

Absence of the Benzylic Effect in Nucleophilic Ring Opening of Oxiranes

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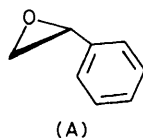
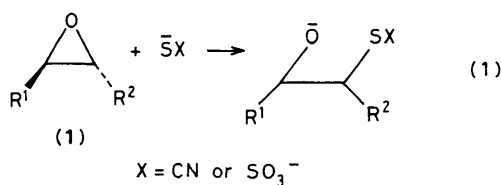
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In reactions of oxiranes with sulphur nucleophiles under conditions in which k_{obs} is pH independent, aryloxiranes show none of the expected enhancement of reactivity; conformational restriction of orthogonal substitution accounts for the observations.

As part of a general study of the effect of strain on reactivity we have examined nucleophilic ring fission of a range of oxiranes.

There is an enormous literature in this field¹ but most work has concentrated on acid catalysed reactions in which protonation at oxygen precedes nucleophilic attack at carbon. In these cases, observed rate constants are composites of the protonation equilibrium constant and the rate constant for nucleophilic ring opening. Because it is difficult to extract values for the protonation equilibria, it is difficult to assess the effect of structure upon reactivity in ring fission under such conditions.

We have studied the reactivity of oxiranes (**1**) with sulphur nucleophiles (equation 1) in the pH range 7–10, this range



being chosen so that the role of pre-protonation can be disregarded. Rate constants were insensitive to pH at the extreme of the pH range studied. Unprotonated oxiranes are not very reactive and in the absence of acid catalysis, the powerful sulphur nucleophiles chosen were required for accurate rate measurements. Results are shown in Table 1.

A long-standing generalisation² that attack in mono-substituted, non-protonated epoxides occurs β to the substituent is understandable on the basis of steric retardation experienced in related electrophiles such as alkyl halides.³ However, benzyl halides are, typically, 10^3 times more

Table 1. Nucleophilic ring fission of oxiranes.

Oxirane	$10^4 k_{\text{SCN}^-}$ ^{a,c} /dm ³ mol ⁻¹ s ⁻¹		$10^4 k_{\text{S}_2\text{O}_3^{2-}}$ ^{b,c} /dm ³ mol ⁻¹ s ⁻¹	
	pH 7	pH 10	pH 7	pH 10
(1a) R ¹ = R ² = H ^d	0.82	1.15	24.3	30.7
(1b) R ¹ = Et, R ² = H	1.01	1.06	23.8	29.8
(1c) R ¹ = CH ₂ Cl, R ² = H	3.53	4.17	124	141
(1d) R ¹ = CCl ₃ , R ² = H	39.1	39.8	—	—
(1e) R ¹ = Ph, R ² = H	1.52	1.03	12.5	13.3
(1f) R ¹ = R ² = Ph ^d	0.08	—	—	—

^a 30 °C. ^b 25 °C. ^c Reactions followed by pH-stat titration in 50:50 v/v aqueous acetone. ^d Rate constants statistically corrected.

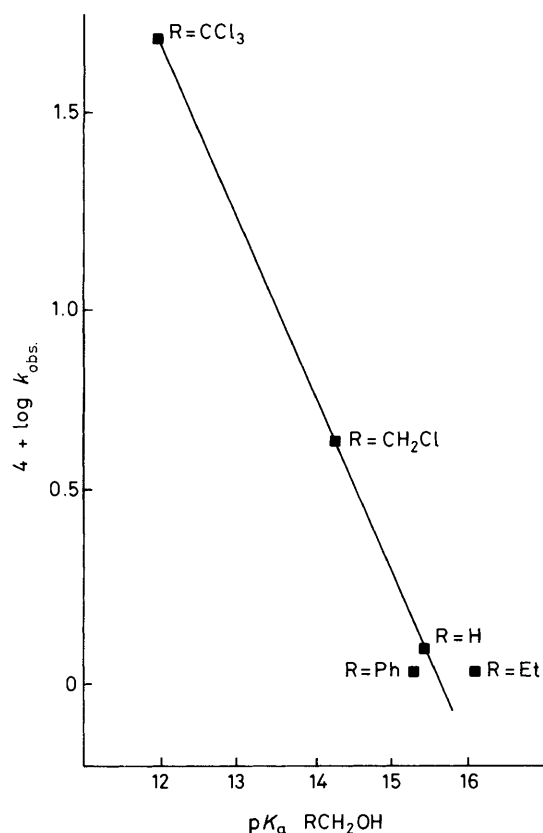


Figure 1. Log k_{obs} for nucleophilic fission of oxiranes (**1**; R² = H) by ^-SCN in acetone-water at pH 10 and 30 °C against pK_a 's of alcohols, RCH₂OH.

reactive than simple alkyl halides in S_N2 reactions.⁴ King and Tsang⁵ have elegantly demonstrated that this is a stereoelectronic phenomenon dependent upon the accessibility of a configuration in which the antiperpendicular alignment of nucleophile, electrophile, and leaving group is orthogonal to the plane of the aromatic nucleus.

A plot of $\log k_{obs}$ for reactions of sulphur nucleophiles vs. the pK_a ⁶ of the alcohol, RCH₂OH, is rectilinear (Figure 1). This is consistent with nucleophilic attack at the β -position and with a considerable degree of C–O bond extension in the transition state.⁷ Contrary to experience with benzylic halides,

however, phenyloxirane (**1e**) conforms closely in behaviour with the other oxiranes studied. It is slightly *less* reactive than oxirane itself and *trans*-2,3-diphenyloxirane is even less reactive. The familiar and expected benzylic acceleration is absent.

Kinetics of reduction of oxiranes with lithium triethylborohydride have recently been measured.⁸ Phenyloxirane is less than half as reactive as 1,2-epoxybutane, in close agreement with our results.

Calculations⁹ show that a nearly bisected conformation (A) is preferred for phenyloxirane (**1e**), the minimum energy being located at an angle of 30° from orthogonality of the two ring planes, so that the C–O bond from the phenyl carrying carbon atom is almost in the plane of the phenyl ring. The rotational energy barrier is 3.2 kcal mol⁻¹ (1 kcal = 4.18 kJ).

In such a conformation for phenyloxirane (**1e**), a trajectory for the nucleophile which is orthogonal to the plane of the aromatic nucleus and antiperpendicular to the leaving (oxygen) group cannot be attained. The abnormally low reactivity of aryloxiranes is thus accounted for.

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