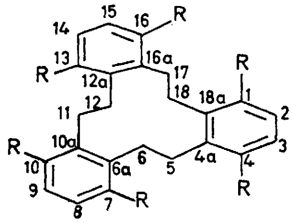
The Conformational Behaviour of 5,6,11,12,17,18-Hexahydrotribenzo[*a*,*e*,*i*]-cyclododecaene and its Derivatives

By David J. Brickwood, W. David Ollis,* and J. Fraser Stoddart

(*Department of Chemistry, The University, Sheffield* S3 7HF)

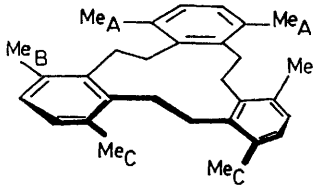
Summary The temperature dependence of the ^{1}H n.m.r. spectrum of 1,4,7,10,13,16-hexamethyl-5,6,11,12,17,18-hexahydrotribenzo[*a,e,i*]cyclododecaene (**2**) has been interpreted in terms of ring inversion between enantiomeric C_2 conformations.

Recently we examined[1] the temperature dependence of the ^{1}H n.m.r. spectrum of 5,6,11,12,17,18-hexahydrotribenzo[*a,e,i*]cyclododecaene[2,3] (**1**) in carbon disulphide solution and found that the sharp singlet (τ 7·07) at +21° for the CH_2–CH_2 protons became a broad *unsymmetrical* multiplet at −80° indicating the presence of a conformation devoid of three-fold symmetry. Clearly the presence of aromatic methyl substituents would assist in the understanding of this conformational behaviour so we have prepared compound (**2**) by a Wurtz reaction on 3,6-dimethyl-1,2-bisbromomethylbenzene.[4]



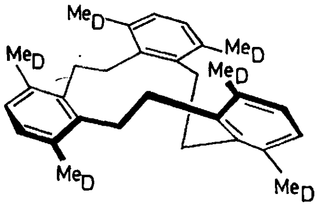
(1) R = H

(2) R = Me



C_2 conformation

(**3**)



D_3 conformation

(**4**)

The ^{1}H n.m.r. spectrum of this hexamethyl derivative (**2**) in $CDCl_3$ showed temperature dependence; the three singlets (τ 7·42, 7·49, and 7·52) for the methyl groups at +20° (Figure) coalesced to a sharp singlet (τ 7·50 at +80°).

Models suggest that the molecule (**2**) could adopt two conformations in the ground state, one with C_2 symmetry (**3**) and the other with D_3 symmetry (**4**). These two conformations (denoted by C_2 and D_3) are analogous to the helical (C_1) and propeller (C_3) conformations of the tri-salicylides.[5] The interconversion between the C_2 and D_3 conformations, (**3**) and (**4**), and their enantiomers (denoted by C_2* and D_3*) involves the following equilibrium: $D_3 \rightleftharpoons C_2 \rightleftharpoons C_2^* \rightleftharpoons D_3^*$.

The most direct qualitative interpretation of the ^{1}H n.m.r. spectrum of the hexamethyl derivative (**2**) would be to assign the three methyl singlets observed at +20° to the three non-equivalent pairs of methyl groups (Me$_A$, Me$_B$, and Me$_C$) of the C_2 conformation (**3**) and conclude that the molecule exists entirely in this conformation in solution. However, closer inspection of these signals (Figure) indicates that the two singlets to lower field are slightly broader than the high field singlet. Two interpretations may be considered: either (i) the non-equivalent methyl groups (Me$_A$, Me$_B$, Me$_C$) of the C_2 conformation (**3**) are exhibiting non-identical relaxation times, or, (ii) there is a small amount (<5%) of the D_3 conformation (**4**) whose equivalent methyl groups (Me$_D$) are giving rise to a signal coincident with that of Me$_C$ in the C_2 conformation (**3**) and exchanging with Me$_A$ and Me$_B$. This second possibility was effectively ruled out by the observation that there were no significant changes in the line-shape down to −40°. Comparison of the observed ^{1}H n.m.r. spectra with theoretical spectra generated by line-shape equations based upon a three-site exchange process between Me$_A$, Me$_B$, and Me$_C$, and involving the same rate constant for all three site exchanges, gave a value for $\Delta G^\ddagger$ of 17·1 ± 0·3 kcal mol^{-1} for $C_2 \rightleftharpoons C_2^*$ inversion.

TABLE

Strain energies (in kcal mol^{-1}) *of selected conformations of compound* (**2**)

Conformation	E_r[a]	E_θ[a]	E_ϕ[a]	E_δ[a]	E_{nb}[a]	E_T[a]
C_2	0·35	2·71	0·76	0·24	0·05	4·11[b]
D_3	0·31	2·47	1·53	0·65	0·00	4·96[b]
TS($C_2 \rightleftharpoons C_2^*$)[c,d]	0·87	15·29	1·43	0·76	2·44	20·79
TS($D_3 \rightleftharpoons C_2$)[c]	0·96	12·99	1·87	0·98	5·05	21·85

[a] The following energy terms[7] have been used: E_r (bond length strain), E_θ (angle strain), E_ϕ (torsional strain), E_δ (out-of-plane strain in aromatic rings), E_{nb} (non-bonded interactional strain). Total strain energy, $E_T = E_r + E_\theta + E_\phi + E_\delta + E_{nb}$. The force constants used were those employed by Boyd[8] for calculating strain energies in cyclophanes. [b] The C_2 conformation is also favoured by entropy: on the basis of symmetry considerations alone, the C_2 conformation, which has a symmetry number of 2, will be R ln 3 cal K^{-1} mol^{-1} higher in entropy than the D_3 conformation which has a symmetry number of 6. [c] Transition-state geometries were defined (*cf.* ref. 5) by holding a CH_2CH_2 unit in the plane of one of the aromatic rings, *e.g.* C-4a to C-11 inclusive. [d] If the difference in strain energies between the C_2 conformation and the transition state for $C_2 \rightleftharpoons C_2^*$ inversion is equated with $\Delta H^\ddagger$ then an approximate estimate for $\Delta G^\ddagger_{calc}$ of 16·3 kcal mol^{-1} follows from recognising that the transition state is favoured on entropy grounds by R ln 2 cal K^{-1} mol^{-1} (*i.e.* the CH_2CH_2 unit can rotate in two equivalent ways).

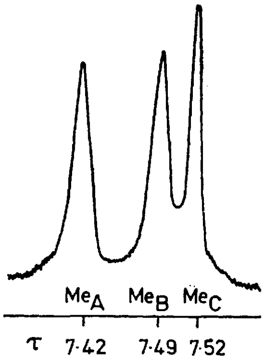
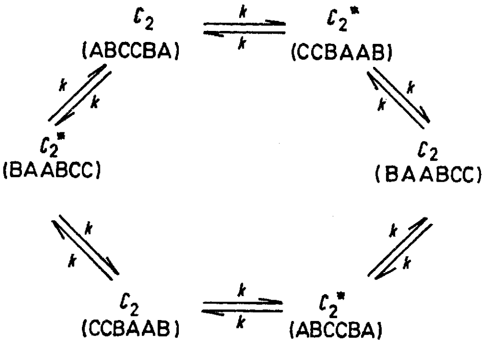


FIGURE. *The* ^{1}H *n.m.r. spectrum of the methyl groups of compound* (**2**) *at* +20° *in* $CDCl_3$.

Strain-energy calculations have been performed[6] on the ground state conformations and on probable transition states for the $D_3 \rightleftharpoons C_2$ ($D_3^* \rightleftharpoons C_2^*$) interconversion and the $C_2 \rightleftharpoons C_2^*$ inversion processes. The results recorded in the Table are in agreement with the conclusion that the C_2 conformation is more stable (ΔG°_{calc} = *ca.* 1·5 kcal mol^{-1}) than the D_3 conformation, but suggest that the D_3 conformation may contribute slightly to the conformational equilibrium. If this were the case, the fact that the calculated energy barrier for $D_3 \rightleftharpoons C_2$ interconversion is of the same order of magnitude as the $C_2 \rightleftharpoons C_2^*$ inversion barrier suggests that a rate process involving a fourth site might be occurring in the temperature range +20° to +80°. This possibility was explored by generating theoretical spectra using line-shape equations[5] based upon a four-site exchange process between Me_A, Me_B, Me_C, and Me_D, with the chemical shifts of the last two sites being made coincident. The results demonstrated that any contribution from the D_3 conformation must be less than 0·8%.



SCHEME. *The sites of the three pairs of methyl groups have been designated* A, B, *and* C (*in parentheses*) *with respect to six designated methyl groups. It is seen that all of the nuclei have been exchanged after two conformational inversions. Consequently the rate constant, k for* $C_2 \rightleftharpoons C_2^*$ *inversion is taken as twice the rate constant for site exchange of the methyl groups.*

The fact that compound (**2**) exists in the less symmetrical C_2 conformation (**3**) in solution is of interest for at least three reasons. Firstly, the situation contrasts with that exhibited by the trisalicylides, where in all cases so far examined[5], both the helical (C_1) and propeller (C_3) conformations are present with the more symmetrical propeller always being preferred. Secondly, Baker and his collaborators[2] concluded, on the basis of an optical examination of the crystals of compound (**1**) that the molecules were unlikely to have trigonal symmetry. Thirdly, there is encouraging agreement between $\Delta G^{\ddagger}_{\text{obs}}$ of 17·1 and $\Delta G^{\ddagger}_{\text{calc}}$ of 16·3 kcal mol^{-1} determined from strain energy calculations (Table).

(*Received*, 9*th April* 1973; *Com.* 500.)

---

[1] T. J. Grant, W. D. Ollis, and J. F. Stoddart, unpublished results.

[2] W. Baker, R. Banks, D. R. Lyon, and F. G. Mann, *J. Chem. Soc.*, 1945, 27; E. Müller and G. Röscheisen, *Chem. Ber.*, 1957, **90**, 543.

[3] H. A. Staab, F. Graf, and B. Junge, *Tetrahedron Letters*, 1966, 743.

[4] E. Buchta and G. Loew, *Annalen*, 1955, **597**, 123.

[5] A. P. Downing, W. D. Ollis, and I. O. Sutherland, *J. Chem. Soc.* (*B*), 1970, 24.

[6] We thank Dr. I. O. Sutherland for a copy of his programme based on the method published by N. L. Allinger, M. T. Tribble, M. A. Miller and D. H. Wertz, *J. Amer. Chem. Soc.*, 1971, **93**, 1637.

[7] J. F. Stoddart, 'Organic Chemistry, Series One,' 'Structure Determination in Organic Chemistry,' ed. W. D. Ollis, Butterworths, London, 1973, p. 1.

[8] R. H. Boyd, *J. Chem. Phys.*, 1968, **49**, 2574.