ring is displaced considerably in the direction of C–C bond cleavage relative to the three-membered ring. The maxima occur at extensions of 98 and 52 pm, respectively. This is in accord with our postulate¹ that the excess of enthalpy decreases less rapidly as a function of bond extension in the four- than in the three-membered ring. Further, at the energy maximum, the C–O bond length has shortened from 127.0 to 122.1 pm for cyclopropoxide; for cyclobutoxide the change is from 127.0 to 120.7 pm.

Conclusions.—The ability of a strained cycloalkanol to expel an unstabilised carbon leaving group in a carbonyl-forming elimination is very striking. The difference in behaviour between three- and four-membered rings, so obvious in all ring-fission reactions studied earlier, is even more exaggerated in carbonyl-forming elimination.

Calculated energy profiles for ring fission are remarkably consistent with the experimental results.

Experimental

For general directions see Part 43.¹

3-Phenylthiopropional had b.p. 127 °C at 10 mmHg (lit.,²⁷ b.p. 128–139 °C at 10 mmHg). Cyclobutanol (Aldrich) was used as supplied. 1-Phenylcyclopropanol was obtained by De Puy's method.²⁸ 1-Phenylcyclobutanol was prepared from phenylmagnesium bromide and cyclobutanone; b.p. 76–78 °C at 0.1 mmHg, m.p. 37 °C (from pentane) (lit.,⁹ 41–43 °C). Treatment of the alcohol (100 mg) in aqueous m-sodium hydroxide at 188 °C for 24 h with subsequent neutralisation (HCl) and extraction gave a residue (90 mg), the i.r. spectrum of which showed no absorption near 3 400 cm⁻¹ and was identical with that of butyrophenone.

Kinetics of the ring fission of cyclopropanol were determined by following the formation of 2-methylprop-2-enal. This is the dehydration product from the aldolisation product of propanal initially formed. Propanal forms this product without the induction period which is characteristic of reactions with cyclopropanol. We have derived rate constants for cyclopropanol on the assumption that aldolisation–dehydration of propanal is fast, and have used a graphical method²⁹ to obtain the ratios of ring fission and aldolisation. Knowledge of the rate of aldolisation of propanal measured separately then yields the rate constant for ring fission of cyclopropanol.

(E)-2-Phenylthiocyclopropanol (**1d**).—The material obtained by Tanaka's²⁹ method (45%) had b.p. 126 °C at 0.8 mmHg and contained up to 20% of 3-phenylthiopropional (by ¹H n.m.r.). The crude alcohol (9 mmol) in pyridine (2 cm³) was kept at 85 °C with 4-nitrobenzoyl chloride (9 mmol) in pyridine (2 ml) for 10 min. After 16 h at 20 °C, the mixture was extracted with hot toluene; removal of the solvent gave the 4-nitrobenzoate (45%), m.p. 117 °C (from toluene–light petroleum) (Found: C, 60.7; H, 4.3; N, 4.4. C₁₆H₁₃NO₄S requires C, 60.9; H, 4.2; N, 4.4%). The 3,5-dinitrobenzoate, prepared similarly, had m.p. 121 °C (from toluene–light petroleum) (Found: C, 53.3; H, 3.1; N, 8.1. C₁₆H₁₂N₂O₆S requires C, 53.3; H, 3.3; N, 7.8%); $\delta_{\text{H}}(\text{CDCl}_3)$ 1.32 [m, 1 H, *J*_{1,3} (*cis*) 6.7 Hz, *J*_{2,3} (*trans*) 6.0 Hz], 1.65 [m, 1 H, *J*_{1,3} (*trans*) 3.6 Hz, *J*_{2,3} (*cis*) 9.0 Hz], 2.72 [m, 1 H, *J*_{1,2} (*trans*) 2.0 Hz], 4.60 (m, 1 H), and 7.1–7.3 (m, 5 H); δ_{C} 15.59, 19.75, 58.09, 122.67, 126.18, 128.13, 128.91, 129.3, 131.07, 135.67, 148.66, and 162.56.

Oxidation of the sulphide *p*-nitrobenzoate (1 mmol)

Table 2. Temperature variation of rate constants of eliminative fission of cycloalkanols

Substrate	5:3 v/v Dioxane–water		Water	
	<i>t</i> /°C	10 ⁵ <i>k</i> ^a	<i>t</i> /°C	10 ⁶ <i>k</i> ^a
(1b)	22.2	2 160	26.1	150
	25.5	3 140	30.4	256
	30.4	5 300	35.6	457
	35.2	8 160	40.0	642
	39.9	12 600	46.4	1 470
	45.2	19 960		
(1d)	35.5	52 100		
	25.5	17 800		
	15.5	4 900		
(4a)			150	1.2 ^c
			158	2.4 ^c
			165	4.6 ^c
(4b)	151	4.4 ^c	159	0.96 ^c
	166	31 ^c	166	1.7 ^c
	188	78 ^c	170	2.0 ^c
			175	3.5 ^c
(4d)			184	7.6 ^c
	70.0	6.2		
	75.0	10.8		
	79.5	16.0		
	88.5	55.0		
(4e)	79.5	1.2		
	88.5	2.8		
	90.5	3.5		
	102.0 ^b	9.7		

^a In dm³ mol⁻¹ s⁻¹. ^b Sealed tube. ^c Pre-conditioned stainless steel tube.

suspended in methanol (100 ml) with aqueous 30% hydrogen peroxide (0.67 cm³) and ammonium molybdate (0.3 g) in water (2 ml) gave, after 17 h at 20 °C, the sulphone (89%), m.p. 122 °C (from ethanol) (Found: C, 55.6; H, 3.9; N, 3.9. C₁₆H₁₃NO₆S requires C, 55.3; H, 3.8; N, 4.0%).

Treatment of 4-nitrobenzoate of (**1d**) with ethanolic sodium ethoxide gave a solution the u.v. spectrum of which (200–300 nm) was identical with that of an equimolecular mixture of benzenethiol, propenal, and 4-nitrobenzoic acid under the same conditions. Treatment of the former solution with methyl iodide showed formation of methyl phenyl sulphide (85%) (by g.l.c.; SE 30, N₂ carrier gas at 126 °C) and 4-nitrobenzoic acid was isolated in 57% yield (m.p. and mixed m.p. 242 °C).

Kinetics were determined by following the release of benzenethiolate ion at 270 nm using a Durrum–Gibson stopped-flow spectrometer the output of which was fed to a Northern Instruments NS 600 multichannel analyser and thence to a teletype giving readings of change of transmittance against time.

(E)- and (Z)-2-Phenylthiocyclobutanol (**4d** and **e**).—2,5-Dimethoxytetrahydrofuran was converted into 1,1,4,4-tetrakisphenylthiobutane (86%), m.p. 93.5 °C (lit.,²¹ 93–94 °C), thence into 1,2-bisphenylthiocyclobutane,¹⁰ and thence (from crude product) into 2-phenylthiocyclobutanone,¹⁰ which was purified (52%) by flash chromatography in light petroleum (b.p. 60–80 °C) containing 10% ether on silica gel. Literature¹⁰ yields were doubled when *t*-butyl-lithium was used in place of *n*-butyl lithium. The ketone was reduced with sodium borohydride¹¹ and sulphur in tetrahydrofuran giving a mixture of the *E*- and *Z*-isomer which were separated by flash chromatography in dichloromethane. The first-eluted *E*-isomer had *n*_D²⁰ 1.5890, m.p. 19 °C; $\delta_{\text{H}}(\text{CDCl}_3)$ 1.83–2.35 (m, 4 H), 2.89 (d, 1 H), 4.09 (m, 1 H), 4.48 (m, 1 H), and 7.13–7.31 (m, 5 H); δ_{C} 21.38, 31.21, 49.72, 67.60, 125.55, 125.85, 128.70, and 136.08 (Found: C, 66.9;

H, 7.0. Calc. for $C_{10}H_{12}OS$: C, 66.6; H, 6.7% (lit.,³¹ b.p. 112 °C at 0.4 mmHg, m.p. 30 °C). The *Z*-isomer, an oil, eluted second, had n_D^{20} 1.5900; $\delta_H(CDCl_3)$ 1.48–2.31 (m, 4 H), 2.58 (s, 1 H), 3.56 (m, 1 H), 4.08 (m, 1 H), and 7.17–7.40 (m, 5 H); δ_C 20.63, 29.27, 49.75, 73.69, 126.27, 128.79, 130.27, and 135.61. The 3,5-dinitrobenzoate had m.p. 132 °C (Found: C, 54.7; H, 3.9; N, 7.6. $C_{17}H_{14}N_2O_6S$ requires C, 54.5; H, 3.8; N, 7.5%).

(*Z*)-2-Phenylsulphonylcyclobutanol (4g).—(*Z*)-2-Phenylthiocyclobutanol (2.78 mmol) in dichloromethane (80 ml) at –30 °C was treated with *m*-chloroperbenzoic acid (9.72 mmol). The mixture was kept at –20 °C for 19 h; successive washing with aqueous sodium disulphite and aqueous sodium hydrogen carbonate and evaporation then gave the sulphone (86%), m.p. 86 °C (from di-isopropyl ether); $\delta_H(CDCl_3)$ 1.6–2.6 (m, 4 H), 3.8–4.1 (m, 1 H), 3.9 (s, 1 H), 4.4–4.7 (m, 1 H), and 7.4–8.0 (m, 5 H); δ_C 21.38, 31.21, 49.72, 67.60, 125.85, 128.55, 128.70, and 136.08 (Found: C, 51.9; H, 6.1. $C_{10}H_{12}O_3S \cdot H_2O$ requires C, 52.1; H, 6.1%). The X-ray crystal structure (Figure 1) confirms the configuration and shows the inclusion of a molecule of water in the crystal.

(*E*)-2-Phenylsulphonylcyclobutanol (4f).—Oxidation of the sulphide as for the *Z*-isomer gave the sulphone (85%) as an oil (Found: C, 56.3; H, 5.3. $C_{10}H_{12}O_3S$ requires C, 56.6; H, 5.3%); $\delta_H(CDCl_3)$ 1.7–2.5 (m, 4 H), 3.5–4.0 (m, 1 H), 4.0 (s, 1 H), 4.4–4.8 (m, 1 H), and 7.3–8.0 (m, 5 H).

Kinetics of reactions of cyclobutanols were monitored by 1H n.m.r. for individual reactions. Typically, *cis*-2-phenylthiocyclobutanol (50 mg) in dioxane (6 cm³) at the reaction temperature (102 °C; sealed tubes) was treated with aqueous *m*-sodium hydroxide (10 cm³); after a measured time the mixture was quenched with dilute hydrochloric acid (30 cm³) and extracted with dichloromethane (3 × 25 cm³). Bisphenylsulphonylmethane (20 mg) was added to the extracts as an integral marker, and these were then washed with brine, dried, and evaporated. The 1H n.m.r. multiplet of the proton α to oxygen (δ 4.5) was compared with that of the standard (δ 4.8), giving the amount of starting material. Results are in Table 2. Reactions of the hydroxycyclobutyl sulphones were complete in less than 5 s at 25 °C; rate constants in Table 1 are minimum values.

Product Analysis.—The *cis*- and *trans*-alcohols were treated under the reaction conditions with omission of the internal standard for 5 half-lives. Work-up gave product mixtures which were identical with each other and with those obtained from an authentic specimen of 4-phenylthiobutanal (see later) by t.l.c. and 1H n.m.r.

4-Phenylthiobutanal.—Benzenethiol (0.19 mol) was added to a solution prepared by the dissolution of sodium (0.175 g atom) in ethanol (250 cm³). 4-Chlorobutyl benzoate³² (0.175 mol) was added and the mixture was kept at 60 °C for 30 min. Dilution with brine and extraction gave the crude sulphide (84%), which on saponification with aqueous methanolic sodium hydroxide and flash chromatography of the crude product gave 4-phenylthiobutanal (85%), m.p. 28 °C (lit.,³³ b.p. 112 °C at 0.1 mmHg) (Found: C, 66.2; H, 7.8. Calc. for $C_{10}H_{14}OS$: C, 65.9; H, 7.7%). Treatment of the alcohol with toluene-*p*-sulphonyl chloride in pyridine gave the tosylate (41%), m.p. 47 °C after flash chromatography (Found: C, 61.0; H, 6.0. $C_{17}H_{20}O_3S_2$ requires C, 60.7; H, 6.0%). The tosylate (3 mmol) was kept in dimethyl sulphoxide (10 cm³) at 150 °C for 15 min with sodium carbonate (1.6 g); dilution with brine and extraction with ether then gave the aldehyde (61%)³⁴ [2,4-dinitrophenylhydrazone, m.p. 102 °C (from ethanol) (Found: C, 53.1; H, 4.5; N, 15.7. $C_{16}H_{16}N_4O_4S$ requires C, 53.3; H, 4.5; N, 15.6%); $\nu_{C=O}$ str. 1 730, ν_{O-C-H} str. 2 720 cm⁻¹; $\delta_H(CDCl_3)$

1.83 (m, 2 H), 2.48 (t, 2 H), 2.82 (t, 2 H), 7.17 (m, 5 H), and 9.62 (t, 1 H).

4-Phenylsulphonylbutanal.—Crude 4-phenylthiobutyl benzoate (0.6 mol)³² in methanol (750 cm³) was treated with aqueous 30% hydrogen peroxide (1.13 mmol) containing ammonium molybdate (0.9 g) in water (9 cm³). The mixture was stirred at 20 °C for 18 h; dilution with brine and extraction then gave the sulphone ester (77%), m.p. 75 °C (from di-isopropyl ether) (Found: C, 64.0; H, 5.7. $C_{17}H_{18}O_4S$ requires C, 64.1; H, 5.7%). The sulphone ester (103 mmol) was saponified (93%) with sodium hydroxide (4.5 g) in 20:1 v/w methanol-water. The crude alcohol (18 mmol) was treated with pyridinium dichromate³⁵ (30 mmol) in dichloromethane (5 cm³). After 20 h at 20 °C, ether (100 cm³) was added, and after filtration through silica gel flash chromatography gave 4-phenylsulphonylbutanal³⁵ (24%), $\nu_{C=O}$ str. 1 716, ν_{SO} str. 1 310 and 1 150 cm⁻¹; $\delta_H(CDCl_3)$ 2.0 (m, 2 H), 2.60 (t, 2 H), 3.2 (t, 2 H), 7.5–8.0 (m, 5 H), and 9.7 (t, 1 H) (24%), characterised as the 2,4-dinitrophenylhydrazone, m.p. 191 °C (from toluene) (Found: C, 48.5; H, 3.7; N, 13.8. $C_{16}H_{16}N_4O_6S$ requires C, 49.0; H, 4.1; N, 14.2%).

Recovery of Cycloalkanols from Reactions in Basic Aprotic Media.—Alcohols (1a and d) (0.14 g) were separately kept with butyl-lithium (0.8 ml of a 1.5M-solution in hexane) in THF (10 ml) for 24 h at 0 °C. Inverse quenching and re-extraction showed negligible ring fission. Similarly, the sulphone (4f) (0.31 g) on treatment with butyl-lithium (1.1 mmol) in THF (5 ml) for 15 min at –10 °C and quenching with D_2SO_4 - D_2O gave 2-phenylsulphonyl[2- 2H]cyclobutan[2H]ol with about 12% of ring-opened product. [1H N.m.r. showed small peaks due to 4-phenylsulphonylbutanal at δ 2.0 (m), 2.6 (t), 3.2 (t), 9.7 (s), and 7.2–8.0 (m); peaks at 4.0 (s) and 4.6 (m) had vanished.]

The 2-phenylthiocyclobutanols were recovered after treatment with an equimolecular amount of butyl-lithium in THF at 25 °C for 18 days.

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