

## Eliminative Fission of Hydroxythietanes: Transition Structures for Cleavage of 4-Membered Rings

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Pathways in nucleophilic fission of hydroxythietanes are determined by the oxidation state of sulphur; for eliminative fission, activation parameters, substituent effects, and comparison with unstrained analogues all suggest a greater degree of ring cleavage in the transition structure for thietanes than for cyclobutanes.

The role of strain in determining reactivity in eliminative fission of cyclobutanols (**1a**) and (**1b**) has been discussed earlier.<sup>1,2</sup> Enormous differences (*ca.*  $10^9$ ) in reactivity between cyclobutanols (**1a**) and (**1b**) and their cyclopropyl analogues in eliminative fission reactions were found.<sup>1</sup> We have concluded elsewhere<sup>2,3</sup> that the origin of such differences lies in the different ways in which strain is released as the rings open. Direct comparison of the reactivity of these strained systems with unstrained systems was, however, frustrated by the non-reactivity of the unstrained analogues.

We now report on eliminative fission [equation (i)] in the thietane derivatives (**1c**–**1g**) and the comparison with the unstrained analogues [equation (ii)] particularly with reference to the effect of strain on reactivity, the nature of the transition state for ring opening, and the competition between eliminative fission and nucleophilic substitutive ring fission [equation (iii)].

Thietanes (**1d**–**1g**) smoothly open in aqueous 1 M-sodium hydroxide giving the carbonyl compounds (**2**) characterised as 2,4-dinitrophenylhydrazones and comparison with authentic specimens. Rate constants and activation parameters are in Table 1. Configurations of the isomeric sulphoxides (**1d**) obtained by oxidation of the thietane (**1c**) have been assigned previously.<sup>4</sup> Their reactivities and activation parameters are similar. Our earlier results for cyclobutanols (**1a**) and (**1b**) are included in Table 1 for comparison.

Table 1 shows that the thietane oxides are much more reactive than the cyclobutanols. This increase in reactivity is to be associated with the attachment of a carbanion-stabilising group to the carbon atom which is detached in ring cleavage. There is evidence (below), however, that this is *not* detached as a free carbanion. The observed accelerations are, presumably, offset by the lower strain energy of thietane (81.9 kJ mol<sup>-1</sup>) compared with that of cyclobutane (106.2 kJ mol<sup>-1</sup>). This is also suggested by the higher reactivity of the cyclobutyl sulphone (**4**) than the thietane dioxide (**1e**) possessing comparable leaving group stabilisation.

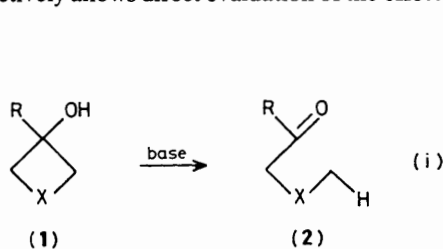
Comparison of the reactivities of (**1f**) and (**1g**) with (**5a**) and (**5b**) respectively allows direct evaluation of the effect of strain

as factors of  $5.2 \times 10^5$  for the sulphoxide and  $4.0 \times 10^4$  for the sulphone. In terms of strain energies, assuming strain in thietanes (81.9 kJ mol<sup>-1</sup>) to be independent of substituent<sup>5</sup> and oxidation state, the strain energy of the 4-membered ring is expressed in acceleration of the reaction to the extent of about 41% for the sulphoxide and 33% for the sulphone. These are to be compared with the value of 26% estimated for alkene-forming eliminations in cyclobutanes.<sup>3</sup>

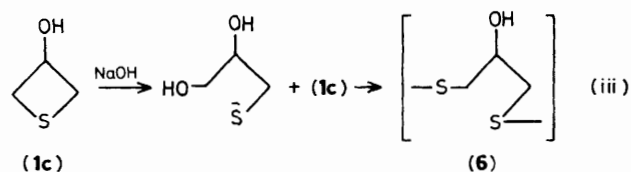
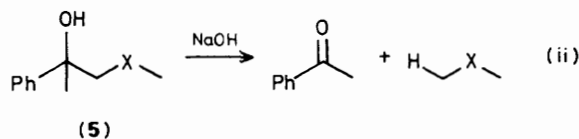
The sensitivity to  $\alpha$ -phenyl substitution in the thietanes [compare (**1d**) with (**1f**) and (**1e**) with (**1g**)] is consistently greater than for cyclobutanes [compare (**1a**) with (**1b**)]. The heat of formation of a phenyl ketone is *ca.* 15 kJ mol<sup>-1</sup> greater than that of the benzylic isomer<sup>6</sup> and the response to  $\alpha$ -phenyl substitution in the thietanes suggests a greater degree of ring cleavage in the thietanes. This is endorsed by the larger contribution of strain energy to acceleration and by the uniformly positive values of the entropies of activation.

In relation to the mechanism of ring fission in the thietanes, sulphoxide (**1f**) shows a  $k_{\text{OH}/\text{H}_2\text{O}}/k_{\text{OD}/\text{D}_2\text{O}}$  value of 0.72. Reactions are effectively zero-order in base (Table 1) and so this is not a primary kinetic isotope effect. This value is the balance of opposing effects. Change from H<sub>2</sub>O to D<sub>2</sub>O increases the 'internal nucleophilicity' of the alkoxide ion but decreases the rate of protonation on the leaving carbon atom. The isotopic discrimination for the formation of (**2f**) from (**1f**), measured by mass spectrometry, gave a value of  $1.7 \pm 0.2$ . This degree of discrimination<sup>7</sup> demonstrates the concertedness of ring fission and protonation and points to enforced catalysis of the overall reaction as seen by Thibblin and Jencks in the cleavage of cyclopropanols.<sup>8</sup>

Finally, thietane (**1c**) shows an interesting difference in behaviour from its analogues with sulphur in a higher oxidation state. Reaction with hydroxide ion gives a hydroxylated polymer whose n.m.r. spectrum is consistent with structure (**6**) [equation (iii)]. We think that reaction occurs by attack of hydroxide ion on C-2 with strain-accelerated displacement of thiolate [equation (iii)]. The resulting thiolate









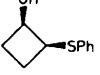
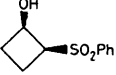
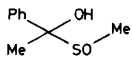
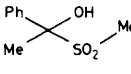


a; R = H, X = CH<sub>2</sub>  
 b; R = Ph, X = CH<sub>2</sub>  
 c; R = H, X = S  
 d; R = H, X = SO  
 e; R = H, X = SO<sub>2</sub>  
 f; R = Ph, X = SO  
 g; R = Ph, X = SO<sub>2</sub>



a; X = SO  
 b; X = SO<sub>2</sub>

Table 1. Eliminative fission of thietanes.

		$k$ (25 °C) <sup>a</sup>	$\Delta H^\ddagger$ <sup>b</sup>	$\Delta S^\ddagger$ <sup>c</sup>
	(1a) <sup>d</sup>	$1.3 \times 10^{-12}$	132 (±1)	-29 (±4)
	(1b) <sup>d</sup>	$1.1 \times 10^{-12}$	125 (±1)	-54 (±4)
	(1c)	$5 \times 10^{-6e}$	—	—
	(1d-cis)	$5.33 \times 10^{-5}$	103 (±2)	+17 (±5)
	(1d-trans) <sup>f</sup>	$4.87 \times 10^{-5}$	109 (±4)	+37 (±2)
	(1e)	$1.40 \times 10^{-2}$	99 (±1)	+50 (±1)
	(1f) <sup>g</sup>	$6.27 \times 10^{-3}$	88 (±1)	+8 (±3)
	(1g)	$6.22 \times 10^{-1}$	94 (±0.1)	+67 (±0.6)
	(3) <sup>d</sup>	$9.0 \times 10^{-8}$	117 (±2)	+12 (±5)
	(4) <sup>d</sup>	$7 \times 10^{-1h}$	—	—
	(5a) <sup>g</sup>	$1.21 \times 10^{-8i}$	96 (±2)	-74 (±5)
	(5b)	$1.57 \times 10^{-5}$	87 (±1)	-46 (±3)

<sup>a</sup> dm<sup>3</sup> mol<sup>-1</sup> s<sup>-1</sup> in NaOH-H<sub>2</sub>O. <sup>b</sup> kJ mol<sup>-1</sup>. <sup>c</sup> J K<sup>-1</sup> mol<sup>-1</sup>. <sup>d</sup> Values from ref. 1. <sup>e</sup> Not elimination, see text. One-point rate constant for nucleophilic *substitutive* fission at 100 °C in 1.5 M NaOH-H<sub>2</sub>O. <sup>f</sup> Reactions carried out on *O*-acetyl compound. <sup>g</sup> Configuration unknown. <sup>h</sup> Minimum value. <sup>i</sup> Estimated from reactions in sealed tubes in the temperature range 67–97 °C.

ion is much more nucleophilic than hydroxide ion and successive nucleophilic attack on new thietane molecules proceeds. This sequence is precluded for the other thietanes by the lower nucleophilicity of the sulphur anion displaced in substitutive ring fission. Cyclobutyl sulphide (3) is more reactive than thietane (1c) in eliminative fission again pointing to the effect of the greater strain of cyclobutanes compared with thietanes.

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