Eliminative Ring Fission. The *retro*-Thorpe–Ingold Effect†

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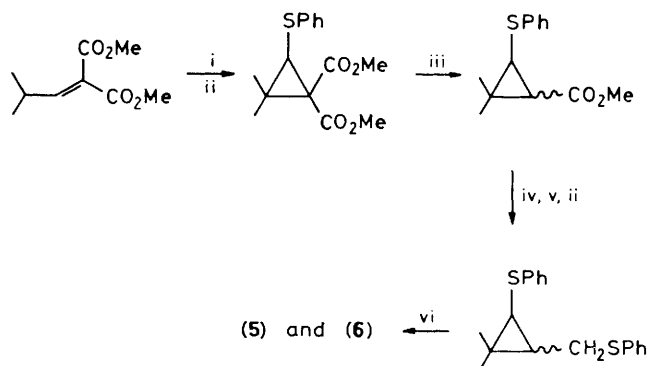
In eliminative ring fission of cyclopropanes by the $(E_1cB)_R$ mechanism, *gem*-dimethyl substitution substantially raises $\Delta H^{\ddagger}$; for oxirans, which react by the $E2$ mechanism, this *retro*-Thorpe–Ingold effect is insufficient to make ring cleavage rate-determining.

In two earlier communications[1,2] the dramatic effect of ring strain on elimination of carbon leaving groups and the influence of substituents at the leaving group upon the transition states for these processes were reported.

We now report on the influence of *gem*-dimethyl substitution upon the cleavage of oxirans and of cyclopropanes. This pattern of substitution was examined because *acceleration of ring closure reactions* by such *gem*-dimethyl substitution is substantial, particularly in formation of small rings. It is generally referred to as the Thorpe–Ingold effect.[3,4] We wished to discover whether this effect would operate in reverse by inhibiting ring fission, the *retro*-Thorpe–Ingold effect.

The reactions studied are in Table 1. Earlier work had shown that the rate constant for eliminative cleavage of oxiran (1)[5] is much larger than that calculated for deprotonation from Taft plots for detritiation of sulphones in ethanolic sodium ethoxide.[6] *gem*-Dimethyl substitution, as in substrate (2) produces a negligible change in k_{obs}. Because $k_{obs} \gg k_1$ we believe that all of these epoxides react by the $E2$ mechanism; evidently any inhibition of ring cleavage is insufficient to reduce the nucleofugality of the strained alkoxy-leaving group to the point where a mechanistic change occurs.

In cyclopropanes, a different situation applies. For substrate (4), the mechanism followed is $(E1cB)_R$; the rate-determining step has been shown to be ring cleavage (k_2).[1]

Table 1. Eliminative ring fission.[a]

Substrate	k_{obs}[b]	k_1[bc]	$\Delta H^{\ddagger}$[d]	$\Delta S^{\ddagger}$[e]
(1) G = EtSO$_2$, X = O, R = H	185[f]	2.5×10^{-1}[f,g]	—	—
(2) G = EtSO$_2$, X = O, R = Me	184	1.1×10^{-1}	—	—
(3) G = PhSO$_2$, X = O, R = H	4177	2.5×10^{-1}	—	—
(4) G = PhSO$_2$, X = CHSO$_2$Ph, R = H (*trans*)	4.8×10^{-3}[h]	8.5×10^{-11}[i]	17.7[j]	-10[j]
(5) G = PhSO$_2$, X = CHSO$_2$Ph, R = Me (*cis*)	2.4×10^{-3}	3.8×10^{-1}	25.5	$+15$
(6) G = PhSO$_2$, X = CHSO$_2$Ph, R = Me (*trans*)	2.7×10^{-3}	3.8×10^{-1}	22.8	$+7$

[a] Reactions in NaOEt–EtOH at 25 °C. [b] Units = dm^3 mol^{-1} s^{-1}. [c] Calculated from $\rho^*\sigma^*$ plot (ref. 6). [d] Units = kcal mol^{-1} (1 kcal = 4.18 kJ). [e] In cal mol^{-1} K^{-1}. [f] Value from ref. 5. [g] Maximum value; see ref. 5. [h] Value from ref. 1. [i] Actual value. [j] Value from ref. 2.

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Scheme 1. i, *N*-Bromosuccinimide–CCl$_4$–(PhCO$_2$)$_2$ (W. Herz, *J. Am. Chem. Soc.*, 1956, **78**, 1485); ii, PhSNa–MeOH (R. Verhe, N. De Kimpe, L. De Buyck, D. Courtheyn, and N. Schamp, *Bull. Soc. Chim. Belg.*, 1977, **86**, 55); iii, NaCl–H$_2$O–dimethyl sulphoxide, 160 °C, 2 h; iv, LiAlH$_4$–Et$_2$O; v, *p*-MeC$_6$H$_4$SO$_2$Cl–pyridine; vi, MeOH–H$_2$O$_2$–(NH$_4$)$_2$MoO$_7$.

Activation parameters and the response to phenyl substitution at the leaving group[2] show that ring fission is little advanced in the transition state. The *gem*-dimethyl cyclopropanes (5) and (6) (Scheme 1) show, in their *values of* k_{obs}, very little evidence of a *retro*-Thorpe–Ingold effect. The reduction in k_{obs} is entirely consistent with a mild effect of distal alkyl substitution on the deprotonation rate, k_1. This small effect is, however, deceptive; the activation parameters for sulphones (4) and (5) show a substantial increase in $\Delta H^{\ddagger}$ consistent with more difficult cleavage of the ring. This is accompanied by a substantially more positive entropy of activation in each case, consistent with a greater degree of ring fission and hence loss of rigidity at the transition state. These results are consistent with the operation of a *retro*-Thorpe–Ingold effect in this system.

References

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