

The Contribution of Ring Strain to Nucleofugality: the First Measurement

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Comparison of eliminative ring fission in a cyclopropane and elimination in an acyclic analogue allows determination of acceleration of elimination by ring strain; a factor of at least $10^{11.7}$ has been found, the largest for any heterolytic reaction.

Acceleration of reactions of cyclopropanes by ring strain is a familiar but unquantified phenomenon. Cyclopropanes thus show reactions, especially nucleophilic displacement of carbon leaving groups, not seen in acyclic analogues.¹ Recently, the nucleofugality² of a carbon leaving group in an elimination reaction has been determined³ and, as cyclopropanes readily undergo eliminative ring fission,⁴ we examined the possibility of determining the nucleofugality of a carbon leaving group whose bond connection is strained by inclusion in a cyclopropane. We now report the first quantitative data on the effect of ring strain on nucleofugality. It is also the largest quantified effect of strain in any heterolytic reaction.

The cyclopropyl sulphone (2) (Scheme 1), obtained using known routes⁵ from the hydroxymethylcyclopropane (1), which was itself obtained using known routes,⁵ reacted with ethanolic sodium ethoxide to give the diene (5), and subsequently the bis-addition product (6). It was established that the intermediate bis-sulphones (3) and (4) gave the diene (5) at least 10^9 times faster than (2). The primary kinetic deuterium isotope effect $[(k_H/k_D)_\beta] = 0.97$ (Table 1) shows that deprotonation is not involved in the rate-determining step of eliminative ring fission and this is confirmed by the rate of β -deprotonation which is much faster than elimination. These results demonstrate that the mechanism of ring fission is $(E1cB)_R$ and the rank⁶ (\equiv nucleofugality $= k_{\text{obs}} - k_{\text{deprotonation}} + 11$) of the strained carbon leaving group is thus directly obtainable.

Comparison of the reactivity of (2) with that of an unstrained analogue presented difficulty because of the very low ranks of unstrained carbon leaving groups.^{2,7} In the system (7; Z = Me or H), no elimination of a sulphonyl-stabilised carbanion can be observed and with Z = SO₂Et, elimination of the benzenesulphonate ion occurs more rapidly than elimination of

the bis-stabilised carbanion (8; R = Me). In the bis-activated system (9) elimination of the anion (8; R = Me) occurs but the reaction is reversible and the reverse reaction is suppressed by addition of the anion (8; R = H). The bis-activated system is calibrated against the mono-activated system *via* the 2-nitropropyl leaving group (Table 1). The rank of this leaving group is assigned the same value in the bis-activated system as in the mono-activated one. Earlier work has shown that rank is insensitive to activating group.³

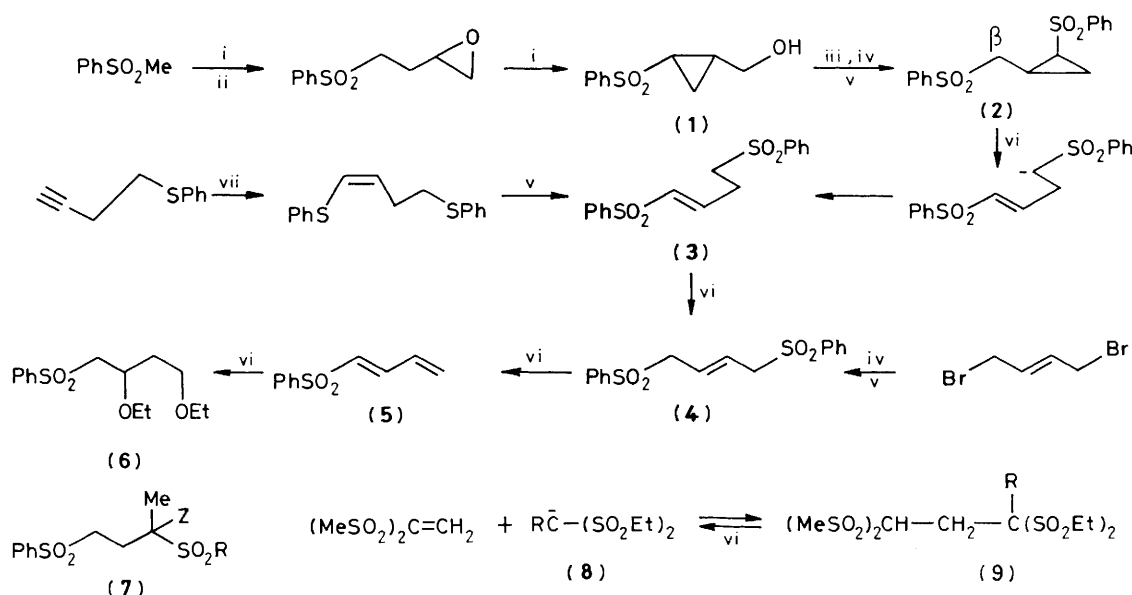
The results show that, even making no allowance for the comparison of a mono-stabilised leaving group in the cyclopropane system with a bis-stabilised group in the acyclic (unstrained) system, the rank difference of the leaving groups in the strained and unstrained systems is 11.7. This corresponds to a $\Delta\Delta G^\ddagger$ value of about 70 kJ mol⁻¹ or about 60% of the strain energy of the cyclopropane ring.

Ruchardt and Beckhaus⁹ have recently shown that in homolysis of strained acyclic and cyclic alkanes, about 60%

Table 1

Substrate	k_{obs}^a	Rank ^b
(2)	$4.7 \times 10^{-3e,d}$	+8.8
(9; R = Me)	2.5×10^{-2e}	-2.9 ^f
(MeSO ₂) ₂ CHCH ₂ CMe ₂ NO ₂	49	+2.6 ^g
PhSO ₂ CH ₂ CH ₂ CMe ₂ NO ₂	4.2×10^{-9}	+2.6

^a Units: l mol⁻¹ s⁻¹ at 25 °C in EtONa-EtOH. ^b $\log k_{\text{obs}} - \log k_{\text{deprotonation}} + 11$. ^c $k_{\text{deprotonation}}$ determined from $k_{\text{deprotonation}}$ and $k_H/k_T = 7.1$ (ref. 8). ^d $(k_H/k_D)_\beta = 0.97$. ^e $k_{\text{deprotonation}} = 1.2 \times 10^{-1}$. ^f Rate measured by the rate of approach to equilibrium with (MeSO₂)₂CHCH₂CH(SO₂Et)₂ in presence of CH₂(SO₂Et)₂. ^g Assigned by comparison with the next entry. ^h Assigned from entry below.



Scheme 1. i, BuⁿLi-hexane-tetrahydrofuran; ii, epibromohydrin; iii, SOCl₂-pyridine, 0 °C; iv, PhSNa-EtOH; v, H₂O₂-MeOH-NH₄MoO₇; vi, EtONa-EtOH; vii, PhSH, *h*v.

of the *calculated* strain energy is released at the transition state.

The synthetic application of sulphonyl-activated eliminative ring fission of cyclobutenes has recently been reported;¹⁰ we are currently investigating the accelerative effect of strained ring fission of cyclobutanes.¹¹

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