Ring Fission of Cycloalkanols: The Different Involvement of Strain in the Reactivity of 3- and 4-Membered Rings

Adrian Bury, Harold A. Earl, and Charles J. M. Stirling*

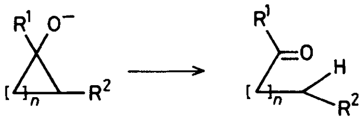
Department of Chemistry, University College of North Wales, Bangor, Gwynedd LL57 2UW, U.K.

Rates of eliminative ring fission of cyclopropanols under basic conditions are 10^5 to 10^9 faster than those of the related cyclobutanols; neither excess enthalpies of the systems nor classical ideas on strain distribution in small rings account for these ratios.

The carbonyl-forming elimination (1) of carbanions is generally restricted, as in the retro-aldol reaction, to examples in which the ejected carbanion is stabilised by the attachment of groups, such as carbonyl. An important exception relates to the situation in which the C–C bond is strained as by incorporation in a strained ring. De Puy[1] has clearly shown that ring opening of cyclopropanols occurs easily under basic conditions and that the regiospecificity of the reaction is entirely consistent with considerable accumulation of negative charge on the (carbon) leaving group. For cyclopropanol itself, an approximate value of the rate constant for ring fission can be extracted (Table 1) from De Puy's data. More recently, Thibblin and Jencks[2] have made accurate measurements of rates of ring opening of aryl cyclopropanols and conclude that the reactions involve enforced general acid catalysis. Departure of the leaving group is contingent upon the availability of a general acid to permit the formation of a C–H bond as part of the concerted processes of carbonyl group formation, ring fission, and carbon protonation.

$$^-\text{O–C–C–G} \rightarrow \text{O=C} + {}^-\text{C–G} \qquad (1)$$

(G = carbanion-stabilising group)

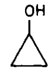
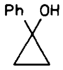
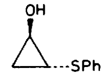
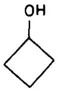
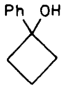
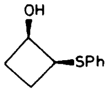
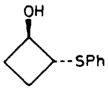
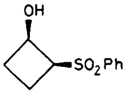


Against this background and as part of our programme of quantifying the effects of strain on reactivity, we have examined the rates of ring fission of a series of cyclopropanols and cyclobutanols (Table 1).

We have not fully defined the detailed mechanisms of these reactions; on the basis of the previous work,[2] each system probably involves enforced acid catalysis. It is most unlikely that a discrete carbanion of very high basicity can be generated in such systems. In this connection, we find that the cyclopropanol (**2**) is recovered quantitatively from long-term treatment of its solution in tetrahydrofuran (THF) with an excess of butyl-lithium when the reaction mixture is rapidly quenched with aqueous buffer (pH 5.5). If, however, water is added slowly to the mixture, the product of ring fission, propiophenone, is obtained.

The cyclopropanols are remarkably more reactive than the cyclobutanols, the latter being disadvantaged relative to the former, both enthalpically and entropically. It is particularly striking that the differences in $\Delta H^\ddagger$ between the cyclobutanols

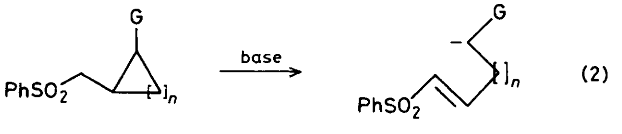
Table 1. Eliminative ring fission of cycloalkanols.

Substrate	$k_{\text{rel.}}$[a]	$\Delta H^{\ddagger}$ [b]	$\Delta S^{\ddagger}$ [c]
 (1)	10^{-3} [d]	—	—
 (2)	1[e]	84	−17
 (3)	1.1×10^{2} [f]	83	+18
 (4)	2.6×10^{-10} [g,h]	—	—
 (5)	7.8×10^{-10} [h,i]	125	−50
 (6)	6.4×10^{-5} [j]	117	+13
 (7)	1.4×10^{-5} [k]	97	−65
 (8)	1×10^{4} [l]	—	—

[a] Reactions in aqueous NaOH–dioxane (5:3 v/v) at 25 °C. Unless otherwise stated rate constants did not vary with base concentration in the range 0.16—1.2 M. [b] kJ mol^{-1}. [c] J K^{-1} mol^{-1}. [d] Estimated from data of ref. 1. [e] k for 1M-NaOH = $1.4 \times 10^{-3}\,\text{M}^{-1}\,\text{s}^{-1}$; for 0.1 M-NaOH, $2.09 \times 10^{-3}\,\text{M}^{-1}\,\text{s}^{-1}$. [f] k for reactions in 0.32 M-NaOH. Rate constant increased slightly, 1.5×10^{-1}—1.9×10^{-1} over the range 0.16—0.60 M-NaOH. [g] Estimated for reactions at 180 °C. [h] Reactions in stainless steel bombs pre-conditioned at > 150 °C. [i] Estimated for reactions at 150—180 °C. [j] Estimated from reactions at 70, 75, 80, and 90 °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 (6) thereby derived.

and cyclopropanols greatly exceed the strain energy differences between cyclopropanol (117 kJ mol^{-1})[3] and cyclobutanol (105[4a] or 111[4b] kJ mol^{-1}). It is possible that α-phenyl substitution alters the strain energy difference between cyclopropanols and cyclobutanols but, if anything, phenyl substitution in the cyclopropanes would be expected[5] to stabilise them relative to the cyclobutanes.

The low reactivity of the cyclobutanols (4) and (5) demanded severe conditions for reactions, several days with 1M-NaOH at 180 °C being typical. This has resulted in the need for very long extrapolations of activation plots to compare data and, accordingly, we have also examined the effect of placing a carbanion-stabilising group on the carbon leaving group. Bordwell[6] has shown that phenylthio groups stabilise localised carbanions in dimethyl sulphoxide (DMSO) by about 10 pK_a units. Comparison of substrate (3) with substrates (6) and (7) shows acceleration of ring fission by factors of about 10^5. An acceleration of this magnitude, which is broadly the same for both ring sizes, is therefore consistent with only a moderate degree of ring fission. Similarly for the cyclobutanol (8), stabilisation of the leaving group by about 20 units[6] produces an acceleration of about 10^{10}. It is striking, however, that the entropies of activation for cyclopropanol fission are very much more positive than for cyclobutanol and that the huge differences in reactivity between the 3- and 4-membered ring systems result from adverse values of both $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$.



(2)

G = CN or PhSO_2; n = 1 or 2

In an earlier communication[7] dealing with reactivity differences between 3- and 4-membered rings in alkene-forming eliminations (2), the cyclopropane : cyclobutane reactivity ratios of 10^3—10^4 could just be accounted for on the basis of relief of strain occurring differently in the two systems. In the 3-membered ring, most of the strain is derived from valence angle distortion and this is relieved rapidly on extension of one bond. By contrast, in the 4-membered ring, the major component of strain is the 1,3 (2,4) interaction[8] and a much greater degree of ring opening is needed to offset this. Reactivity differences between cyclobutanes and cyclopropanes could *just* be accounted for[7] on the basis of simple molecular mechanics calculations of the dissipation of excess enthalpy as a result of bond extension, provided this extension was the same in each case. Such arguments cannot account for the present results; instead the activation parameters show that the transition structure for cyclobutanol fission not only relieves less strain ($\Delta H^{\ddagger}$ more positive) but is less open ($\Delta S^{\ddagger}$ less positive) than for cyclopropanol fission.

We are presently engaged in MNDO calculations to attempt to understand this situation better.

We thank the S.E.R.C. and the University College of North Wales for the support of this work, Professor P. v. R. Schleyer and Dr. J. N. Macdonald for their generous help and advice, and Dr. M. B. Hursthouse (Queen Mary College) for the determination of the X-ray crystal structure of the cyclobutane (6).

Received, 27th November 1984; Com. 1677

References

1 C. H. De Puy and L. R. Mahoney, *J. Am. Chem. Soc.*, 1964, **86**, 2653.
2 A. Thibblin and W. P. Jencks, *J. Am. Chem. Soc.*, 1979, **101**, 4963.
3 J. D. Dill, A. Greenberg, and J. F. Liebman, *J. Am. Chem. Soc.*, 1979, **101**, 6814.
4 (a) J. Rocek and A. E. Radkowsky, *J. Am. Chem. Soc.*, 1973, **95**, 7123; (b) H. J. Schneider, G. Schmidt, and F. Thomas, *ibid.*, 1983, **105**, 3556.
5 A. Greenberg and J. F. Liebman, 'Strained Organic Molecules,' Academic Press, New York, 1978, Section 5E2; A. Sevin and P. Chaquin, *J. Org. Chem.*, 1982, **47**, 4145.
6 F. G. Bordwell and D. L. Hughes, *J. Org. Chem.*, 1983, **48**, 2216.
7 H. A. Earl, D. R. Marshall, and C. J. M. Stirling, *J. Chem. Soc., Chem. Commun.*, 1983, 779.
8 N. L. Bauld, J. Cessac, and R. L. Holloway, *J. Am. Chem. Soc.*, 1977, **99**, 8140.