Highly Unsaturated Three-bladed Propeller Molecules. Synthesis and Ring Inversion Dynamics of Two [4.4.4]Propellatrienetriones

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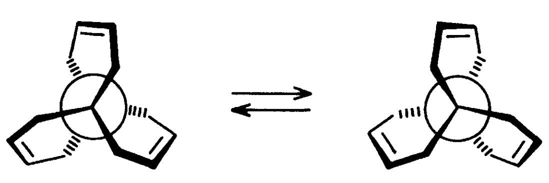
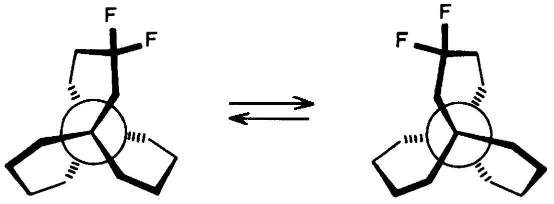
The kinetic parameters for antipodal ring inversion were measured for two [4.4.4]propellatrienetriones; the $\Delta G^{\ddagger}$(298 K) values show that incorporation of three –CH=CHCO– units does little to increase the barrier and allow for their possible isolation in optically active form.

The [4.4.4]propellane framework has elicited interest because the constituent six-membered rings radiate as blades from a common axis.[1,2] The presence of a shared single bond forces each blade to be twisted in the *same* sense with the result that a helical conformation is conferred to the molecule. Enantiomer interconversion within the D_3-symmetric triene (**1**), *i.e.* (**1a**) ⇄ (**1b**), which may involve *synchronous* three-ring flipping, proceeds readily. In fact, the $\Delta G^{\ddagger}$(300 K) associated with flexing of the molecule in the manner shown is sufficiently low (16.7 kcal/mol)[3]† to preclude its isolation in optically active form. A prediction that the fully saturated congener would enjoy greater conformational rigidity has not been fulfilled. Analysis of the dynamic properties of the 3,3-difluoro derivative (**2**) has revealed its $\Delta G^{\ddagger}$(300 K) for ring inversion to fall below that of (**1**).[3] For this pattern of substitution, the ring inversions need not be synchronous and may proceed by three consecutive chair ⇄ boat processes.

Although the *sense of twist* is important for chirality, the conformational dynamics of the system might well be controlled to a large extent by the *angle of twist,* the nature and sequencing of functional groups, and the presence or lack of conjugation. Because this facet of the question has not been examined, we have prepared the pair of isomeric trienetriones



(**1a**) (**1b**)



(**2a**) (**2b**)

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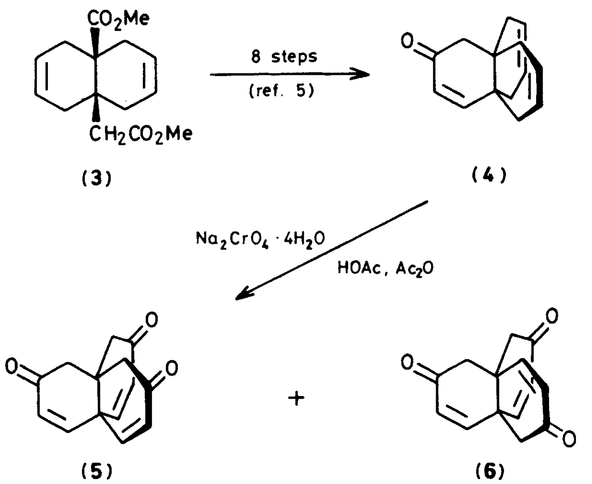
† 1 kcal = 4.18 kJ.

Table 1. Activation parameters for ring inversion in (**5**) and (**6**).

Compd.	Solvent	E_a (kcal/mol)[a]	$\Delta H^‡$(298 K) (kcal/mol)[a]	$\Delta G^‡$(298 K) (kcal/mol)[a]	$\Delta S^‡$(298 K) (kcal/mol)
(**5**)	$CDCl_3$	12.4 ±0.1	11.8 ±0.1	16.5 ±0.1	−15.6
	C_6D_5Cl	12.0 ±0.2	11.4 ±0.2	16.2 ±0.1	−15.8
(**6**)	C_6D_5Cl	12.8 ±0.1	12.2 ±0.1	15.8 ±0.1	−11.9

[a] The error limits were estimated by inserting into the Eyring equation the worst possible combinations of rate and temperature data within the estimated error limits of the measurements.



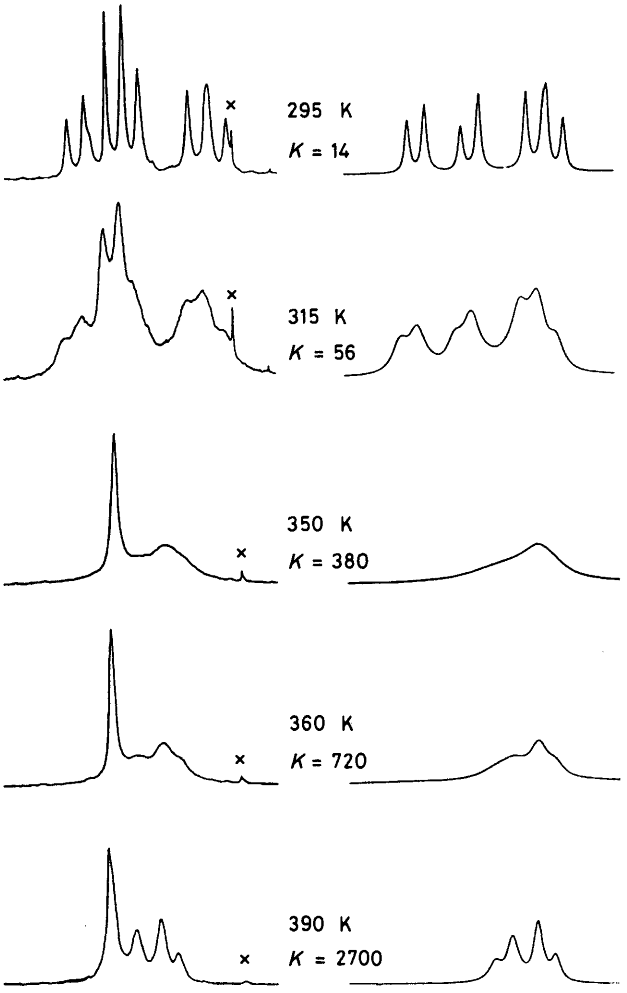


Figure 1. Representative variable-temperature 300 MHz ^1H n.m.r. spectra of (**6**) in C_6D_5Cl (left) and computer-simulated spectra (right). Temperatures are considered accurate to ±1 K.

(**5**) and (**6**), and have assessed the barriers to interconversion of their enantiomeric forms.

Following eight-step conversion of diester (**3**)[4] into (**4**) as previously described,[5] the [4.4.4]propellatrienone was oxidized with sodium chromate tetrahydrate (8 equiv.) in acetic acid–acetic anhydride (5:3) at ambient temperature (20 h).[6] Triketones (**5**) and (**6**)‡ were separated by medium pressure chromatography and easily distinguished on the basis of their ^1H and ^{13}C n.m.r. spectra. For the highly symmetric (**5**), only six carbon signals were seen. In the case of (**6**), the fourteen carbon signals proved especially revealing of the prevailing propeller topography. Rapid conformational equilibration under these conditions would have reduced the number of signals to ten.

Dynamic ^1H n.m.r.[7] (DNMR) was utilized to obtain the activation parameters for ring inversion in the trienetriones. For each compound, the fitting parameters were calculated from the slow exchange (room temperature) spectra. T_2 Relaxation times for each temperature were calculated in the usual way from the line-width at half-height of an internal, non-exchanging reference peak ($SiMe_4$ or $CDCl_3$). When ($^2H_5$)chlorobenzene was used as solvent, slight chemical shift changes occurred on heating the sample. The DNMR parameters were adjusted accordingly when this occurred, except under fast exchange conditions where, out of necessity, this effect was assumed to be negligible.

In the case of (**5**), all 3 methylene groups are magnetically equivalent and the system was treated as a simple AB $\rightleftarrows$ BA exchange: $\delta_{AB}(CDCl_3)$ 0.56 (J_{AB} 16.52 Hz), δ_{AB} (C_6D_5Cl) 0.53 (J_{AB} 16.53 Hz). For (**6**), all 3 methylene groups are magnetically non-equivalent and 2 of them show mutual exchange: δ_{AB} (C_6D_5Cl) 0.44 (J_{AB} 16.30 Hz), δ_{CD} (C_6D_5Cl) 0.20 (J_{CD} 16.94 Hz). The final data are collected in Table 1. The third methylene group which overlaps with the system under study (Figure 1) showed normal AB exchange.

The sizeable negative entropies of activation are consistent with the premise that substantial ground state conformational mobility is frozen out in that mid-point geometry where all rings necessarily become almost completely planar. Dreiding models reveal that substantial stress is placed on the central bond at this stage of the interconversion. Since our $\Delta G^‡$

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‡ *Spectroscopic data:* (**5**), m.p. 225 °C decomp. (from chloroform–pentane); i.r. (cm^{-1}, KBr) 1680; ^{13}C n.m.r. ($CDCl_3$) δ 195.47, 144.13, 129.31, 45.50, 43.70, 41.95. (**6**), m.p. 187—188 °C (from chloroform–pentane); i.r. (cm^{-1}, KBr) 1670; ^{13}C n.m.r. ($CDCl_3$) δ 194.52, 193.65, 151.28, 148.27, 146.25, 131.87, 130.01, 127.50, 47.13, 45.27, 44.61 (2 × C), 43.36, 42.54.

values[8] are very similar to those previously reported for (**1**) and (**2**), it may well be that the energetic demands associated with stretching of this bond overshadow those contributions offered by the peripheral substituents. Although further studies are necessary to quantify matters more broadly,§ our findings do demonstrate that the combined conjugative properties of three α,β-unsaturated carbonyl moieties do little to improve the possibilities for optical resolution.

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§ Following completion of this work, the conformational dynamics of [4.4.4]propellane-2,7-dione were reported (R. W. Alder, R. J. Arrowsmith, M. R. Bryce, P. Eastment, and A. G. Orpen, *J. Chem. Soc., Perkin Trans. 2*, 1983, 1519). On the basis of a coalescence temperature of 241 K, this tricyclic molecule was determined to exhibit a $\Delta G^{\ddagger}$ of 11.2 kcal/mol, a value significantly lower than that observed for (**1**), (**2**), (**5**), and (**6**). These workers attribute the reduced barrier to increased facilitation of a stepwise inversion mechanism. This scheme can hardly apply to compounds (**5**) and (**6**) in which the intermediate conformations must tend toward planar six-membered rings and the transition state and intermediates become difficult to distinguish.

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