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 nucleofugality[2] of a carbon leaving group in an elimination reaction has been determined[3] 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 routes[5] 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 10^3 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-detritiation which is much faster than elimination. These results demonstrate that the mechanism of ring fission is $(E1cB)_R$ and the rank[6] (=nucleofugality $= k_{obs} - k_{deprotonation} + 11$) 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 = SO_2Et, elimination of the benzenesulphinate 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]

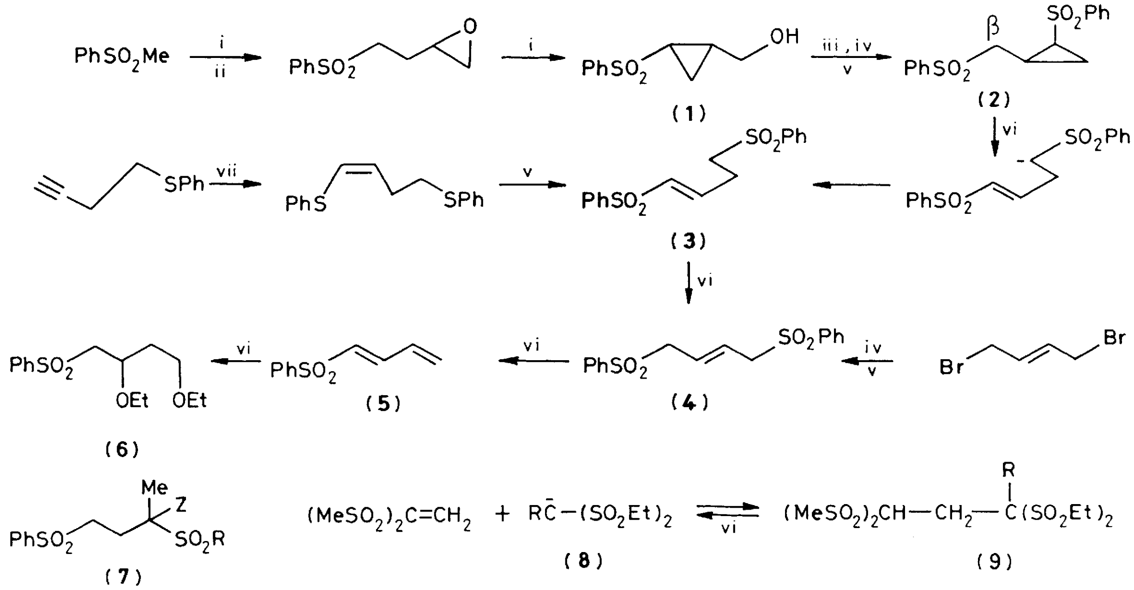
The results show that, even making no allowance for the comparison of a mono-stabilised leaving group in the cyclopropane system with a bis-stabilised group in the acyclic (unstrained) system, the rank difference of the leaving groups in the strained and unstrained systems is 11.7. This corresponds to 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 Beckhaus[9] have recently shown that in homolysis of strained acyclic and cyclic alkanes, about 60%

Table 1

Substrate	k_{obs}[a]	Rank[b]
(**2**)	4.7×10^{-3}[c,d]	+8.8
(**9**; R = Me)	2.5×10^{-2}[e]	−2.9[f]
$(MeSO_2)_2CHCH_2CMe_2NO_2$	49	+2.6[g]
$PhSO_2CH_2CH_2CMe_2NO_2$	4.2×10^{-9}	+2.6

[a] Units: l mol^{-1} s^{-1} at 25 °C in EtONa–EtOH. [b] log k_{obs} − log $k_{deprotonation}$ + 11. $k_{deprotonation}$ determined from $k_{detritiation}$ and $k_H/k_T = 7.1$ (ref. 8). [c] $(k_H/k_D)_\beta = 0.97$. [d] $k^\beta_{detritiation} = 1.2 \times 10^{-1}$. [e] Rate measured by the rate of approach to equilibrium with $(MeSO_2)_2CHCH_2CH(SO_2Et)_2$ in presence of $CH_2(SO_2Et)_2$. [f] Assigned by comparison with the next entry. [g] Assigned from entry below.



Scheme 1. i, Bu^nLi–hexane–tetrahydrofuran; ii, epibromohydrin; iii, $SOCl_2$–pyridine, 0 °C; iv, PhSNa–EtOH; v, H_2O_2–MeOH–NH_4MoO_7; vi, EtONa–EtOH; vii, PhSH, *h*ν.

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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