

Conformational Behaviour of Medium-sized Rings. Part 8.¹ 6*H*,12*H*,18*H*-Tribenzo[*b,f,j*][1,5,9]trithiacyclododecin and its 5,5,11,11,17,17-Hexaoxide

By W. David Ollis,* Julia Stephanidou Stephanatou, and J. Fraser Stoddart, Department of Chemistry, The University, Sheffield S3 7HF
 Michael Nógrádi, Institute of Organic Chemistry, Technical University, Budapest XI, Gellért tér 4, Hungary

The temperature-dependences of the ¹H n.m.r. spectra of 6*H*,12*H*,18*H*-tribenzo[*b,f,j*][1,5,9]trithiacyclododecin (7) and its 5,5,11,11,17,17-hexaoxide (8) have been interpreted in terms of ring inversions between enantiomeric helical conformations. The free energy of activation for conformational inversion in the cyclic trisulphide (7) is compared with that previously obtained for the ring inversion of the enantiomeric C₂ conformations of the parent hydrocarbon, 5,6,11,12,17,18-hexahydrotribenzo[*a,e,i*]cyclododecene (1).

OUR earlier interest² in the conformational behaviour of twelve-membered ring systems encouraged us to investigate the conformational properties of the hexahydrotribenzocyclododecene (1)³ and its 2,3,8,9,14,15- (2)³ and 1,4,7,10,13,16- (3)^{3,4} hexamethyl derivatives by dynamic ¹³C and ¹H n.m.r. spectroscopy and strain energy calculations. Although the hydrocarbons (1)–(3) are conformationally mobile in solution, they all exist³ preferentially in ground state conformations with C₂ symmetry. The temperature-dependences of their n.m.r. spectra have been interpreted³ in terms of ring inversion between enantiomeric C₂ conformations and the barrier heights for this conformational change were found^{3,4} to depend on the nature of the substituent atoms or groups at the *ortho*-positions of the aromatic rings. A comparison between the activation parameters for the hexahydrotribenzocyclododecene (1) and its 2,3,8,9,14,15- (2) and 1,4,7,10,13,16- (3) hexamethyl derivatives shows³ that approximately the same barrier (ΔG^\ddagger 9.9–10.1 kcal mol⁻¹) is associated with ring inversion in compounds (1) and (2) whereas a much higher barrier (17.4 kcal mol⁻¹) is associated with the same ring inversion process in compound (3). The activation parameters for the conformational changes experienced by the trisalicylides (4)–(6) in solution were also found² to correlate in a predictable manner with the

steric bulk of the various alkyl substituents occupying the *ortho*-positions of the aromatic rings. Thus, the free energies of activation² for ring inversion and interconversion processes are considerably less for tri-3,6-dimethylsalicylide (4) than they are for tri-*o*-thymotide (5) or tri-*o*-carvocrotide (6). However, whereas the hydrocarbons (1)–(3) adopt^{3,4} only one conformation with C₂ symmetry in solution, both helical (C₁ symmetry) and propeller (C₃ symmetry) conformations are present² at equilibrium in solutions of the trisalicylides (4)–(6) with the more symmetrical propeller always preferred.

In the light of these results it was of interest to discover the effect on the conformational behaviour of the twelve-membered ring when single methylene groups in the three dimethylene bridges of the hexahydrotribenzocyclododecene (1) are replaced by heteroatoms in a constitutionally symmetrical manner. The first compounds of this type we chose to study were the readily available trithia-analogue (7) of the hydrocarbon (1) and the easily derived cyclic tris-sulphone (8). The cyclic trisulphide (7) is obtained, together with the dithiocin (9) and higher oligomers including the cyclic tetra- and penta-sulphides, when *o*-mercaptobenzyl chloride (10) reacts⁵ with sodium hydroxide in ethanol. Oxidation of the cyclic trisulphide (7) with hydrogen peroxide in glacial acetic acid afforded the cyclic tris-sulphone (8).

In this paper, we report the results of our investigations

¹ Part 7, F. E. Elhadi, W. D. Ollis, and J. F. Stoddart, preceding paper.

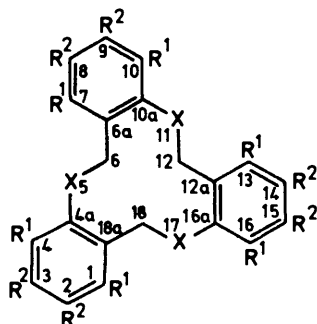
² W. D. Ollis and I. O. Sutherland, *Chem. Comm.*, 1966, 402; A. P. Downing, W. D. Ollis, and I. O. Sutherland, *ibid.*, 1967, 171; A. P. Downing, W. D. Ollis, I. O. Sutherland, J. Mason, and S. F. Mason, *ibid.*, 1968, 329; A. P. Downing, W. D. Ollis, and I. O. Sutherland, *J. Chem. Soc. (B)*, 1970, 24.

³ Part 6, D. J. Brickwood, W. D. Ollis, J. S. Stephanatou, and J. F. Stoddart, *J.C.S. Perkin I*, 1398.

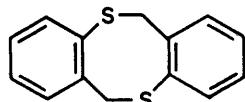
⁴ D. J. Brickwood, W. D. Ollis, and J. F. Stoddart, *J.C.S. Chem. Comm.*, 1973, 638.

⁵ G. W. Stacey, F. W. Villaescusa, and T. E. Wollner, *J. Org. Chem.*, 1965, 30, 4074.

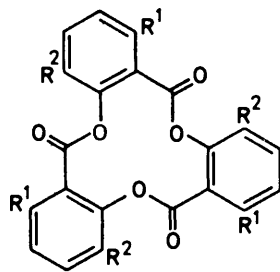
on the conformational behaviour of the cyclic trisulphide (7) and tris-sulphone (8) in solution by dynamic ^1H n.m.r. spectroscopy. Part of this investigation has been the



- (1) $\text{X} = \text{CH}_2$, $\text{R}^1 = \text{R}^2 = \text{H}$
 (2) $\text{X} = \text{CH}_2$, $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{Me}$
 (3) $\text{X} = \text{CH}_2$, $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{H}$
 (7) $\text{X} = \text{S}$, $\text{R}^1 = \text{R}^2 = \text{H}$
 (8) $\text{X} = \text{SO}_2$, $\text{R}^1 = \text{R}^2 = \text{H}$



(9)



(10)

- (4) $\text{R}^1 = \text{R}^2 = \text{Me}$
 (5) $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{CHMe}_2$
 (6) $\text{R}^1 = \text{CHMe}_2$, $\text{R}^2 = \text{H}$

subject of a preliminary communication ⁶ and has also been discussed briefly in a recent review ⁷ on the conformational behaviour of some medium-sized ring systems. In addition, one of us has described ⁸ the X-ray crystal structure of the cyclic trisulphide (7).

EXPERIMENTAL

The general methods have been discussed in Parts 3 ⁹ and 6.³

Reaction of *o*-Mercaptobenzyl Chloride (10) with Sodium Hydroxide in Ethanol.⁵—A solution of *o*-mercaptobenzyl chloride (10) ⁵ (10.1 g) in ethanol (1 l) was added during 4 h to a solution of sodium hydroxide (25 g) in ethanol (1.5 l). Evaporation of the solvent was followed by repeated extraction with chloroform. The chloroform solution was evaporated and the residue was subjected to column chromatography on silica gel using benzene–light petroleum (b.p. 60–80 °C) (1 : 4) as eluant. Fraction 1 corresponded to the cyclic disulphide, 6H,12H-dibenzo[b,f][1,5]dithiocin (9) (2.1 g, 27%), m.p. 170–173° (lit.,⁵ 174–176°). Fraction 2 corresponded to the cyclic trisulphide, 6H,12H,18H-tribenzo[b,f,j][1,5,9]trithiacyclododecin (7) (0.5 g, 6.4%), m.p. 197–198° [Found: C, 68.6; H, 5.9%; *M* (mass spec.), 366. $\text{C}_{21}\text{H}_{18}\text{S}_3$ requires C, 68.8; H, 4.95%; *M*, 366], $\tau(\text{CS}_2)$ 2.30–2.96 (12 H, m, aromatic) and 5.51 (6 H, s, $3 \times \text{CH}_2$). However, t.l.c. of the original reaction mixture

on silica gel using benzene–light petroleum (b.p. 60–80 °C) (2 : 3) as eluant indicated the presence of two slower moving components in addition. These were separated by preparative t.l.c. on silica gel using this solvent system as eluant to give (i) the cyclic tetrasulphide, 6H,12H,18H,24H-tetrabenzo[b,f,j,n][1,5,9,13]tetrahiacyclohexadecin, obtained pure after recrystallisation from chloroform–ether–light petroleum (b.p. 60–80 °C) (210 mg, 2.8%), m.p. 195–196° [Found: *M* (mass spec.), 488.076 3. $\text{C}_{28}\text{H}_{24}\text{S}_4$ requires *M*, 488.076 1], $\tau(\text{CDCl}_3)$ 2.46–2.90 (16 H, m, aromatic) and 5.84 (8 H, s, $4 \times \text{CH}_2$), and (ii) the cyclic pentasulphide, 6H,12H,18H,24H,30H-pentabenzo[b,f,j,n,r][1,5,9,13,17]pentathiacycloicosin, which was recrystallised from light petroleum (b.p. 60–80 °C) (120 mg, 1.5%), m.p. 120–122° [Found: *M* (mass spec.), 610.094 9. $\text{C}_{35}\text{H}_{30}\text{S}_5$ requires *M*, 610.095 1], $\tau(\text{CDCl}_3)$ 2.54–3.00 (20 H, m, aromatic) and 5.83 (10 H, s, $5 \times \text{CH}_2$).

6H,12H,18H-Tribenzo[b,f,j][1,5,9]trithiacyclododecin 5,5,11,11,17,17-Hexaoxide (8).—Acetic acid (10 ml) and 30% hydrogen peroxide (5 ml) were added to a solution of the cyclic trisulphide (7) (60 mg) in chloroform (10 ml) and the mixture was refluxed for 3 days. On cooling, the cyclic tris-sulphone (8) separated as a crystalline compound (55 mg, 73%), m.p. >305° [Found: C, 54.7; H, 4.25; S, 20.6%; *M* (mass spec.), 462. $\text{C}_{21}\text{H}_{18}\text{O}_6\text{S}_3$ requires C, 54.5; H, 4.05; S, 20.8%; *M*, 462], $\tau(\text{CD}_2\text{Cl}_2\text{-CF}_3\text{CO}_2\text{H})$ 1.56–2.38 (12 H, m, aromatic) and 4.62 (6 H, s, $3 \times \text{CH}_2$).

Determination of Rates of Conformational Changes by Dynamic ^1H N.m.r. Spectroscopy.—A program VI* for exchange of nuclei between all six sites of three AB systems, A1B1, A2B2, and A3B3 was written (coded in FORTRAN IV) using simultaneous equations obtained from a density matrix approach.^{10–12} This program was used to simulate the ^1H n.m.r. spectral line-shapes associated with (i) the methylene protons of the cyclic trisulphide (7) between –36 and –106 °C and (ii) the methylene protons of the cyclic tris-sulphone (8) between –77 and +6 °C.

The problem in relation to the spectral line-shapes for compounds (7) and (8) can be stated as follows. The conformational itinerary (see Results and Discussion section) dictates (i) that each of the six sites is visited by each of the six methylene protons H_C , H_D , H_E , H_F , H_G , and H_H , and (ii) that the site visits can be represented by two cyclic permutations. It transpires that a clockwise sequence of site visits on the conformational itinerary leads to one cyclic permutation (CFHDEG) (read: C is replaced by F, F is replaced by H, . . . , G is replaced by C). The other cyclic permutation (CGEDHF) is the inverse of the first and corresponds to an anticlockwise sequence of site visits on the conformational itinerary. It is now necessary to enumerate all cyclic permutations of six spins which can be made to correspond with these two cyclic permutations of protons given the restriction that the six spins consist of three paired systems. Each spin system will be designated by a numeral (1, 2, or 3) and each spin in a pair by a letter (A and B). By definition, C is paired with D, E with F, and G with H. Reference to the two cyclic permutations of protons shows

⁸ L. Párkányi, A. Kálmán, and M. Nógrádi, *Acta Cryst.*, 1975, **B31**, 2716.

⁹ Part 3, W. D. Ollis and J. F. Stoddart, *J.C.S. Perkin I*, 1976, 926.

¹⁰ J. I. Kaplan, *J. Chem. Phys.*, 1958, **28**, 278; 1958, **29**, 462.

¹¹ S. Alexander, *J. Chem. Phys.*, 1962, **37**, 967, 974; 1963, **38**, 1787; 1964, **40**, 2741.

¹² C. S. Johnson, *J. Chem. Phys.*, 1964, **41**, 3277; *Adv. Magnetic Resonance*, 1965, **1**, 33; *J. Magnetic Resonance*, 1969, **1**, 98.

* The program numbers (*viz.* I–V) have been established in Parts 3,⁹ 6,³ and 7¹ and this present program (*i.e.* VI) represents the latest addition to the series; programs I–VI will form the basis of a collection for reference in future Parts of this series.

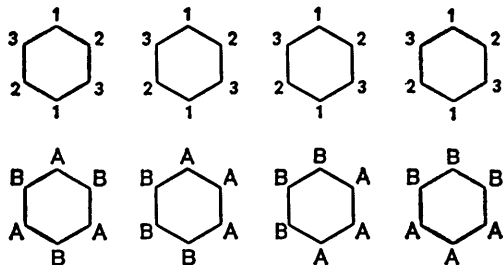
⁶ W. D. Ollis, J. F. Stoddart, and M. Nógrádi, *Angew. Chem. Internat. Edn.*, 1975, **14**, 168.

⁷ W. D. Ollis, J. F. Stoddart, and I. O. Sutherland, *Tetrahedron*, 1974, **30**, 1903.

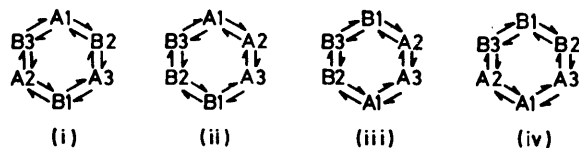
that the paired spins are separated antipodally in the cycle. It follows that there are two and only two cycles of numerals, (123123) and its inverse (132132), and two and only two cycles of letters, (AAABBB) and (ABABAB). There is one and only one combination of (123123) and its inverse with (ABABAB); there are three and only three combinations of (123123) and its inverse with (AAABBB). Consequently, there are four and only four combinations which can be expressed by the following mappings:

$$\left\{ \begin{array}{c} 1\ 2\ 3\ 1\ 2\ 3 \\ \text{ABABAB} \end{array} \right\} \left\{ \begin{array}{c} 1\ 2\ 3\ 1\ 2\ 3 \\ \text{AAABBB} \end{array} \right\} \left\{ \begin{array}{c} 1\ 2\ 3\ 1\ 2\ 3 \\ \text{BAAABB} \end{array} \right\} \left\{ \begin{array}{c} 1\ 2\ 3\ 1\ 2\ 3 \\ \text{BBAAAB} \end{array} \right\}$$

and the inverses. The situation can be visualised easily in terms of the pairwise superposition of hexagons:



from which the four site exchange schemes:



can be written down. Figure 1 shows the density matrix elements associated with each transition and the rate constants associated with each site exchange of nuclei between the six sites A1, B1, A2, B2, A3, and B3 of the three AB systems corresponding to the site exchange schemes (i)—(iv). The density matrix approach¹⁰⁻¹² was used to examine all four site exchange schemes. Attempts to perform line-shape analysis on the temperature-dependent ¹H n.m.r. spectra (Figure 2) of the cyclic trisulphide (7) indicated that only the computer program constructed on the basis of site exchange scheme (iv) provides good matches between computed and experimental spectra. The temperature-dependent ¹H n.m.r. spectra of the cyclic trisulphone (8) were amenable to line-shape analysis using site exchange schemes (ii)—(iv). The method of computation will now be illustrated for site exchange scheme (iv).

$$k_{21}\rho_{13}^2 + k_{31}\rho_{13}^3 - k_{12}\rho_{13}^1 - k_{13}\rho_{13}^1 - \rho_{13}^1/t_{2A1} - 2\pi i\rho_{13}^1(\nu_{A1} - \nu + \frac{1}{2}J_1) + i\rho_{13}^1\pi J_1 + p_1 iC = 0 \quad (1)$$

$$k_{12}\rho_{13}^1 + k_{32}\rho_{13}^2 - k_{21}\rho_{13}^2 - k_{23}\rho_{13}^2 - \rho_{13}^2/t_{2A2} - 2\pi i\rho_{13}^2(\nu_{A2} - \nu + \frac{1}{2}J_2) + i\rho_{13}^2\pi J_2 + p_2 iC = 0 \quad (2)$$

$$k_{13}\rho_{13}^1 + k_{23}\rho_{13}^2 - k_{31}\rho_{13}^3 - k_{32}\rho_{13}^3 - \rho_{13}^3/t_{3A3} - 2\pi i\rho_{13}^3(\nu_{A3} - \nu + \frac{1}{2}J_3) + i\rho_{13}^3\pi J_3 + p_3 iC = 0 \quad (3)$$

$$k_{21}\rho_{12}^2 + k_{31}\rho_{12}^3 - k_{12}\rho_{12}^1 - k_{13}\rho_{12}^1 - \rho_{12}^1/t_{2B1} - 2\pi i\rho_{12}^1(\nu_{B1} - \nu + \frac{1}{2}J_1) + i\rho_{12}^1\pi J_1 + p_1 iC = 0 \quad (4)$$

$$k_{12}\rho_{12}^1 + k_{32}\rho_{12}^3 - k_{21}\rho_{12}^2 - k_{23}\rho_{12}^2 - \rho_{12}^2/t_{2B2} - 2\pi i\rho_{12}^2(\nu_{A2} - \nu + \frac{1}{2}J_2) + i\rho_{12}^2\pi J_2 + p_2 iC = 0 \quad (5)$$

$$k_{13}\rho_{12}^1 + k_{23}\rho_{12}^2 - k_{31}\rho_{12}^3 - k_{32}\rho_{12}^3 - \rho_{12}^3/t_{2B3} - 2\pi i\rho_{12}^3(\nu_{B3} - \nu + \frac{1}{2}J_3) + i\rho_{12}^3\pi J_3 + p_3 iC = 0 \quad (6)$$

For three AB systems undergoing the exchange of nuclei between the sites illustrated in scheme (iv) in Figure 1 the

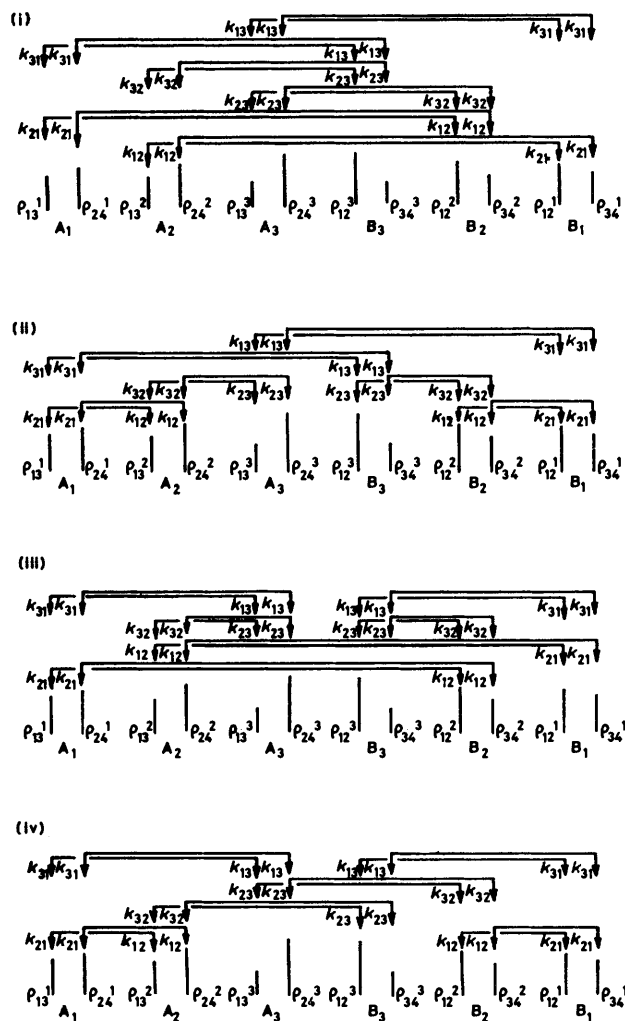


FIGURE 1 The site exchange schemes (i)—(iv) for exchange of nuclei between six sites (A1, B1, A2, B2, A3, and B3) of three AB systems. The density matrix element corresponding to each transition is indicated. The double-headed arrows represent site exchanges with the appropriate rate constant given alongside each arrow

density matrix approach¹⁰⁻¹² gives two sets of six simultaneous equations in the density matrix elements for the twelve allowed transitions corresponding to the twelve lines observed in three AB systems. The first set of six simultaneous equations involves the density matrix elements ρ_{12}^1 , ρ_{12}^2 , ρ_{12}^3 , ρ_{13}^1 , ρ_{13}^2 , and ρ_{13}^3 . The subscripts have their usual significance in referring to spin states; the superscripts 1, 2, and 3 refer to the three different AB system in scheme (iv) in Figure 1. By considering the effects of the site exchanges shown in scheme (iv) in Figure 1 upon the basis functions, the simultaneous equations (1)—(6) in ρ parameters may be obtained for 'steady-state' conditions ($\partial\rho_{12}^1/\partial t = 0$, etc.). A second set of six simultaneous equations may be obtained in the density matrix elements ρ_{24}^1 , ρ_{24}^2 , ρ_{24}^3 , ρ_{34}^1 , ρ_{34}^2 , and ρ_{34}^3 which differ from the first set [(1)—(6)] only in the sign of the J parameters. These twelve complex simultaneous equations were solved for the

ρ parameters at each input value of the frequency ν by use of a MASTER SIX SITE computer program. Values for the site frequencies ν_{A1} , ν_{A2} , ν_{A3} , ν_{B1} , ν_{B2} , and ν_{B3} , the populations p_1 , p_2 , and p_3 and relaxation times t_{2A1} , t_{2A2} , t_{2A3} , t_{2B1} , t_{2B2} , and t_{2B3} were obtained initially from chemical

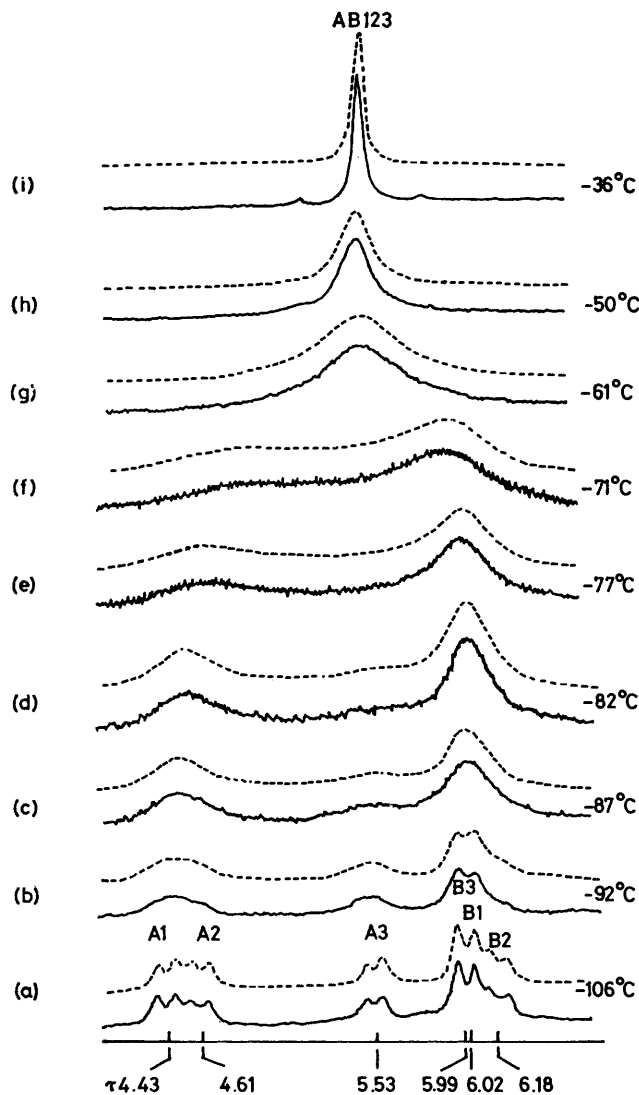


FIGURE 2 Observed (full line) and computed (broken line) spectra of the methylene protons of 6H,12H,18H-tribenzo-[b,f,j][1,5,9]trithiacyclododecin (7) using program VI for exchange of nuclei between six equally-populated sites A1, B1, A2, B2, A3, and B3 (the input values for all the rate constants, k_{12} , etc., were the same so they will be referred to collectively as k): (a) at -106°C , k 5.5 s^{-1} ; (b) at -92°C , k 17.5 s^{-1} ; (c) at -87°C , k 47.2 s^{-1} ; (d) at -82°C , k 75.2 s^{-1} ; (e) at -77°C , k 173 s^{-1} ; (f) at -71°C , k 345 s^{-1} ; (g) at -61°C , k $1\,318\text{ s}^{-1}$; (h) at -50°C , k $3\,630\text{ s}^{-1}$; (i) at -36°C , k $19\,500\text{ s}^{-1}$

shifts, relative intensities, and half-peak widths for the individual signals of the three AB systems in the low temperature spectra. The absorption intensity at frequency ν is proportional to the imaginary part of $\Sigma \rho_{rs}^n$ for all the twelve allowed transitions. Solutions to the simultaneous equations for a range of values for ν which cover the appropriate region of the spectrum give line shapes for selected input values of the rate constants k_{12} , k_{21} , k_{13} ,

k_{31} , k_{23} , and k_{32} . Since the input values for all these rate constants were the same in the present instances, they will be referred to collectively as k . A spectrum consisting of the absorption intensities at 500 values of ν required a computing time of only 46 s on an I.C.L. 1907 computer. The density matrix approach¹⁰⁻¹² can be applied to schemes (i)–(iii) in Figure 1 in analogous fashion to that described for scheme (iv).

RESULTS AND DISCUSSION

The ^1H n.m.r. spectrum of the cyclic trisulphide (7) in carbon disulphide showed temperature-dependence (see

TABLE 1
Temperature-dependent ^1H n.m.r. spectral parameters (100 MHz) for compounds (7) and (8)

Compound (7)	X	Solvent	Temp. ($^\circ\text{C}$)	Group	τ (J/Hz) ^a		
(7)	S	CS_2	-106	C_6H_4	2.30–2.96 (m)		
				CH_2	4.43 (A1), 6.02 (B1) (J 9.0) ^b		
					4.61 (A2), 6.18 (B2) (J 9.0) ^b		
					5.53 (A3), 5.99 (B3) (J 9.0) ^b		
				-36	C_6H_4	2.30–2.96 (m)	
					CH_2	5.51 (AB123)	
					-77	C_6H_4	1.52–2.40 (br,m)
						CH_2	3.64 (A1), 5.24 (B1) (J 15.0) ^c
							3.86 (A2), 5.35 (B2) (J 15.0) ^c
							4.12 (A3), 5.37 (B3) (J 15.0) ^c
+30	C_6H_4	1.56–2.38 (m)					
	CH_2	4.62 (AB123)					

^a Sites are designated A1, B1, A2, B2, A3, and B3 for six-site systems where there is coupling in the form of three AB systems. Sites that represent six time-averaged signals are designated AB123. ^b The three AB systems were identified unambiguously by homonuclear INDOR spectroscopy (see text). ^c The assignment of the pairing of these three AB systems is arbitrary.

Table 1). Three AB systems for the six methylene protons were identified (see Figures 2 and 4) at -106°C and the pairing of each AB system was established by homonuclear INDOR spectroscopy (Figure 4). The three AB systems coalesced to give a sharp singlet at -36°C and above. This observation indicates that the ground-state conformation of the cyclic trisulphide (7) has C_1 symmetry. Temperature-dependence was also observed (see Table 1) when the ^1H n.m.r. spectrum of the cyclic trisulphide (8) was examined in dichloro-dideuteriomethane containing a few drops of trifluoroacetic acid. At $+30^\circ\text{C}$, a singlet was observed for the six methylene protons. On cooling to -77°C , the singlet was resolved into three AB systems. Thus, the ground-state conformation of the cyclic trisulphide (8) must also have C_1 symmetry. The pairing of the three AB systems given in Table 1 is arbitrary since all attempts to unravel the coupling pattern by (i) spin-spin decoupling and (ii) homonuclear INDOR spectroscopy were unsuccessful on account of the insoluble nature of the sample at low temperatures. However, because of the relatively large chemical shift differences between the

A and B protons in all cases, the theoretical line-shapes (see later and Figure 3) are in fact quite insensitive to the actual assignment of AB systems to chemical shifts.

Acceptance of the requirement for ground-state conformations with C_1 symmetry and examination of molecular models suggest that the molecules (7) and (8) both adopt helical conformations (*cf.* ref. 2) in solution. There are two enantiomeric conformations of this type (11a and b) and they will be referred to by the descriptors H and H*. These conformations are analogous to the C_2 and C_2^* conformation^{3,4} of the hydrocarbons

consideration of the $H \rightleftharpoons H^*$ inversion process. The itinerary of $H \rightleftharpoons H^*$ inversion processes which are required to exchange the six methylene protons of (7) and (8) with the six different sites conveniently labelled 1-OUT, 1-IN, 2-OUT, 2-IN, 3-OUT, and 3-IN is shown in Figure 5. The sites occupied by the three pairs of diastereotopic methylene groups have been labelled by the numbers 1, 2, and 3 in an arbitrary fashion. Furthermore, the protons are considered to occupy IN or OUT sites depending on whether they are oriented inside or outside the diagrams in Figure 5. This notation is

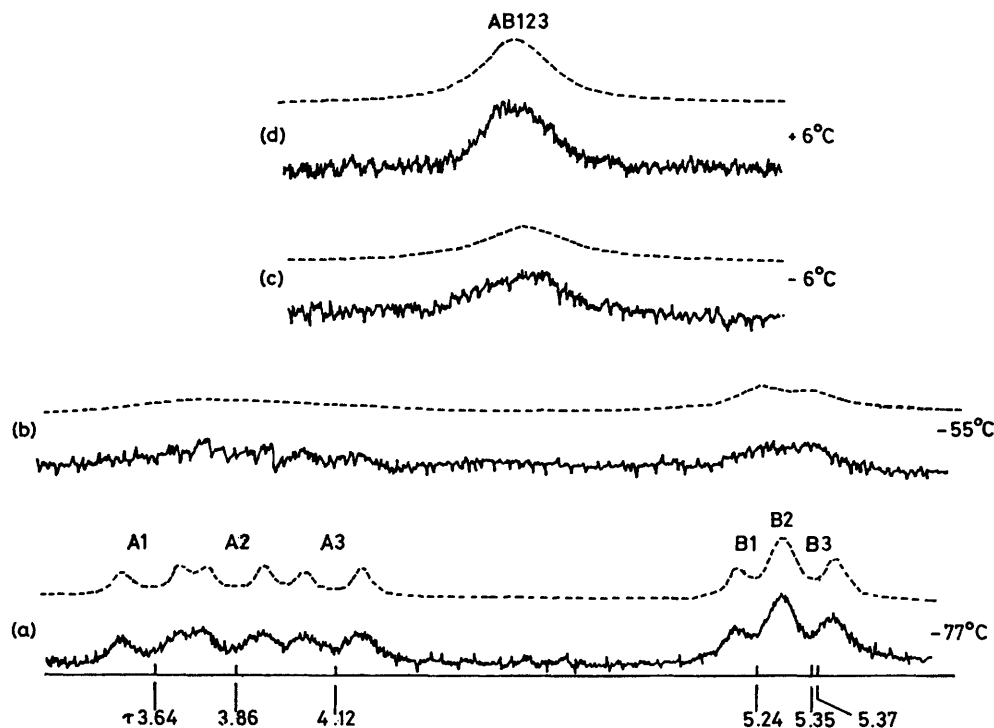
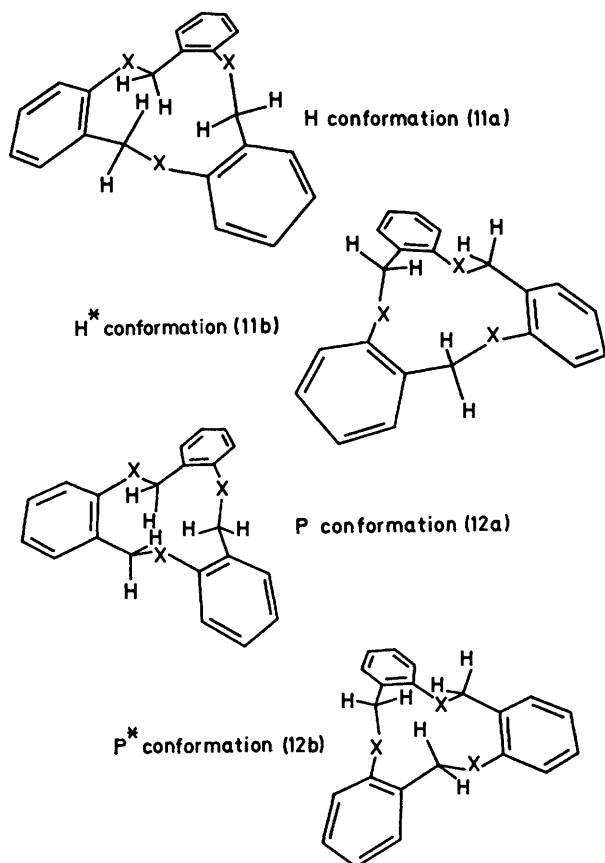


FIGURE 3 Observed (full line) and computed (broken line) spectra of the methylene protons of 6H,12H,18H-tribenzo[*b,f,j*][1,5,9]-trithiacyclododecin 5,5,11,11,17,17-hexaoxide (8) using program VI for exchange of nuclei between six equally-populated sites A1, B1, A2, B2, A3, and B3 (the input values for all the rate constants, k_{12} , etc., were the same so they will be referred to collectively as k): (a) at -77°C , k 3.7 s^{-1} ; (b) at -55°C , k 44.6 s^{-1} ; (c) at -6°C , k $2\,488\text{ s}^{-1}$; (d) at $+6^\circ\text{C}$, k $3\,558\text{ s}^{-1}$

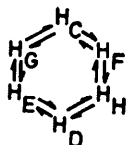
(1)–(3). In common with these hydrocarbon molecules where none of the more symmetrical D_3 and D_3^* conformations were detected in solution, the molecules (7) and (8) do not appear to populate the more symmetrical propeller conformations with C_3 symmetry to any extent in solution. Formally, there are two enantiomeric conformations of this type (12a and b) which can be recognised with molecular models and they can be denoted by the descriptors P and P*. The conformational inversion and interconversion processes involving these enantiomeric and diastereoisomeric conformations are represented by the equilibria $P \rightleftharpoons H \rightleftharpoons H^* \rightleftharpoons P^*$ in a manner reminiscent of the case of the trisallycylides (4)–(6).² However, in order not to complicate unnecessarily the problem involving the site exchanges between the six sites and the protons of the three pairs of diastereotopic methylene groups in the H and H* conformations (11a and b), the discussion will now be limited to a

necessary because a unique assignment of protons to the sites A1, B1, A2, B2, A3, and B3 is not possible and an arbitrary assignment could be misleading (see Experimental section). If the identity of the protons in Figure 5 is established using subscripts C, D, E, F, G, and H, then the six diastereotopic protons H_C , H_D , H_E , H_F , H_G , and H_H can be associated with the six different options corresponding to three degenerate H conformations [(11a)–I, (11a)–II, and (11a)–III] and three degenerate H* conformations [(11b)–I, (11b)–II, and (11b)–III] in Figure 5. Simultaneous torsion about a carbon-sulphur (*e.g.* 4a,5) and a carbon-carbon (*e.g.* 6,6a) bond linking a particular X-CH₂ group to two aromatic rings (*e.g.* those defined by atoms 1, 2, 3, 4, 4a, 18a and 6a, 7, 8, 9, 10, 10a) can formally lead to $H \rightleftharpoons H^*$ inversion. Previously, we have likened this synchronous torsional change to a pedalling motion. Pedalling of the X-CH₂ bridges II or III of H–I, I or III of H–II, I or II of H–III

effects $H \rightleftharpoons H^*$ inversion such that H-I is inverted to either H*-III or H*-II, H-II to either H*-III or H*-I,



and H-III to either H*-II or H*-I. From a consideration of Figure 5 it is obvious that each one of the six protons visits a particular site in the order:



This cyclic array determines (see Experimental section) the two cyclic permutations [(CFHDEG) and its inverse (CGEDHF)] which lead to the four possible site exchange schemes (i)–(iv) involving sites A1, B1, A2, B2, A3, and B3 observable in the low temperature 1H n.m.r. spectra (see Figures 2 and 3) of compounds (7) and (8). Inspection of Figure 5 in relation to the site exchange schemes (i)–(iv) shows that the $H \rightleftharpoons H^*$ inversion process is associated with a first-order rate constant k which in turn may be related directly to the site exchange rate constants k_{12} , k_{21} , k_{13} , k_{31} , k_{23} , and k_{32} . The rate constants for $H \rightleftharpoons H^*$ inversion at different temperatures were determined (see Figures 2 and 3) for compounds (7) and (8) by comparing 1H n.m.r. spectra for the methylene protons in each case with theoretical spectra generated by the line-shape procedure outlined in the Experimental section. Values of the free energies

of activation for the $H \rightleftharpoons H^*$ inversion process were determined at different temperatures. Table 2 records

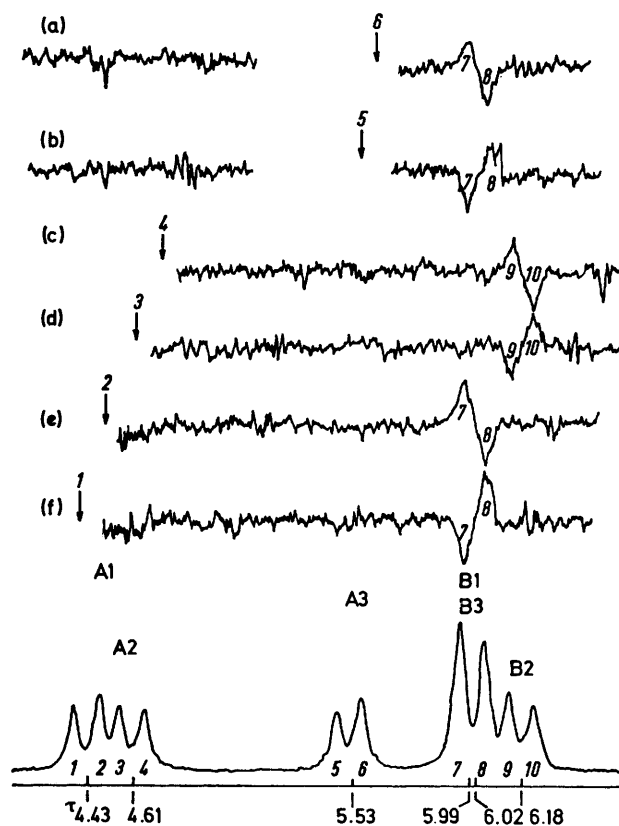


FIGURE 4 Assignment of the three AB systems, A1B1, A2B2, and A3B3 of 6H,12H,18H-tribenzo[*b,f,j*][1,5,9]trithiacyclo-dodecin (7) by homonuclear INDOOR spectroscopy. An observing frequency ν_{obs} monitors a single spectral line while a second irradiating frequency ν_{irr} sweeps the spectrum. When ν_{irr} crosses a spectral line which has an energy level in common with the observed spectral line, a positive (+) or negative (-) intensity change occurs depending upon the sign of the generalised Overhauser effect. The following information can be gleaned from the INDOOR spectra (a)–(g):

Spectrum	Line observed	Lines exhibiting intensity change
(a)	6	7 (+); 8 (-)
(b)	5	7 (-); 8 (+)
(c)	4	9 (+); 10 (-)
(d)	3	9 (-); 10 (+)
(e)	2	7 (+); 8 (-)
(f)	1	7 (-); 8 (+)

the average values of ΔG^\ddagger ($H \rightleftharpoons H^*$) for compounds (7) and (8).

TABLE 2

Compound	X	Solvent	1H N.m.r. probe ^{a,b}	ΔG^\ddagger /kcal mol ⁻¹
(7)	S	CS ₂	CH ₂	9.3 ± 0.2 ^c
(8)	SO ₂	CD ₂ Cl ₂ -CF ₃ CO ₂ H (10 : 1)	CH ₂	11.3 ± 0.4 ^d

^a Details of the 1H n.m.r. chemical shifts are given in Table 1.
^b The site exchanges involving sites A1, B1, A2, B2, A3, and B3 are described in the text with reference to Figures 1 and 4. Line-shape analyses were carried out using program VI.
^c Value obtained from 1H n.m.r. line-shape analysis (see Figure 2).
^d Value obtained from 1H n.m.r. line-shape analysis (see Figure 3).

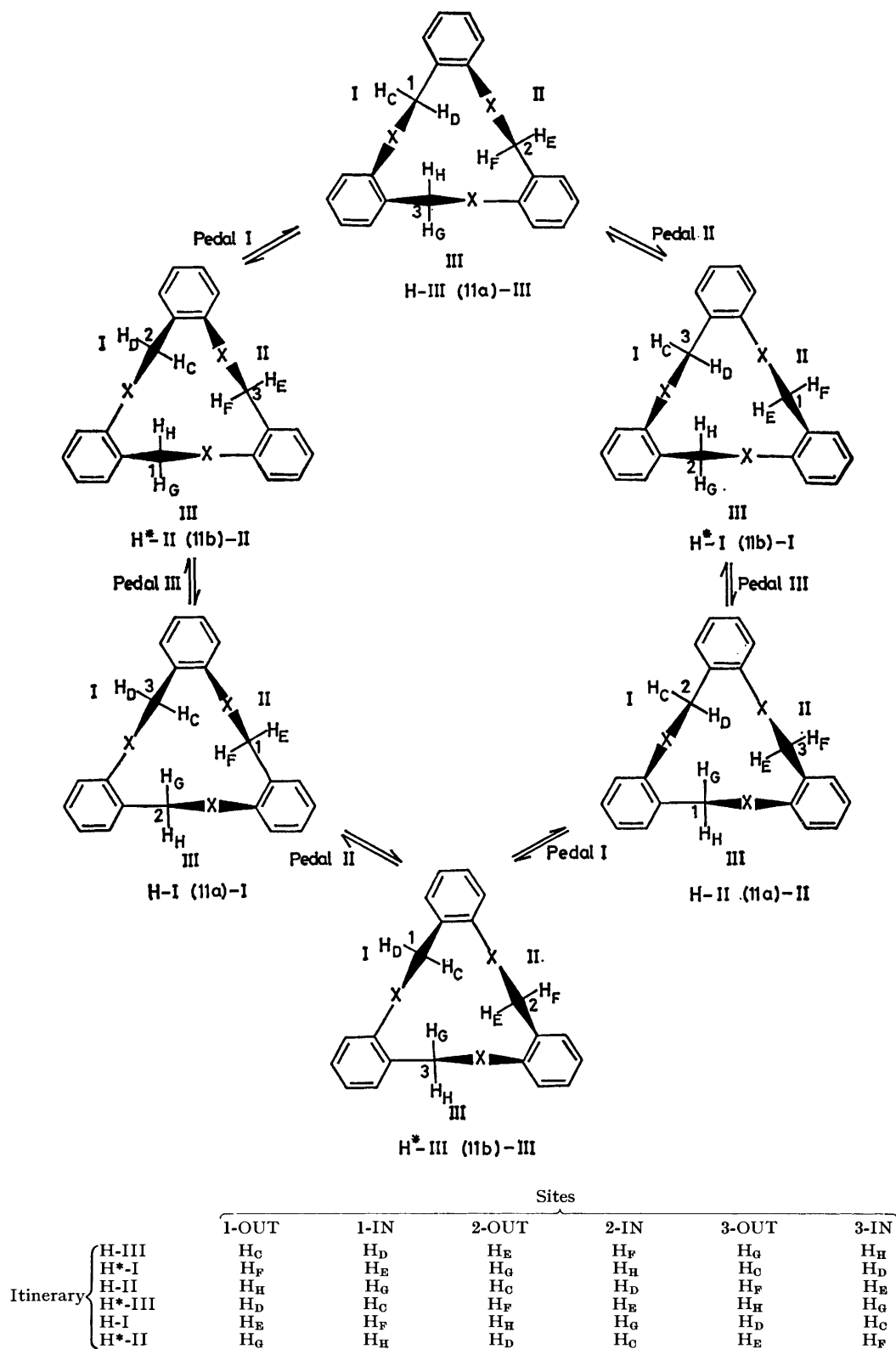
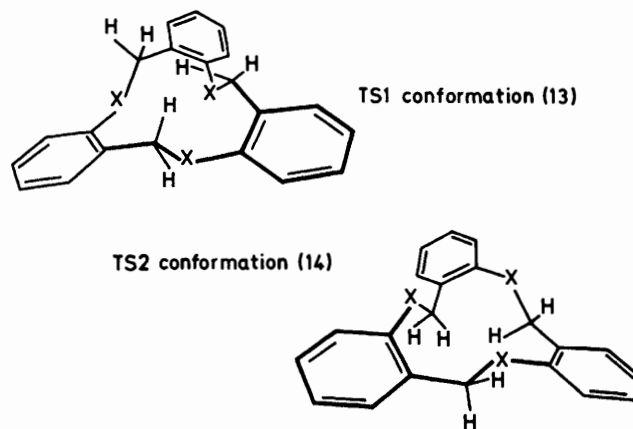


FIGURE 5 The itinerary of $H \rightleftharpoons H^*$ inversion processes required to exchange the six different methylene protons H_C , H_D , H_E , H_F , H_G , and H_H with the six different sites 1-OUT, 1-IN, 2-OUT, 2-IN, 3-OUT, and 3-IN in the cyclic trisulphide (7) and the cyclic tris-sulphone (8)

Molecular models of the cyclic trisulphide (7) and the cyclic trisulphone (8) reveal that two diastereoisomeric transition states to $H \rightleftharpoons H^*$ inversion need to be considered in each case. These are the TS1 (13) and TS2 (14) conformations which differ as a result of pedalling of an appropriate CH_2X group in an H (11a) or H^* (11b) conformation in opposite directions. In the TS1 conformation (13) the methylene group passes through the interior of the ring whereas in the TS2 conformation (14) a sulphur atom or sulphone grouping experiences this transformation. In the diagrams (13) and (14) the portions of the molecule indicated by thickened bonds are coplanar in each case. Attempts to manipulate CPK space-filling molecular models demonstrate that the passage of either a sulphur atom or a sulphone grouping through the interior of the ring is a highly unattractive proposition compared with an internal passage of a methylene group. Thus, only the TS1 conformation (13) in each case is worthy of further consideration. The fact that the free energy of activation for $H \rightleftharpoons H^*$ inversion in the cyclic trisulphide is not much smaller (indeed only by $0.8 \text{ kcal mol}^{-1}$) than the barrier of $10.1 \text{ kcal mol}^{-1}$ for $C_2 \rightleftharpoons C_2^*$ ring inversion in the analogous hydrocarbon (1) is of particular interest. If the transition state conformation for $H \rightleftharpoons H^*$ inversion in the cyclic trisulphide (7) is indeed of the TS1 type (13) then any conjugative stabilisation of the TS1 conformation (13) as a result of electron delocalisation between the lone pairs on sulphur and the π -system of the aromatic rings is rather small in energy terms.

Finally, it should be noted that the asymmetrical helix conformation (11a and b) which has been established as the only observable ground-state conformation



of the cyclic trisulphide (7) in solution also corresponds⁸ to the solid-state conformation of the molecule (7).

We thank Professor K. Mislow for criticism and discussions on the interpretation and presentation of the results, and Dr. A. G. Ferrige (Wellcome Research Laboratories) for recording homonuclear INDOR spectra. We gratefully acknowledge financial support (to J. S. S.) from the State Scholarship Foundation of the Government of Greece.

[7/1694 Received, 26th September, 1977]