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CONCERTED VERSUS STEPWISE PROCESSES IN ELIMINATIVE FISSION OF OXACYCLES

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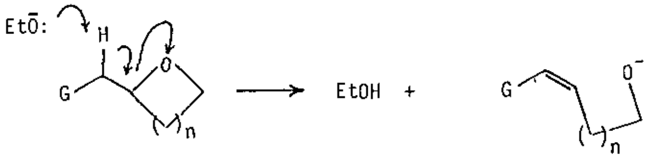
Abstract – 2-Phenylsulphonylmethyloxetan (2a) has been synthesised and the kinetics of base-promoted eliminative ring fission have been determined. The results show, by comparison with the behaviour of related substrates studied previously, that (i) the 3-ring:4-ring differential for concerted processes is much smaller than for stepwise processes, particularly those in which the extent of ring fission is large and (ii) the effect of gem-dimethyl substitution (Thorpe-Ingold effect) is to restrain ring fission but only to a small extent when compared with stepwise processes.

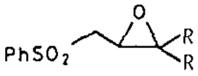
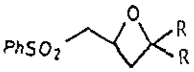
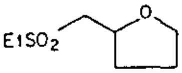
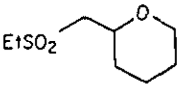
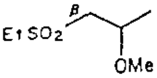
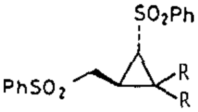
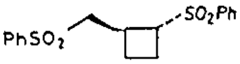
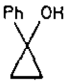
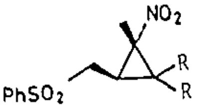
In an initial attempt[1] to evaluate the effect of strain upon reactivity, we examined the reactivity of the series of oxacycles (1), (3), and (4) in eliminative fission reactions of the general type:



We found, as expected, that the oxiran (1a) was very much more reactive than the larger ring homologues (3) and (4). The kinetic data however could not be processed to give information about the effect of strain on reactivity because, as shown in the Table, the mechanisms of reaction are different as between the oxiran on the one hand and the 5- and 6-membered rings on the other. The striking result was, however, that strain in the oxiran turned a sluggish nucleofuge such as methoxy [cf substrate (5)] into one which enforced a concerted (E_2) pathway typical of the very highest ranked nucleofuges such as halide.[2]

At the time of these studies[1] we were unable, because of synthetic difficulties, to study the 4-ring analogue (2a) so as to compare its behaviour with the more (1a) and less (3) and (4) strained substrates. In particular we wished to explore the effect of change of strain on both reactivity and mechanism. A further intriguing question remained. Would gem-dimethyl substitution, well known qualitatively in the 'Thorpe-Ingold' effect,[3] to

TABLE 1. ELIMINATIVE RING FISSION

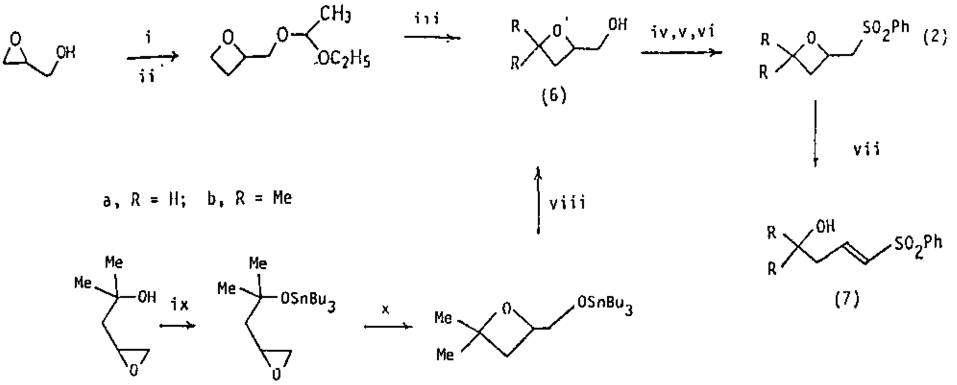
(1)		(a)	4170	2.5×10^{-1}	E_2	1
		(b)	4160	1.1×10^{-1}	E_2	11
(2)		(a)	23.4	2.5×10^{-1}	E_2	
		(b)	15	1.1×10^{-1}	E_2	10
(3)			1.4×10^{-3}	2.5×10^{-1} [c]	$(E_1cB)_R$	1
(4)			2.0×10^{-3}	2.5×10^{-1} [c]	$(E_1cB)_R$	1
(5)			7.5×10^{-5}	2.0×10^{-1} [c]	$(E_1cB)_R$	1
(8)		(a)	4.8×10^{-3} [d]	8.5×10^{-1}	$(E_1cB)_R$	6
		(b)	2.7×10^{-3} [e]	5.0×10^{-1}	$(E_1cB)_R$	11
(9)			8.2×10^{-8}	8.5×10^{-1}	$(E_1cB)_R$	8
(10)			3.1×10^{-3}	–	Enforced acid[f,g] catalysis	9, 13
(11)			2.3×10^{-12}	–	Enforced acid[g,h] catalysis	9
(12)		(a)	16.7	3.5	E_2	11
		(b)	5.3	1.6	E_2 [i]	11

Footnotes: [a] Units: $M^{-1} s^{-1}$ for EtONa/EtOH at 25°C; [b] Units: $M^{1} s^{-1}$ for EtONa/EtOH at 25° see ref. 7; [c] for Et = Ph; [d] $\Delta H^{\neq}$ 74.0 kJ mol^{-1}; [e] $\Delta H^{\neq}$ 95.3 kJ mol^{-1}; [f] ref. 13; [g] for NaOH in aqueous solutions; [h] assigned on basis of arguments of ref. 13 and behaviour of more highly stabilised system discussed in ref. 14; [i] tentative assignment; $k_{obs}:k_i$ ratio too small for definite assignment.

encourage ring-closure reactions,[3,4] restrain ring fission and if so how much ? This communication addresses both of these questions.

ELIMINATIVE RING FISSION OF OXETAN (2a). The key to obtaining this substrate was synthesis of the oxetan methanol (6a) using a very recently published procedure (Scheme).[5] Conversion of (6a) into the desired sulphone via the tosylate and sulphide was straightforward. Treatment with sodium ethoxide-ethanol under standard conditions[6] gave the ring opened alcohol (7a). The observed rate constant is in the Table.

SCHEME



Reagents: i, $EtOCH{=}CH_2$—TsOH; ii, $\overset{-}{C}H_2\overset{+}{S}Me_2$; iii, AcOH; iv, TsCl—py; v, PhSNa—EtOH; vi, H_2O_2—MeOH—NH_4MoO_7; vii, EtONa—EtOH; viii, isophthalic acid; ix, Bu_3SnOMe. x, 200°

Rates of deprotonation of sulphones in ethanolic sodium ethoxide have been evaluated earlier[7] and the observed overall rate constant for (2a) shows that elimination occurs more rapidly than deprotonation, pointing to a concerted (E_2) mechanism for the reaction. When this rate constant for the concerted process is compared with that for the oxiran (1a) under the same conditions, it is seen that the ratio $k_{3\text{-ring}}:k_{4\text{-ring}}$ is small at 178 when compared with the 3-ring:4-ring ratio (6.7×10^4) for the stepwise $(E_1cB)_R$ eliminative fission of carbocycles[8] (8) and (9) and very small by comparison with that ($\approx 10^{10}$ for cycloalkanols (10) and (11).[9] For rapid concerted processes, therefore, it appears that the factors which differentiate rates of fission of 3- and 4-membered rings are less marked than in those processes (above) which are either stepwise or in which the very slow reactions appear to involve a large extent of ring cleavage in the transition structure. We have discussed earlier the nature of the differential operation of strain relief in the fission of small rings and it seems clear that, at very small extents of ring cleavage, the 3-ring:4-ring ratio should also be small. This makes sense of the present findings; when strain so greatly enhances the nucleofugality of a medium-ranked nucleofuge such as alkoxy, it seems likely that little ring fission is present in the transition structure.

THE THORPE-INGOLD EFFECT. We have recently examined the effect of *gem*-dimethyl substitution on the fission of oxirans[10] and two sets of cyclopropanes.[11] For the oxiran pair (1a) and (1b), the latter being obtained from the alcohol (6b) (Scheme) derived by a literature procedure,[12] *gem*-dimethyl substitution has no effect on the rate constant for the E_2 reactions within experimental error. For the sulphonylcyclopropane pair[11] (8a) and (8b) which react by the stepwise $(E_1cB)_R$ mechanism, rate constants were closely similar but $\Delta H^{\neq}$ values showed considerable enthalpic restraint (Table) amounting to 20 KJ mol^{-1} compensated for by a more favourable entropy term for the *gem*-dimethyl substrate. For the nitrocyclopropane pair (12a) and (12b) for which the mechanism is probably concerted E_2, the rate ratio is small at 11.6. Comparison of the oxetans (2a) and (2b), both of which clearly react by the E_2 mechanism, shows a rate ratio of 1.5, a small but discernibly greater factor than for the oxirans (1).

It appears therefore that in the most highly reactive oxacycle system that we have studied, not only is the 3-ring:4-ring ratio the smallest indicating the lowest differential extent of strain relief in the transition structure but that, in addition, the Thorpe-Ingold effect is also the smallest, consistent with a low degree of ring cleavage in the transition-structure for these reactions.

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