Conformational Behaviour of Medium-sized Rings. Part 6.[1] 5,6,11,12,17,18-Hexahydrotribenzo[*a,e,i*]cyclododecene and its 2,3,8,9,14,15- and 1,4,7,10,13,16-Hexamethyl Derivatives. 2,3,8,9- and 1,4,7,10-Tetramethyl-5,6,11,12-tetrahydrodibenzo[*a,e*]cyclo-octene

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The temperature dependences of (i) the broad-band decoupled ^{13}C n.m.r. spectrum of 5,6,11,12,17,18-hexahydrotribenzo[*a,e,i*]cyclododecene (1) and (ii) the ^{1}H n.m.r. spectra of its 2,3,8,9,14,15- (2) and 1,4,7,10,13,16- (3) hexamethyl derivatives have been interpreted in terms of ring inversion between enantiomeric C_2 conformations. Conformational analysis on these molecules has been carried out with the aid of strain energy calculations on selected conformations of the parent hydrocarbon (1) and its 1,4,7,10,13,16-hexamethyl derivative (3). Useful correlations between calculated and experimental thermodynamic parameters were found. The temperature dependences of the ^{1}H n.m.r. spectra of the 2,3,8,9- (15) and 1,4,7,10- (16) tetramethyl derivatives of 5,6,11,12-tetrahydrodibenzo[*a,e*]cyclo-octene (14) have been interpreted in terms of interconversion of chair- and boat-like conformations. Strain energy calculations on selected conformations of the 1,4,7,10-tetramethyl derivative (14) have led to useful correlations between calculated and experimental thermodynamic parameters.

THE conformational properties of the hexahydrotribenzocyclododecene (1) were first discussed in a prescient publication in 1945 by Baker, Banks, Lyon, and Mann.[2] Inspection of molecular models led these authors to consider the four conformations (1a—d) shown in Figure 1 as possible forms for the molecule in the crystalline state. A preliminary *X*-ray study indicated that the occurrence of conformations (1a) and (1d), with trigonal symmetry, in the crystal was improbable, without providing any information concerning the relative merits of conformations (1b) and (1c). It is significant that several years before the wide recognition of conformational analysis as a stereochemical discipline,[3] the ready interconversion of conformations (1a)—(1d) was seen to involve only those changes in stereochemistry commonly described nowadays as torsional processes. Hexahydrotribenzocyclododecene (1) is the parent hydrocarbon of a series of twelve-membered ring systems which include the trisalicylide derivatives (4)—(6). The recognition[4] that tri-3,6-dimethylsalicylide (4), tri-*o*-thymotide (5), and tri-*o*-carvocrotide (6) all exist in solution in diastereoisomeric propeller and helical conformations encouraged us in 1972 to examine the conformational behaviour of the hydrocarbon (1) and its hexamethyl derivatives (2) and (3) in solution.

In 1945, Baker *et al.*[2] reported the synthesis of the hexahydrotribenzocyclododecene (1) from *o*-xylylene dibromide with sodium in (i) dioxan and (ii) ether

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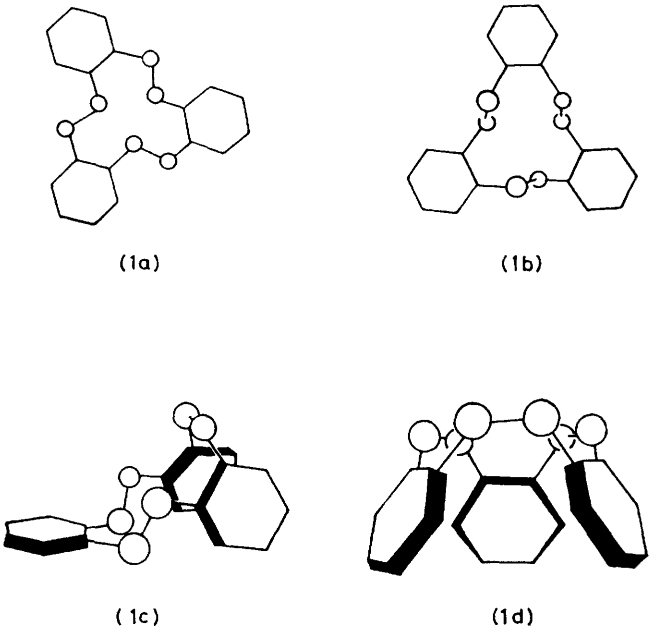
[1] Part 5, D. J. Brickwood, A. M. Hassan, W. D. Ollis, J. S. Stephanatou, and J. F. Stoddart, preceding paper.

[2] W. Baker, R. Banks, D. R. Lyon, and F. G. Mann, *J. Chem. Soc.*, 1945, 27.

[3] D. H. R. Barton, *Experientia*, 1950, **6**, 316; *Topics Stereochem.*, 1971, **6**, 1; O. Hassel, *Tidsskr. Kjemi Bergvesen og Metallurgi*, 1943, **3** [5], 32; *Topics Stereochem.*, 1971, **6**, 11.

[4] 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.

containing small amounts of ethyl acetate. In our hands, a Wurtz reaction employing the solvent conditions in (ii) gave a low yield of the hydrocarbon (1) together with small amounts of the acyclic hydrocarbons (7), (10), and (13). This reaction has been the subject of several investigations[5-8] and the yield of the tribenzocyclododecene (1) has been improved[5,6,8] (i) by varying the relative concentrations of the reactants[5,8] and (ii) by incorporating tetraphenylethylene as catalyst.[5,6] Tetrahydrodibenzocyclo-octene (14)[2,5-14] was obtained as the major product in 45% yield along with 16% of the tribenzocyclododecene (1) and small amounts of *o*-ditolylethane (7) when we carried out the Wurtz reaction in tetrahydrofuran in the presence of tetraphenylethylene (*cf.* ref. 6).

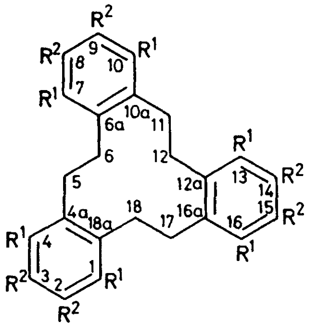

(1a) (1b)

(1c) (1d)

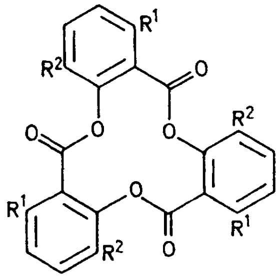
FIGURE 1 Reproductions of the photographs of molecular models shown in ref. 2 for four 'strainless phases' (1a—d) of hexahydrotribenzocyclododecene (1); (1a) with C_{3h} symmetry, (1b) with C_2 symmetry, (1c) with C_s symmetry, and (1d) with C_{3v} symmetry

The 2,3,8,9,14,15-hexamethyl derivative (2) of (1) and the 2,3,8,9-tetramethyl derivative (15) of (14) were obtained together with the acyclic hydrocarbons (8) and (11) by a tetraphenylethylene-catalysed Wurtz reaction on the dibromide (21) in tetrahydrofuran. The dibromide (21) was synthesized by a route involving (i) a Diels–Alder cycloaddition[15] between 2,3-dimethylbuta-1,3-diene and diethyl acetylenedicarboxylate to give diethyl 4,5-dimethylcyclohexa-1,4-diene-1,2-dicarboxylate (17) together with small amounts of the aromatic oxidation product (18), (ii) oxidation of (17) with 2-chloro-2-nitropropane[16] in methanolic sodium methoxide to the known[16] dimethyl diester (19), (iii) reduction of (19) with lithium aluminium hydride to the diol (20), and finally (iv) treatment of (20) with phosphorus tribromide.

The 1,4,7,10,13,16-hexamethyl derivative (3) of (1) and the 1,4,7,10-tetramethyl derivative (16) of (14) were obtained together with the acyclic hydrocarbons (9) and (12) and 1,2,3,4-tetramethylbenzene (26) by a Wurtz reaction on the dibromide (25) in ether–ethyl acetate. The synthesis of the dibromide (25) was based on known procedures[17,18] involving (i) a Diels–Alder condensation[17] between 2,5-dimethylfuran and maleic



(1) $R^1 = R^2 = H$
(2) $R^1 = H, R^2 = Me$
(3) $R^1 = Me, R^2 = H$



(4) $R^1 = R^2 = Me$
(5) $R^1 = Me, R^2 = CHMe_2$
(6) $R^1 = CHMe_2, R^2 = Me$

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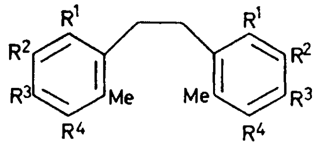
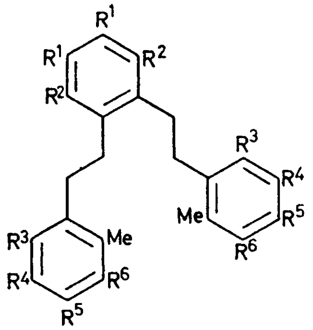
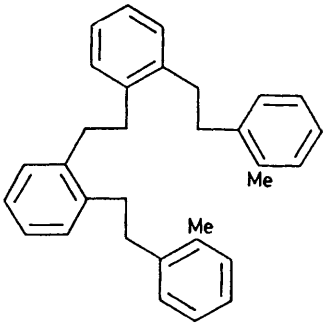
anhydride to give the adduct (22), (ii) acid-catalysed dehydration of (22) to yield 3,6-dimethylphthalic anhydride (23), (iii) reduction[18] of (23) with lithium aluminium hydride to the diol (24), and finally (iv) treatment[18] of (24) with phosphorus tribromide.



(7) $R^1 = R^2 = R^3 = R^4 = H$
(8) $R^1 = R^4 = H, R^2 = R^3 = Me$
(9) $R^1 = R^4 = Me, R^2 = R^3 = Me$



(10) $R^1 = R^2 = R^3 = R^4 = R^5 = R^6 = H$
(11) $R^1 = R^4 = R^5 = Me, R^2 = R^3 = R^6 = H$
(12) $R^1 = R^4 = R^5 = H, R^2 = R^3 = R^6 = Me$



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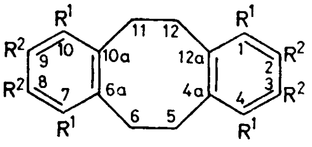
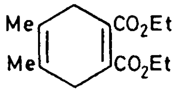


(14) $R^1 = R^2 = H$
(15) $R^1 = H, R^2 = Me$
(16) $R^1 = Me, R^2 = H$

In this paper, results of studies on the conformational behaviour of the twelve-membered ring hydrocarbon (1) and its 1,4,7,10,13,16-hexamethyl derivative (3) in solution by dynamic ^{13}C and ^1H n.m.r. spectroscopy are compared with the conclusions reached on the basis of strain energy calculations.[11,19] In this way, the influence on the conformational behaviour of aromatic methyl substituents in the *ortho*-positions with respect to the twelve-membered ring can be assessed. In the 2,3,8,9,14,15-hexamethyl derivative (2) the methyl substituents occupy simultaneously *meta*- and *para*-positions on the benzene rings relative to the twelve-membered ring. Since it has hydrogen atoms in all six *ortho*-positions, and since it contains good ^1H n.m.r. probes in the form of the aromatic protons and methyl protons, the hydrocarbon (2) may be considered as an ideal model for the parent hydrocarbon (1). This means that a comparison is possible between the results obtained in solution by dynamic ^{13}C n.m.r. spectroscopy with the parent hydrocarbon (1) and by dynamic ^1H n.m.r. spectroscopy with the 2,3,8,9,14,15-hexamethyl derivative (2). Part of this investigation has been the subject of a preliminary communication[20] and has also been discussed briefly in a recent review[11] on the conformational behaviour of some medium-sized ring systems. Finally, the availability from the syntheses of (2) and (3) of the 2,3,8,9- (15) and 1,4,7,10- (16) tetramethyl derivatives of tetrahydrodibenzocyclo-octene (14) has prompted us to examine the conformational properties of these '6,8,6' systems in solution and compare our results with those in the literature[10-14] for (14). In particular, the 2,3,8,9-tetramethyl derivative (15), with its four *ortho*-hydrogen atoms on the benzene rings and its good ^1H n.m.r. probes in the form of the aromatic protons and methyl protons, may be regarded as a suitable model for the parent hydrocarbon (14).



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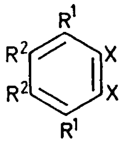
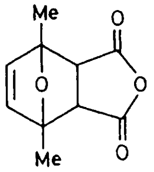


(18) $R^1 = H, R^2 = Me, X = CO_2Et$
(19) $R^1 = H, R^2 = Me, X = CO_2Me$
(20) $R^1 = H, R^2 = Me, X = CH_2OH$
(21) $R^1 = H, R^2 = Me, X = CH_2Br$
(24) $R^1 = Me, R^2 = H, X = CH_2OH$
(25) $R^1 = Me, R^2 = H, X = CH_2Br$



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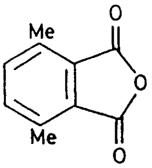

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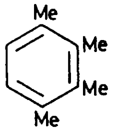

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EXPERIMENTAL

Apart from ^{13}C n.m.r. spectroscopy, the general methods are described in Part 3.[21] Broad-band decoupled ^{13}C n.m.r. spectra were recorded on a JEOL SP 100 spectrometer with dichlorodideuteriomethane as ' lock ' and tetramethylsilane as internal standard.

Reaction between Sodium and o-*Xylylene Dibromide* (*with* T. J. GRANT).[2]—Sodium wire (35.4 g) was added to a solution of *o*-xylylene dibromide (93.4 g) in dry ether (600 ml) and the mixture was heated under reflux for 24 h. Additions of ethyl acetate (2 ml) were made initially, and at the end of 5, 15, and 20 h. After the reaction was complete, the resulting amorphous solid was removed by filtration. Evaporation of the filtrate gave an oily residue which was separated into four fractions by fractional distillation. Fraction 1 had b.p. 50—56° at 20 mmHg, fraction 2 b.p. 80—140° at 0.1 mmHg, fraction 3 b.p. 140—210° at 0.1 mmHg, and fraction 4 b.p. 210—260 at 0.1 mmHg. Fraction 1 crystallised from ethanol as needles of *o*-ditolylethane (7) (0.11 g, 1%), m.p. 65° (lit.,[2] 65—66°), M^+ 210, $\tau(CDCl_3)$ 2.90 (8 H, s, aromatic), 7.18 (4 H, s, CH_2CH_2), and 7.72 (6 H, s, 2 × Me). Fraction 2 was purified by distillation to give 1,2-*bis*-(o-*methylphenethyl*)*benzene* (10) (0.25 g, 1%), b.p. 210° at 0.5 mmHg [Found: C, 92.1; H, 8.25%; *M* (mass spec.), 314. $C_{24}H_{26}$ requires C, 91.7; H, 8.3%; *M*, 314], $\tau(CDCl_3)$ 2.74—2.96 (12 H, m, aromatic), 7.15 (8 H, s, 2 × CH_2CH_2), and 7.74 (6 H, s, 2 × Me). Column chromatography of fraction 3 on silica gel using benzene–light petroleum (b.p. 60—80°) (1 : 1) as eluant yielded 5,6,11,12,-17,18-hexahydrotribenzo[*a,e,i*]cyclododecene (1) (0.022 g, 0.1%), m.p. 189° (lit.,[2] 184.5°), M^+ 312, $\tau(CDCl_3)$ 2.60—2.92 (12 H, m, aromatic) and 6.97 (12 H, s, 3 × CH_2CH_2). Fraction 4 crystallised from ethanol to yield 2,2′-*bis*-(o-*methylphenethyl*)αα′-*bibenzyl* (13) (0.023 g, 0.1%), m.p. 69° [Found: C, 90.9; H, 7.95%; *M* (mass spec.), 418. $C_{32}H_{34}$ requires C, 91.9; H, 8.14%, *M*, 418], $\tau(CDCl_3)$ 2.76—2.98 (16 H, m, aromatic), 7.12 (4 H, s, bibenzyl CH_2CH_2), 7.17 (8 H, s, other CH_2CH_2), and 7.76 (6 H, s, 2 × Me).

The reaction was also carried out in dry tetrahydrofuran with tetraphenylethylene as catalyst.[6] Column chromatography on silica gel using benzene–light petroleum (b.p. 60—80°) (15 : 1) as eluant gave 5,6,11,12-tetrahydrodibenzo[*a,e*]cyclo-octene (14) (45%), m.p. 109—111° (lit.,[6] 110—112°) in addition to *o*-ditolylethane (7) (2%) and 5,6,11,12,17,18-hexahydrotribenzo[*a,e,i*]cyclododecene (1) (16%).

Diethyl 4,5-*Dimethylcyclohexa*-1,4-*diene*-1,2-*dicarboxylate* (17).[15]—2,3-Dimethylbuta-1,3-diene (820 mg) and diethyl acetylenedicarboxylate (1.7 g) were heated in an autoclave at 120 °C for 6 h. T.l.c. indicated that two products were formed. They were separated by column chromatography on silica gel using light petroleum (b.p. 60—80°)–ethyl acetate (8 : 1) as eluant. Fraction 1 corresponded to the diene (17) (2.05 g, 81%), M^+ 252, $\tau(CDCl_3)$ 5.78 (4 H, q, *J* 7.8 Hz, 2 × $CO_2CH_2CH_3$), 7.10 (4 H, s, methylene protons), 8.35 (6 H, s, 2 × Me), and 8.71 (6 H, t, *J* 7.8 Hz, 2 × $CO_2CH_2CH_3$). Fraction 2 was characterised as diethyl 4,5-dimethylbenzene-1,2-dicarboxylate (18) (190 mg, 8%), M^+ 250, $\tau(CDCl_3)$ 2.55 (2 H, s, aromatic), 5.69 (4 H, q, *J* 7.5 Hz, 2 × $CO_2CH_2CH_3$), 7.72 (6 H, s, 2 × Me), and 8.68 (6 H, t, *J* 7.5 Hz, 2 × $CO_2CH_2CH_3$).

The same products were obtained when 2,3-dimethylbuta-1,3-diene (820 mg) and diethyl acetylenedicarboxylate (1.7 g) were heated under reflux in ethanol (15 ml) for 24 h.

Dimethyl 4,5-*Dimethylbenzene*-1,2-*dicarboxylate* (19).[16]—The diene diester (17) (8.0 g) was added to M-sodium methoxide (500 ml) containing 2-chloro-2-nitropropane (40 ml) and the mixture was refluxed in nitrogen for 1 h. The solution was acidified with hydrochloric acid and then excess of acid was destroyed by addition of ethereal diazomethane. Extraction with ether yielded the crude product as an oil. Crystallisation from methanol gave the diester (19) (7.2 g, 92%), m.p. 54—55° (lit.,[16] 56°).

1,2-*Bishydroxymethyl*-4,5-*dimethylbenzene* (20).—The diester (19) (1.3 g) was refluxed for 6 h with lithium aluminium hydride (650 mg) in dry ether (40 ml). The excess of hydride was destroyed by addition of moist ether followed by water. The mixture was filtered and the residual solid was washed thoroughly with dilute hydrochloric acid and then with water. The combined filtrates were extracted with ether, and the ethereal layer was dried (Na_2SO_4) and evaporated. The crude product was recrystallised from light petroleum (b.p. 60—80°) to give the *diol* (20) (760 mg, 88%), m.p. 95—98° [Found: C, 72.5; H, 8.8%; *M* (mass spec.), 166. $C_{10}H_{14}O_2$ requires C, 72.3; H, 8.5%; *M*, 166], $\tau(CDCl_3)$ 2.94 (2 H, s, aromatic), 5.41 (4 H, s, 2 × CH_2OH), 6.58 (2 H, br s, 2 × OH), and 7.87 (6 H, s, 2 × Me).

1,2-*Bisbromomethyl*-4,5-*dimethylbenzene* (21).—Phosphorus tribromide (4.2 ml) in dry ether (56 ml) was added dropwise with stirring to the diol (20) (3.5 g) dissolved in dry benzene (40 ml) and dry ether (40 ml). The mixture was stirred for 2 h and then poured into water (160 ml). The organic layer was washed with 10% sodium hydrogen carbonate solution (2 × 25 ml) and then with water (2 × 40 ml), then dried (Na_2SO_4) and evaporated. Recrystallisation of the residue from ethanol gave the *dibromide* (21) (5.6 g, 92%), m.p. 113—116° (decomp.) [Found: C, 41.1; H, 4.3; Br, 54.5%; *M* (mass spec.), 290. $C_{10}H_{12}Br_2$ requires C, 41.1; H, 4.1; Br, 54.8%; *M*, 290], $\tau(CDCl_3)$ 2.89 (2 H, s, aromatic), 5.40 (4 H, s, 2 × CH_2Br), and 7.79 (6 H, s, 2 × Me).

Reaction between Sodium and the Dibromide (21).—A solution of the dibromide (21) (4.5 g) in dry tetrahydrofuran (20 ml) was added with stirring during 10 h to sodium (1.5 g) and tetraphenylethylene (260 mg) in dry tetrahydrofuran (30 ml) cooled to −80 °C in acetone–solid CO_2. After the reaction was complete moist ether was added followed by water. Separation of the organic layer was followed by further extraction with chloroform; the material from the organic solutions was subjected to column chromatography on silica gel using benzene–light petroleum (b.p. 60—80°) (1 : 30) as eluant to give four components. Component 1 was recrystallised from ether–ethanol to afford *bis*-(2,4,5-*trimethylphenyl*)*ethane* (8) (96 mg, 5%), m.p. 136—137° [Found: *M* (mass spec.), 266.203 4. $C_{20}H_{26}$ requires *M*, 266.203 5], $\tau(CDCl_3)$ 3.03 and 3.06 (4 H, two equal intensity singlets, aromatic), 7.24 (4 H, s, CH_2CH_2), and 7.72 and 7.78 (18 H, 2 × s, 6 × Me). Component 2 was recrystallised from chloroform–ethanol to give 2,3,8,9-*tetramethyl*-5,6,11,12-*tetrahydrodibenzo*[a,e]*cyclo-octene* (15) (225 mg, 11%), m.p. 246—248°, [Found: *M* (mass spec.), 264.187 2. $C_{20}H_{24}$ requires *M*, 264.187 9], $\tau(CDCl_3–CS_2)$, 3.31 (4 H, s, aromatic), 7.09 (8 H, s, 2 × CH_2CH_2), and 7.91 (12 H, s, 4 × Me). Component 3 was characterised after recrystallisation from ether–ethanol as 1,2-*dimethyl*-4,5-*bis*-(2,4,5-*trimethylphenethyl*)*benzene* (11) (136 mg, 6%), m.p. 139—140.5° [Found: *M* (mass spec.), 398.296 6. $C_{30}H_{38}$ requires

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

M, 398.297 3], $\tau(CDCl_3)$ 3.01, 3.06, and 3.09 (6 H, 3 equal intensity singlets, aromatic), 7.22 (8 H, s, 2 × CH_2CH_2), and 7.74, 7.77, and 7.81 (24 H, 3 × s, 8 × Me). Component 4 was recrystallised from chloroform–ethanol to afford needles of 2,3,8,9,14,15-*hexamethyl*-5,6,11,12,17,18-*hexahydrotribenzo*[a,e,i]*cyclododecene* (2) (242 mg, 11%), m.p. >310° [Found: M (mass spec.), 396.280 1. $C_{30}H_{36}$ requires M, 396.281 7], $\tau(CDCl_3)$ 2.93 (6 H, s, aromatic), 7.07 (12 H, s, 3 × CH_2CH_2), and 7.76 (18 H, s, 6 × Me).

Diels–Alder Adduct (22) *of* 2,5-*Dimethylfuran and Maleic Anhydride*.[17]—2,5-Dimethylfuran (500 ml) was added dropwise with vigorous stirring during 1 h to maleic anhydride (44 g) in dry ether (100 ml). Stirring was continued for 16 h and then the crystalline product was collected. The filtrate was cooled in an ice-bath for 2 h to yield additional product. The yellow crystalline adduct (22) (54.5 g, 66%) had m.p. 70—72° (lit.,[17] 59—63°), M^+ 194, $\tau[(CD_3)_2CO]$ 3.59 (2 H, s, olefinic), 6.65 (2 H, s, methine), and 8.35 (6 H, s, 2 × Me).

3,6-*Dimethylphthalic Anhydride* (23).[17]—The Diels–Alder adduct (22) (54 g) was added in portions to a rapidly stirred solution of 90% sulphuric acid (600 ml) maintained between 0 and −6 °C. Stirring was continued for 1 h at 0 °C and then the temperature was allowed to rise to +10 °C. The mixture was then poured on to ice (1.5 kg) and the precipitate was collected, washed with ice–water, and dissolved in water (800 ml) containing sodium hydroxide (40 g). Upon addition of glacial acetic acid (150 ml) a small quantity of 2,5-dimethylbenzoic acid (m.p. 132—134°; lit.,[17] 132—134°) was obtained. Crude 3,6-dimethylphthalic anhydride was isolated from the filtrate by adding 5N-hydrochloric acid until the solution was acidic. Recrystallisation from benzene gave the pure anhydride (23) (34.5 g, 71%), m.p. 140—141° (lit.,[17] 142—143°), M^+ 176, $\tau[(CD_3)_2CO]$ 2.30 (2 H, s, aromatic) and 7.40 (6 H, s, 2 × Me).

1,2-*Bishydroxymethyl*-3,6-*dimethylbenzene* (24).[18]—3,6-Dimethylphthalic anhydride (23) (30 g) was extracted (Soxhlet) into refluxing dry ether (900 ml) containing lithium aluminium hydride (15 g). Heating under reflux was continued for 28 h and then excess of hydride was destroyed by addition of moist ether followed by water. The mixture was filtered and the residual solid was washed thoroughly with dilute hydrochloric acid and then with water. The combined filtrates were extracted with ether; the ethereal layer was dried (Na_2SO_4) and evaporated. The crude product was recrystallised from light petroleum (b.p. 60—80 °C) to give needles of the diol (24) (25.2 g, 87%), m.p. 69—70° (lit.,[18] 70°), M^+ 166, $\tau(CDCl_3)$ 2.95 (2 H, s, aromatic), 5.35 (4 H, br s, 2 × CH_2OH), 6.10 (2 H, br s, 2 × OH), and 7.68 (6 H, s, 2 × Me).

1,2-*Bisbromomethyl*-3,6-*dimethylbenzene* (25).[18]—Phosphorus tribromide (30 ml) in dry ether (400 ml) was added dropwise with stirring to the diol (24) (25 g) dissolved in benzene (250 ml) and dry ether (250 ml). The mixture was stirred for 16 h, and then poured into water (1 l). The organic layer was washed with 10% sodium hydrogen carbonate solution (2 × 150 ml) and then with water (2 × 150 ml), dried (Na_2SO_4), and evaporated to yield a crystalline residue. Recrystallisation from ethanol gave the dibromide (25) (36 g, 94%), m.p. 101—102° (lit.,[18] 100°), M^+ 290, $\tau(CDCl_3)$ 2.90 (2 H, s, aromatic), 5.30 (4 H, s, 2 × CH_2Br), and 7.65 (6 H, s, 2 × Me).

Reaction between Sodium and the Dibromide (25).—Sodium wire (5.35 g) was added to a solution of the dibromide (25) (14 g) in dry ether (100 ml) and the mixture was heated under reflux for 24 h. Additions of ethyl acetate (2 ml) were made initially and at the end of 5, 10, and 20 h. After the reaction was complete, the inorganic material was removed by filtration. Evaporation of the filtrate gave an oily residue which was separated by fractional distillation at 5 mmHg. Fraction 1 (0.89 g) had b.p. 64—88° and fraction 2 (1.7 g) b.p. 90—220°. Fraction 1 was redistilled at 4.5 mmHg to give 1,2,3,4-tetramethylbenzene (26) (370 mg, 6%), b.p. 78—80° at 4.5 mmHg (lit.,[17] 78.5—80.5° at 10 mmHg). Fraction 2 was subjected to column chromatography on silica gel using benzene–light petroleum (b.p. 60—80 °C) (1 : 19) as eluant to give four crystalline components. Component 1 was recrystallised from light petroleum (b.p. 40—60°) to give *bis*-(2,3,6-*trimethylphenyl*)-*ethane* (9) (110 mg, 9%), m.p. 97—100° [Found: M (mass spec.), 266.203 8. $C_{20}H_{26}$ requires M, 266.203 4], $\tau(CDCl_3)$ 3.09 (4 H, s, aromatic), 7.17 (4 H, s, CH_2CH_2), and 7.66, 7.72, and 7.75 (18 H, 3 equal intensity singlets, 6 × Me). Component 2 was recrystallised from light petroleum (b.p. 60—80 °C) to give 1,4,7,10-*tetramethyl*-5,6,11,12-*tetrahydrodibenzo*[a,e]*cyclo-octene* (16) (45 mg, 4%), m.p. 128—130° [Found: M (mass spec.), 264.187 7. $C_{20}H_{24}$ requires M, 264.187 9], $\tau(CDCl_3)$ 3.29 (4 H, s, aromatic), 6.91 (8 H, s, 2 × CH_2CH_2), and 7.76 (12 H, s, 4 × Me). Component 3 was recrystallised from light petroleum (b.p. 60—80 °C) to give 1,2-*dimethyl*-3,6-*bis*-(2,3,6-*trimethylphenylethyl*)*benzene* (12) (63 mg, 3%), m.p. 166—168° [Found: M (mass spec.), 398.296 1. $C_{30}H_{38}$ requires M, 398.297 3] $\tau(CDCl_3)$ 3.20—3.24 (6 H, m, aromatic), 7.16 (8 H, s, 2 × CH_2CH_2), and 7.73, 7.78, 7.83, and 7.88 (24 H, 4 equal intensity singlets, 8 × Me). Component 4 was recrystallised from benzene–light petroleum (b.p. 60—80 °C) to give 1,4,7,10,-13,16-*hexamethyl*-5,6,11,12,17,18-*hexahydrotribenzo*[a,e,i]-*cyclododecene* (3) (4 mg, <1%), m.p. >290° [Found: M (mass spec.), 396.280 7. $C_{30}H_{36}$ requires M, 396.281 7], $\tau(CDCl_3)$ 2.95—3.05 (6 H, m, aromatic), 6.70—7.10 (12 H, m, 3 × CH_2CH_2), and 7.42, 7.50, and 7.54 (18 H, 3 equal intensity signals, 6 × Me).

Determination of Rates of Conformational Changes by Dynamic ^1H *and* ^{13}C *N.m.r. Spectroscopy*.—The methods used are fully described in Parts 1—4.[10, 21–23] The computer programs (coded in FORTRAN IV) used to generate the theoretical line-shapes are now described for the general methods I—III.

Method I. A program (I) * for exchange of nuclei between two equally or unequally populated sites, A and B, with no mutual coupling. The aromatic protons of eight-membered ring compounds (15) and (16) both gave two singlet signals of unequal intensities at low temperatures and so spectral line-shapes were simulated using this program. Calculated and observed spectra are shown in Figures 2 and 3 for compounds (15) and (16), respectively. The methyl protons of compounds (15) and (16) both gave two singlets at low temperatures as well. In the case of compound (16), spectral line-shapes were also simulated using this program. Calculated and observed spectra are shown in Figure 3.

Method II. A program (IV) † for exchange of nuclei

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* The program numbers (I—III) established in Part 3 [21] are adhered to in this paper, and together with the additional programs (IV and V) described here, these programs will form the basis of a collection for reference in future Parts of this series.

[22] Part 2, R. P. Gellatly, W. D. Ollis, and I. O. Sutherland, *J.C.S. Perkin I*, 1976, 913.

[23] Part 4, D. J. Brickwood, W. D. Ollis, and J. F. Stoddart, *J.C.S. Perkin I*, 1978, 1385.

between three equally or unequally populated sites, A, B, and C, with no mutual coupling. The modified form of the Bloch equations introduced by McConnell[24] can be extended[25] to cases involving exchange between more than two sites with no mutual coupling. For a j site problem, the general equation (1) may be written for the complex magnetic moment G_j of the jth site. The assumption is made that all spectra were recorded under steady-state conditions so that all the time derivatives of the complex magnetic moments may be set to zero.[24,26]

$$\alpha_jG_j - \Sigma_{1\neq j}(k_{1j}G_1 - k_{j1}G_j) = -i\gamma H_1M_0P_j \qquad (1)$$

where

$$\alpha_j = T_{2j}^{-1} - i(\omega_j - \omega) \qquad (2)$$

ω is the observing frequency * and is therefore that of the rotational frequency ‡ of the applied field H_1, ω_j is the Larmor frequency ‡ corresponding to the jth site, T_{2j} is the transverse relaxation time of nuclei in the jth site, p_j is the population of site j expressed as a mole fraction, M_0 is the nuclear magnetic moment per unit volume, γ is the gyromagnetic ratio for the nucleus under investigation and k_{1j} *etc.* is the rate constant for exchange from site 1 to site j *etc.* For an exchange process between three sites A, B, and C with no mutual coupling, the complex simultaneous equations (3)—(5) can be derived from the general equation (1) as follows:

$$G_A(\alpha_A + k_{AB} + k_{AC}) + G_B(-k_{BA}) + G_C(-k_{CA}) = -\gamma iH_1M_0p_A \qquad (3)$$

$$G_A(-k_{AB}) + G_B(\alpha_B + k_{BA} + k_{BC}) + G_C(-k_{CB}) = -i\gamma H_1M_0p_B \qquad (4)$$

$$G_A(-k_{AC}) + G_B(-k_{BC}) + G_C(\alpha_C + k_{CA} + k_{CB}) = -i\gamma H_1M_0p_C \qquad (5)$$

These equations were solved for the complex magnetic moments G_A, G_B, and G_C by use of a MASTER THREE SITE computer program. Values for site frequencies, ω_j, populations, p_j, and relaxation times, T_{2j} were obtained initially from chemical shifts, relative intensities, and half-height peak widths for the singlet signals A, B, and C in the low temperature spectra. The absorption intensity at frequency ω is proportional to the imaginary part of $G_A + G_B + G_C$. The solutions to equations (3)—(5) for a range of values for ω which cover the appropriate region of the spectrum give line-shapes for selected input values of the rate constants, k_{AB} *etc.* All three twelve-membered ring compounds (1)—(3) exhibited low temperature spectra consistent with a conformation which renders constitutionally identical atoms and groups in these compounds diastereotopic. Thus, the methyl protons of compound (3) give rise to three singlet signals at room temperature and below. The spectral line-shapes associated with the high temperature spectra were simulated (see Figure 4) using this program. Compound (2) exhibited low temperature spectral dependence for its aromatic protons whilst the quaternary aromatic carbons and bismethylene carbons of compound (1) each gave rise to three singlets at low temperatures in its broad-band decoupled ^{13}C n.m.r. spectrum (see Figure 5). In all cases, spectral line shapes were simulated using this program. Calculated and observed spectra are shown in Figures 6—8.

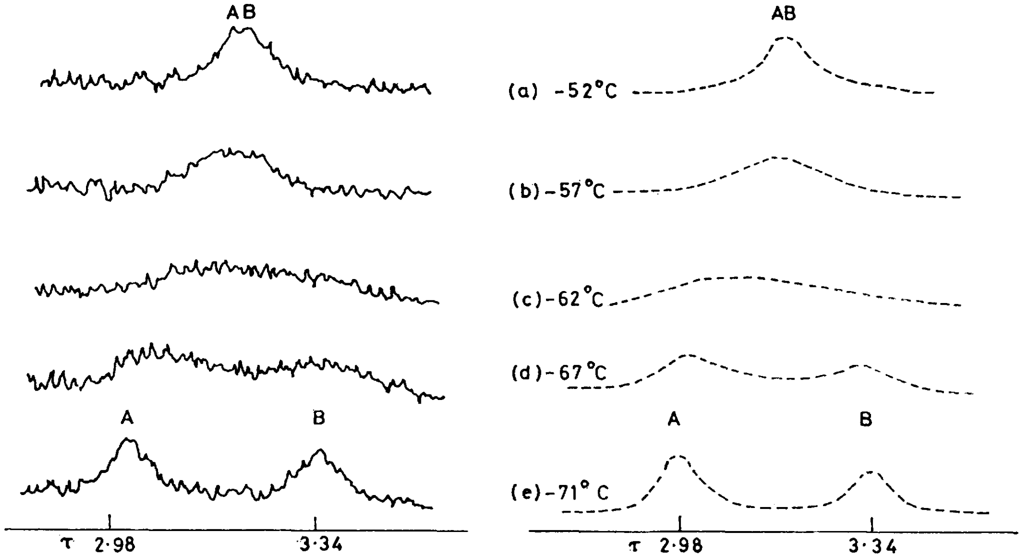

FIGURE 2 Observed (full line) and computed (broken line) spectra of the aromatic protons of 2,3,8,9-tetramethyl-5,6,11,12-tetrahydrodibenzo[*a,e*]cyclo-octene (15): (a) at −52 °C, k_{AB} 215 s^{-1}, p_A 0.6, p_B 0.4; (b) at −57 °C, k_{AB} 126 s^{-1}, p_A 0.6, p_B 0.4; (c) at −62 °C, k_{AB} 68 s^{-1}, p_A 0.6, p_B 0.4; (d) at −67 °C, k_{AB} 34 s^{-1}, p_A 0.6, p_B 0.4; (e) at −71 °C, k_{AB} 15 s^{-1}, p_A 0.6, p_B 0.4

Method III. A program (V) † for exchange of nuclei between four equally or unequally populated sites A, B, C, and D with no mutual coupling. This computer program (MASTER FOUR SITE) was written to solve the four complex simultaneous equations which can be derived from the general equation (1) in an analogous manner to that described in method II. The problem has already been discussed by us at some length in our publications[4] on the conformational behaviour of the trisalicylide derivatives (4)—(6). This program was used to simulate the spectral

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* Angular frequency units (radians s^{-1}) are used for all frequencies in these equations.

† We thank Professor I. O. Sutherland for a copy of his program.

[24] H. M. McConnell, *J. Chem. Phys.*, 1958, **28**, 430.

[25] C. S. Johnson, *Adv. Magnetic Resonance*, 1965, **1**, 33.

[26] L. W. Reeves, *Adv. Phys. Org. Chem.*, 1965, **3**, 187; A. Allerhand, H. S. Gutowsky, J. Jonas, and R. A. Meinzer, *J. Amer. Chem. Soc.*, 1966, **88**, 3185.

line-shapes of the methyl protons of compound (3) in order to examine the possibility that a small amount of a second conformation in a diastereoisomeric mixture was populating a fourth site. Calculated spectra are shown in Figure 4 beside the observed spectra and the spectra calculated using Method II assuming only three-site occupancy.

Strain Energy Calculations.—These were carried out on compounds (1), (3), and (16) using a program * (coded in FORTRAN) based upon the procedure reported by Allinger *et al.*[19] Details of the force field employed have been given in a recent review.[11]

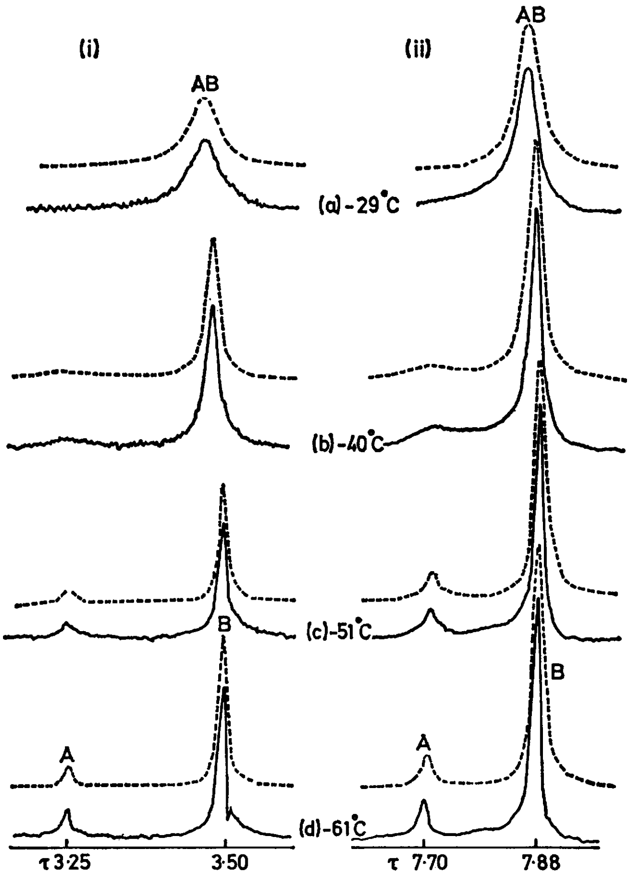

FIGURE 3 Observed (full line) and computed (broken line) spectra of (i) the aromatic protons and (ii) the methyl protons of 1,4,7,10-tetramethyl-5,6,11,12-tetrahydrodibenzo[*a,e*]cyclooctene (16): (a) at −29 °C, k_{AB} 129 s^{-1} for (i) k_{AB} 124 s^{-1} for (ii), p_A 0.12, p_B 0.88; (b) at −40 °C, k_{AB} 20 s^{-1} for (i) and (ii), p_A 0.12, p_B 0.88; (c) at −51 °C, k_{AB} 2.0 s^{-1} for (i), k_{AB} 2.2 s^{-1} for (ii), p_A 0.12, p_B 0.88; (d) at −61 °C, k_{AB} 0.36 s^{-1} for (i), k_{AB} 0.35 s^{-1} for (ii), p_A 0.12, p_B 0.88

RESULTS AND DISCUSSION

The temperature-dependent n.m.r. spectra and the conformational properties of the twelve-membered ring compounds (1)—(3) are presented first, and the discussion of the corresponding results for the ' 6,8,6 ' systems (15) and (16) follows.

The Temperature-dependent N.m.r. Spectra and the Conformational Properties of 5,6,11,12,17,18-*Hexahydrotribenzo*[a,e,i]*cyclododecene* (1) *and its* 2,3,8,9,14,15- (2) *and* 1,4,7,10,13,16- (3) *Hexamethyl Derivatives*.—The ^1H n.m.r. spectrum of the hexahydrotribenzocyclododecene (1) at room temperature in carbon disulphide containing a small amount of deuteriochloroform showed (see Table 1) a multiplet for the aromatic protons and a singlet for the CH_2–CH_2 protons which became a broad *unsymmetrical* multiplet at —80 °C indicating the presence of a conformation devoid of three-fold symmetry. Molecular models suggest that compounds (1)—(3) could adopt (see Figure 9) two conformations in the ground state, one with C_2 symmetry (27a) and the other with D_3 symmetry (28a). These two conformations (denoted by C_2 and D_3) are topologically analogous to the helical (C_1) and propeller (C_3) conformations of the trisalicylides.[4] Since the C_2 conformation (27a) has only one C_2 axis of symmetry it follows that the CH_2 groups of the two homotopic CH_2CH_2 groups are diastereotopic while the CH_2CH_2 group which is bisected by the C_2 axis contains homotopic CH_2 groups. Thus, this conformation (27a; $R^1 = R^2 = H$) should give rise to two superimposable ABCD systems and one AA'BB' system (*i.e.* an *unsymmetrical* multiplet) for the CH_2CH_2 protons in the low temperature ^1H n.m.r. spectrum of (1). The D_3 conformation (28a; $R^1 = R^2 = H$) has three C_2 axes and one C_3 axis of symmetry which render all the CH_2 groups of the CH_2CH_2 groups homotopic. This conformation (28a; $R^1 = R^2 = H$) should therefore give rise to three coincident AA'BB' systems (*i.e.* a *symmetrical* multiplet) for the CH_2CH_2 protons in the ^1H

TABLE 1

Temperature-dependent ^{13}C n.m.r. spectral parameters (25.14 MHz) for compound (1) and ^1H n.m.r. spectral parameters (100 MHz) for compounds (1)—(3)

Compound	Solvent	Temp. (°C)	Group	δ(^{13}C) or τ [a]
(1)	CD_2Cl_2–CS_2 (2 : 1)	−104	$\mathit{C}_6\mathrm{H}_4$	δ 140.0 (A), 139.7 (B), 139.3 (C), 130.2, 126.7
			$\mathit{C}\mathrm{H}_2\mathit{C}\mathrm{H}_2$	δ 38.2 (A), 36.8 (B), 36.0 (C)
		+20	$\mathit{C}_6\mathrm{H}_4$	δ 139.9 (ABC), 130.4, 126.7
			$\mathit{C}\mathrm{H}_2\mathit{C}\mathrm{H}_2$	δ 37.4 (ABC)
(1)	CS_2 [b]	−90	$\mathrm{C}_6\mathit{H}_4$	τ 2.92 (br,s)
			$\mathrm{C}\mathit{H}_2\mathrm{C}\mathit{H}_2$	τ 6.64—7.64 (m)
		+21	$\mathrm{C}_6\mathit{H}_4$	τ 2.74—3.00 (m)
			$\mathrm{C}\mathit{H}_2\mathrm{C}\mathit{H}_2$	τ 7.07 (s)
(2)	$CDCl_3$–CS_2 (1 : 1)	−90	$\mathrm{C}_6\mathit{H}_2$	τ 2.82 (s) (A), 2.91 (s) (BC) [c]
			$\mathrm{C}\mathit{H}_2\mathrm{C}\mathit{H}_2$	τ 6.60—7.80 (m)
			$\mathrm{C}\mathit{H}_3$	τ 7.74 (br,s)
		+20	$\mathrm{C}_6\mathit{H}_2$	τ 3.03 (s) (ABC)
			$\mathrm{C}\mathit{H}_2\mathrm{C}\mathit{H}_2$	τ 7.15 (s)
			$\mathrm{C}\mathit{H}_3$	τ 7.80 (s)
(3)	$CDCl_3$	+20	$\mathrm{C}_6\mathit{H}_2$	τ 2.95—3.05 (m)
			$\mathrm{C}\mathit{H}_2\mathrm{C}\mathit{H}_2$	τ 6.70—7.10 (m)
			$\mathrm{C}\mathit{H}_3$	τ 7.42 (s) (A), 7.50 (s) (B), 7.54 (s) (C)
		+80	$\mathrm{C}_6\mathit{H}_2$	τ 3.04 (s)
			$\mathrm{C}\mathit{H}_2\mathrm{C}\mathit{H}_2$	τ 6.91 (br,s)
			$\mathrm{C}\mathit{H}_3$	τ 7.50 (s) (ABC)

[a] Sites are designated A, B, and C for the three-site systems. Sites that represent three time-averaged signals are designated ABC. [b] Contains a few drops of $CDCl_3$. [c] The chemical shifts of the B and C protons are coincident.

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* See footnote on p. 1403.

n.m.r. spectrum of (1) at low temperatures. One of two conclusions can be drawn from the fact that an *unsymmetrical* multiplet is observed for the CH_2CH_2 protons at −80 °C: either (i) compound (1) exists in solution entirely in the C_2 conformation (27a; $R^1 = R^2 = H$), or (ii) it exists as a mixture of the C_2 and D_3 conformations, (27a; $R^1 = R^2 = H$) and (28a; $R^1 = R^2 = H$).

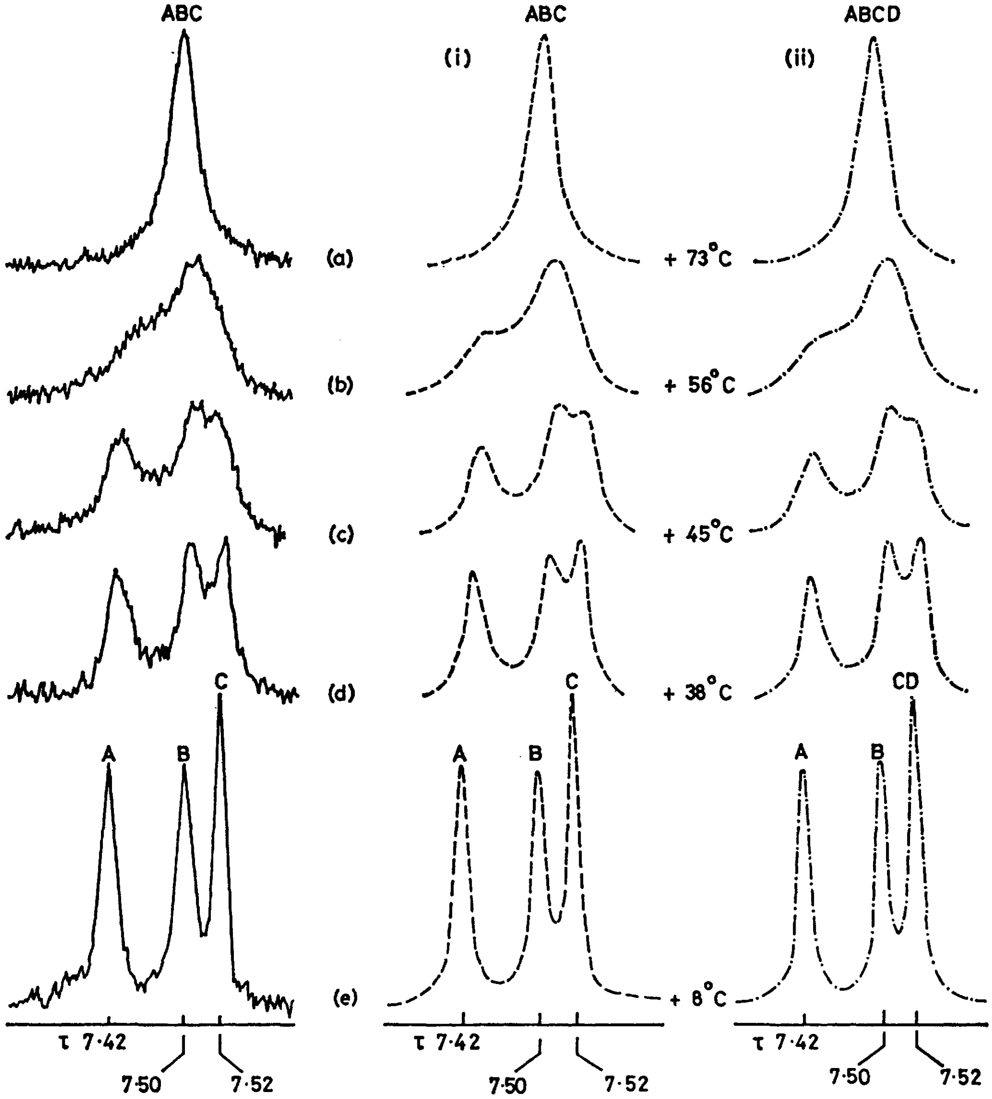


FIGURE 4 Observed (full line) and computed spectra of the methyl protons of 1,4,7,10,13,16-hexamethyl-5,6,11,12,17,18-hexahydrotribenzo[*a*,*e*,*i*]cyclododecene (3) using (i) program IV for exchange of protons among three equally populated sites, A, B, and C (– – – –) and (ii) program V for exchange of protons among three equally populated sites, A, B, and C, and a fourth site D (p_D 0.8) coincident with C (— · — · —) (in both cases the input values for all the rate constants, k_{AB} *etc.* were the same and so they will be referred to collectively as *k*): (a) at +73 °C, *k* 106 s^{-1} for (i), *k* 63 s^{-1} for (ii); (b) at + 56 °C, *k* 16.9 s^{-1} for (i), *k* 13 s^{-1} for (ii); (c) at + 45 °C, *k* 6.3 s^{-1} for (i), *k* 4.8 s^{-1} for (ii); (d) at +38 °C, *k* 3.7 s^{-1} for (i), *k* 2.9 s^{-1} for (ii); (e) at +8 °C, *k* 0.01 s^{-1} for (i), *k* 0.07 s^{-1} for (ii)

In order to obtain a better understanding of the conformational behaviour of the hexahydrotribenzocyclododecene (1), the 2,3,8,9,14,15-hexamethyl derivative (2) was studied as a suitable model. This compound (2) was chosen for two reasons: (i) the methyl groups are sufficiently remote from the twelve-membered ring not to influence the conformatioan behaviour of the ring and (ii) good ^1H n.m.r. probes are potentially present in the form of the methyl protons and aromatic protons. At +20 °C, the ^1H n.m.r. spectrum of compound (2) in deuteriochloroform–carbon disulphide (1 : 1) consisted of three singlets for the aromatic, CH_2CH_2, and aryl-methyl protons (see Table 1). Interest was centred around the signal for the aromatic protons because they responded to temperature changes over a shorter range than did the signals for the CH_2CH_2 and aryl-methyl protons. As the temperature was lowered to −90 °C the singlet for the aromatic protons separated into two singlets with relative intensities 1 : 2 (see Figure 6). Over this temperature range, the signal for the aryl-methyl protons broadened and the CH_2CH_2 signal became a broad unsymmetrical multiplet as in the low temperature ^{1}H n.m.r. spectra for compound (1). The most obvious interpretation of the low temperature ^{1}H n.m.r. spectrum of (2) is to assign the two singlets in the aromatic region to the three pairs of diastereotopic aromatic protons in the C_2 conformation (27a; $R^1 = H$, $R^2 = Me$). This interpretation recognises that the chemical shifts of two of the three pairs of diastereotopic aromatic protons are apparently coincident. For this reason, the aromatic protons give rise to two singlets with relative intensities 1 : 2 rather than to three singlets of equal intensity.

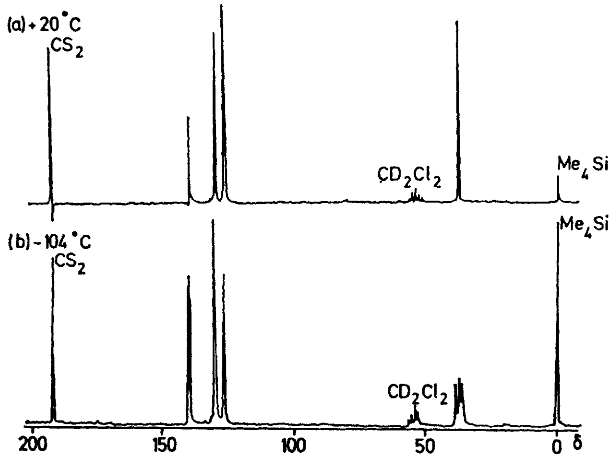


FIGURE 5 The broad-band decoupled ^{13}C n.m.r. spectra of 5,6,11,12,17,18-hexahydrotribenzo[*a*,*e*,*i*]cyclododecene (1) at (a) +20 °C and (b) −104 °C in CD_2Cl_2–CS_2 (2 : 1); see Table 1 for chemical shift data

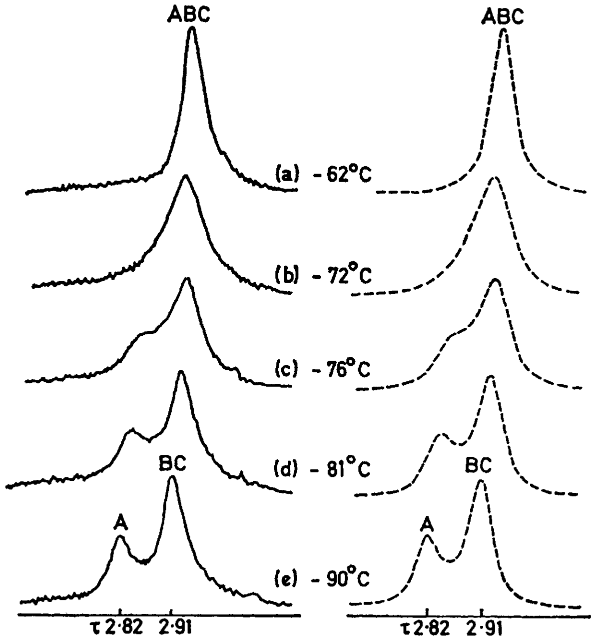


FIGURE 6 Observed (full line) and computed (broken line) spectra of the aromatic protons of 2,3,8,9,14,15-hexamethyl-5,6,11,12,17,18-hexahydrotribenzo[*a*,*e*,*i*]cyclododecene (2) using program IV for exchange of protons between three equally populated sites, A, B, and C (the input values for all the rate constants, k_{AB} *etc.* were the same and so they will be referred to collectively as k): (a) at −62 °C, k 94.1 s^{-1}; (b) at −72 °C, k 32.2 s^{-1}; (c) at −76 °C, k 17.4 s^{-1}; (d) at −81 °C, k 10.6 s^{-1}; (e) at −90 °C, k 7.5 s^{-1}

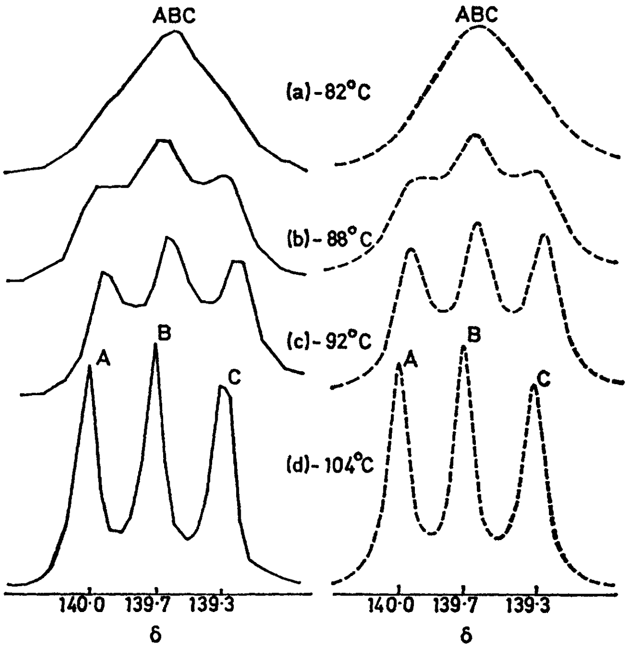


FIGURE 7 Observed (full line) and computed (broken line) spectra of the quaternary aromatic carbons of 5,6,11,12,17,18-hexahydrotribenzo[*a*,*e*,*i*]cyclododecene (1) using program IV for exchange of broad-band decoupled carbons between three equally populated sites, A, B, and C (the input values for all the rate constants, k_{AB} *etc.* were the same and so they will be referred to collectively as k): (a) at −82 °C, k 19.3 s^{-1}; (b) at −88 °C, k 9.3 s^{-1}; (c) at −92 °C, k 5.0 s^{-1}; (d) at −104 °C, k 0.52 s^{-1}

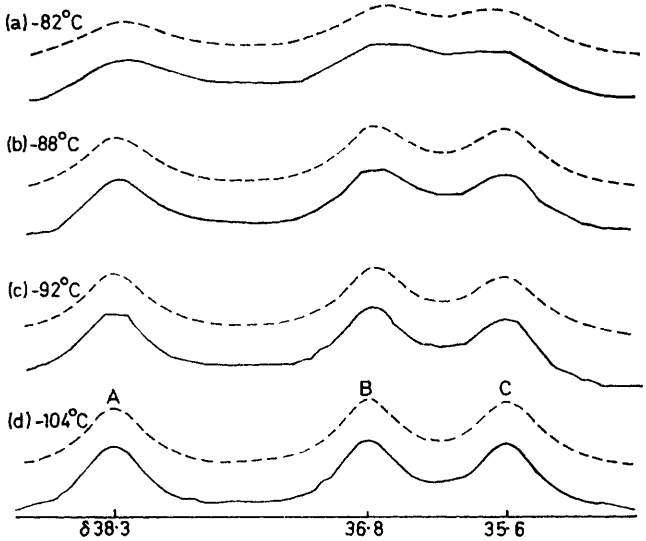
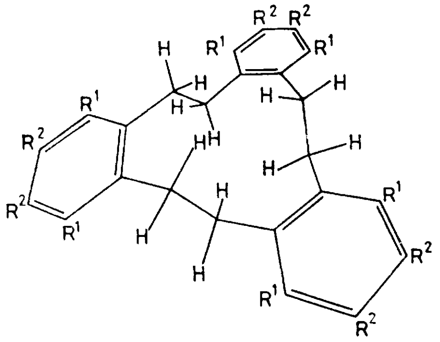


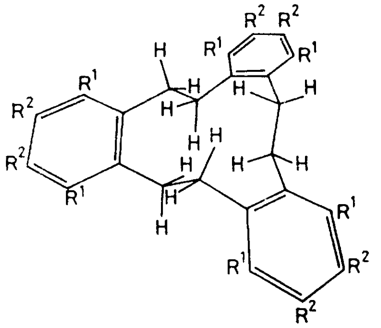
FIGURE 8 Observed (full line) and computed (broken line) spectra of the dimethylene carbons of 5,6,11,12,17,18-hexahydrotribenzo[*a*,*e*,*i*]cyclododecene (1) using program IV for exchange of broad-band decoupled carbons between three equally populated sites, A, B, and C (the input values for all the rate constants, k_{AB} *etc.* were the same and so they will be referred to collectively as k): (a) −82 °C, k 110 s^{-1}; (b) at −88 °C, k 4.3 s^{-1}; (c) at −92 °C, k 1.9 s^{-1}; (d) at −104 °C, k 0.34 s^{-1}

Although the conformational interconversion and inversion processes involving the C_2 (27a; $R^1 = H$, $R^2 = Me$) and D_3 (28a; $R^1 = H$, $R^2 = Me$) conformations and their enantiomers (denoted by C_2* and D_3*) can be discussed in terms of the equilibria $D_3 \rightleftharpoons C_2 \rightleftharpoons C_2^* \rightleftharpoons D_3^*$, the site exchange between sites A, B, and C involving the three pairs of diastereotopic aromatic protons ($R^1 = H_A$, H_B, or H_C) of the C_2 and C_2* conformations (27a and b; $R^1 = H$, $R^2 = Me$) can only be fully understood by reference to Figures 10 and 11. [The designations H_A, H_B, and H_C of the three pairs of diastereotopic aromatic protons of the C_2 conformations (27a and b) in Figure 10 do not reflect the relative chemical shifts of these protons. Individual assignments are, of course, quite arbitrary.] Despite the fact that the D_3 and D_3* conformations (28a and b; $R^1 = H$, $R^2 = Me$) are not detectable by ^1H n.m.r. spectroscopy at low temperatures they must be considered as possible intermediates in the site exchange processes involving the C_2 and C_2* conformations (27a and b; $R^1 = H$, $R^2 = Me$). Formally, the site occupied by the homotopic aromatic protons ($R^1 = H_D$) of the D_3 conformations (28a and b; $R^1 = H$, $R^2 = Me$) is designated as site D in Figures 10 and 11 even although its occupancy has not been detected experimentally. In Figure 10, each formula represents a ground state conformation on the conformational itinerary. The conformations are drawn such that the mean plane of the twelve-membered ring lies in the plane of the paper and the methylene groups are indicated as being oriented above (●) or below (○) the mean plane. Formally at least, D_3 conformations (28a and b; $R^1 = H$, $R^2 = Me$) can be interconverted with C_2 conformations (27a and b; $R^1 = H$, $R^2 = Me$), and $C_2 \rightleftharpoons C_2^*$ ring inversions can occur by processes which involve simultaneous torsion about the two carbon–carbon bonds (*e.g.* 4a,5 and 6,6a) linking a particular dimethylene group (*e.g.* 4,5) to two aromatic rings (*e.g.* those defined by 1,2,3,4,4a,18a and 6a,7,8,9,10,10a). These processes, when executed with molecular models, are reminiscent of pedalling motions. Pedalling of any one of the three homotopic dimethylene bridges (1, 2, or 3) of the D_3 conformation (28a; $R^1 = H$, $R^2 = Me$) leads to a C_2 conformation (27a; $R^1 = H$, $R^2 = Me$). However, since the sites of the three pairs of diastereotopic protons designated H_A, H_B, and H_C are different with respect to the six designated aromatic protons (H-1,4,7,10,13,16) according as to whether the C_2 axis bisects dimethylene bridge 1, 2, or 3, it is convenient to identify the C_2 conformations (27a; $R^1 = H$ $R^2 = Me$) as C_2-*1*, C_2-*2*, and C_2-*3*, respectively. Pedalling of either of the two homotopic dimethylene bridges (*2* or *3* for C_2-*1*, *1* or *3* for C_2-*2*, and *1* or *2* for C_2-*3*) of C_2-*1*, C_2-*2*, or C_2-*3* effects $C_2 \rightleftharpoons C_2^*$ ring inversion such that C_2-*1* is inverted to give either C_2*-*3* or C_2*-*2*, C_2-*2* to give either C_2*-*3* or C_2*-*1*, and C_2-*3* to give either C_2*-2 or C_2*-1. Pedalling of any of the three dimethylene bridges, *1*, *2*, or *3* bisected by the C_2 axis in C_2*-*1*, C_2*-*2*, and C_2*-*3*, respectively, leads to the D_3* conformation (28b; $R^1 = H$, $R^2 = Me$). The complete site exchange scheme for H_A, H_B, H_C, and H_D is summarised by the cubic array diagram in Figure 11. The designation of sites within the square brackets reading from left to right correspond to H-1,4,7,10,13,16. Since the D_3 conformations (28a and b; $R^1 = H$, $R^2 = Me$) are undetected intermediates in the low temperature ^1H n.m.r. spectra, further discussion of the conformational behaviour of compound (2) can be restricted to a consideration of the C_2 conformations (27a and b; $R^1 = H$, $R^2 = Me$). Figures 10 and 11 show that the $C_2 \rightleftharpoons C_2^*$ inversion process is associated with a first-order rate constant *k* which in turn may be related to the rate constants for the aromatic protons' site exchanges [$H_A \longrightarrow H_B$, $H_A \longrightarrow H_C$, $H_B \longrightarrow H_A$, $H_B \longrightarrow H_C$, $H_C \longrightarrow H_A$, $H_C \longrightarrow H_B$]. Thus, the rate constants for $C_2 \rightleftharpoons C_2^*$ ring inversion at different temperatures were determined (see Figure 6) by comparing experimental ^1H n.m.r. spectra for the aromatic protons with theoretical spectra generated by the line-shape procedure described in method II (see Experimental section). Values for the free energy of activation for the $C_2 \rightleftharpoons C_2^*$ ring inversion process were determined at the various temperatures. Table 2 records the average value (10.1 kcal mol^{-1}) for $\Delta G^\ddagger$ ($C_2 \rightleftharpoons C_2^*$) in compound (2).

During our investigations on the conformational



C_2 conformation (27a)



D_3 conformation (28a)

FIGURE 9 The ground-state C_2 (27a) and D_3 (28a) conformations of compounds (1)—(3). For (1), $R^1 = R^2 = H$; for (2), $R^1 = H$, $R^2 = Me$; for (3), $R^1 = Me$, $R^2 = H$. The enantiomeric ground-state conformations are denoted by C_2* (27b) and D_3* (28b) in the text

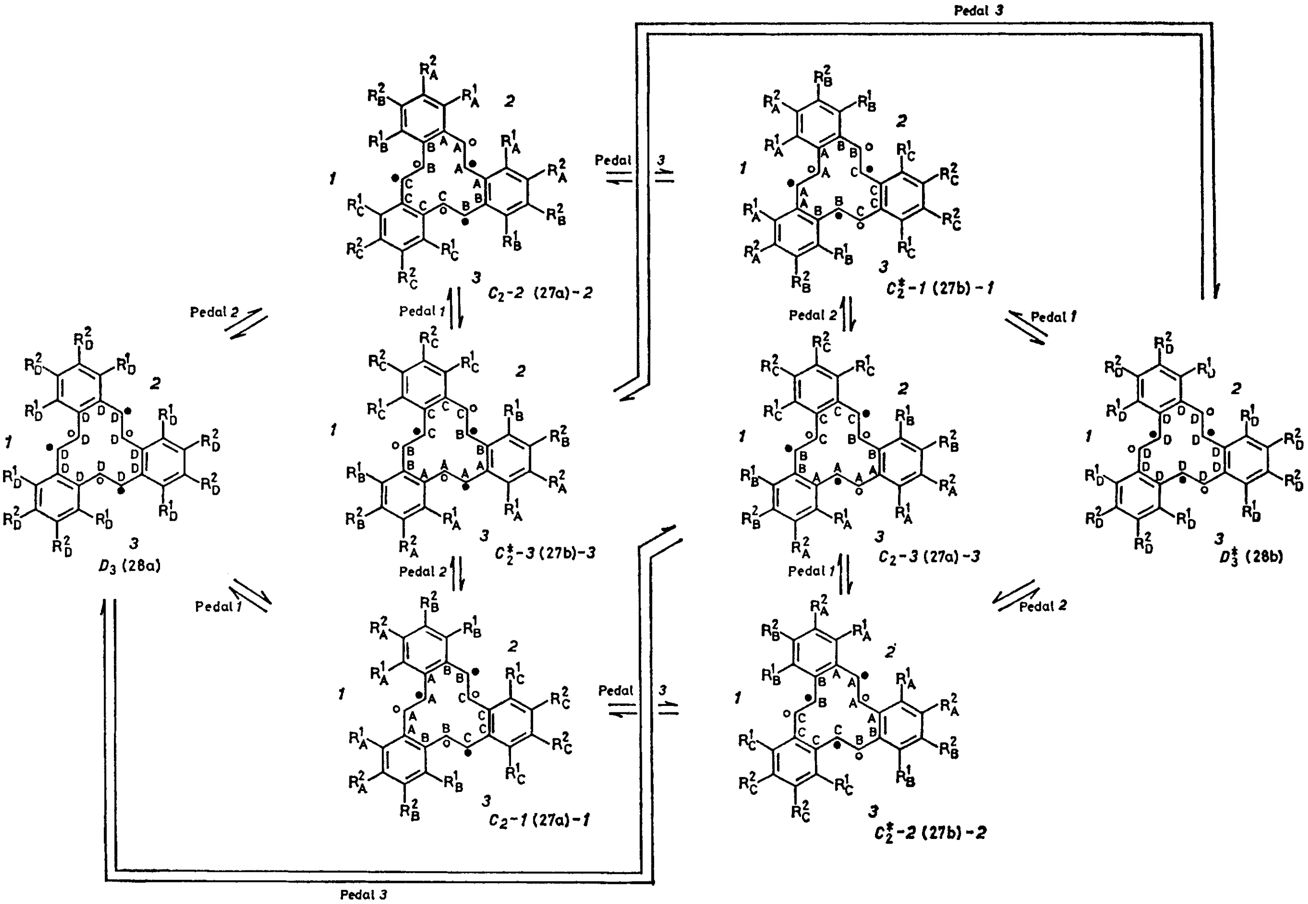


FIGURE 10 Conformational itinerary and site-exchange scheme for different nuclei and groups of nuclei involving the C_2 (27a), C_2* (27b), D_3 (28a), and D_3* (28b) conformations of compounds (1)—(3). For (1), $R^1 = R^2 = H$; for (2), $R^1 = H$, $R^2 = Me$; for (3), $R^1 = Me$, $R^2 = H$. ● ≡ a methylene group above the mean plane of the ring. ○ ≡ a methylene group below the mean plane of the ring

behaviour of compound (2), an FT ^{13}C n.m.r. spectrometer became available to us. Consequently, we decided to investigate the temperature dependence of the broad-band decoupled ^{13}C n.m.r. spectrum of the parent compound (1) in order to establish that (i) the 2,3,8,9,14,15-hexamethyl derivative (2) is indeed a good model for (1) and (ii) line-shape analysis of broad-band decoupled ^{13}C n.m.r. spectra constitutes a reliable means of obtaining activation parameters for conformational changes in medium-sized ring compounds. At +20 °C, the broad-band decoupled ^{13}C n.m.r. spectrum of compound (1) in dichlorodideuteriomethane–carbon disulphide (2 : 1) consisted of three singlets for the aromatic carbon atoms and one for the CH_2CH_2 carbons (see Table 1 and Figure 5). As the temperature was lowered to −104 °C, the singlet for the CH_2CH_2 carbon atoms (C-5,6,11,12,17,18) separated into three singlets of approximately equal intensities. The low-field singlet for the quaternary aromatic carbons (C-4a,6a,10a,12a,16a,18a) also separated into three singlets of approximately equal intensities at −104 °C. Over this temperature range the signals for the other two sets of aromatic carbons remained as singlets. Taken together, these observations indicate that compound (1) also adopts predominantly C_2 conformations (27a and b; $R^1 = R^2 = H$) in solution. Of course, small contributions (<2%) from the D_3 conformations (28a and b; $R^1 = R^2 = H$) would not necessarily be detected by variable temperature broad-band decoupled ^{13}C n.m.r. spectroscopy. As before, the site exchanges between sites A, B, and C involving (i) the three pairs of diastereotopic quaternary aromatic carbons and (ii) the three pairs of diastereotopic CH_2CH_2 carbons of the C_2 and C_2* conformations (27a and b; $R^1 = R^2 = H$) can only be fully appreciated by reference to Figures 10 and 11. The situation is analogous to that already discussed for the three pairs of diastereotopic aromatic protons in compound (2). Rate constants for $C_2 \rightleftharpoons C_2^*$ ring inversion at various temperatures were determined by comparing the experimental broad-band decoupled ^{13}C n.m.r. spectra for (i) the quaternary aromatic carbons (see Figure 7) and (ii) the CH_2CH_2 carbons (see Figure 8) with theoretical spectra generated by the line-shape procedure described in method II (see Experimental section). Values for the free energy of activation for the $C_2 \rightleftharpoons C_2^*$ ring inversion process were determined at the various temperatures. The average value for $\Delta G^{\ddagger}$ ($C_2 \rightleftharpoons C_2{}^*$) was found (Table 2) to be (i) 9.9 kcal mol^{-1} derived from the quaternary aromatic carbons and (ii) 10.1 kcal mol^{-1} derived from the CH_2CH_2 carbon atoms. Not only is the agreement between these two values for the same conformational process in compound (1) obtained from use of two different ^{13}C n.m.r. probes satisfying, but the close correspondence with the average value (10.1 kcal mol^{-1}) for $\Delta G^{\ddagger}$ ($C_2 \rightleftharpoons C_2{}^*$) from from ^1H n.m.r. line shape analysis of compound (2) is encouraging. Clearly, the 2,3,8,9,14,15-hexamethyl derivative (2) is a good model for the tribenzocyclododecene (1). Finally, application of dynamic ^{13}C n.m.r. spectroscopy obviously leads to results which agree with those obtained by dynamic ^1H n.m.r. spectroscopy (*cf.* ref. 27). This observation is reassuring.

TABLE 2

Thermodynamic parameters associated with $C_2 \rightleftharpoons C_2{}^*$ ring inversion in compounds (1)—(3)

Compound	R^1	R^2	Solvent	N.m.r. probe [a, b]	$\Delta G^{\ddagger}$/kcal mol^{-1}
(1)	H	H	CD_2Cl_2–CS_2 (2 : 1)	C-4a,6a,10a,12a, 16a,18a	9.9 ± 0.2 [c]
				C-5,6,11,12,17, 18	10.1 ± 0.1 [d]
(2)	H	Me	$CDCl_3$–CS_2 (1 : 1)	H-1,4,7,10,13,16	10.1 ± 0.3 [e]
(3)	Me	H	$CDCl_3$	Me-1,4,7,10,13, 16	17.4 ± 0.3 [f]

[a] Details of ^{13}C and ^1H chemical shifts are given in Table 1. [b] The site exchanges involving sites A, B, and C are described in Figures 10 and 11. Line-shape analysis was carried out using program IV described in method II. [c] Value from ^{13}C n.m.r. line-shape analysis (see Figure 7). [d] Value from ^{13}C n.m.r. line-shape analysis (see Figure 8). [e] Value from ^1H n.m.r. line-shape analysis (see Figure 6). [f] Value from ^1H n.m.r. line-shape analysis (see Figure 4).

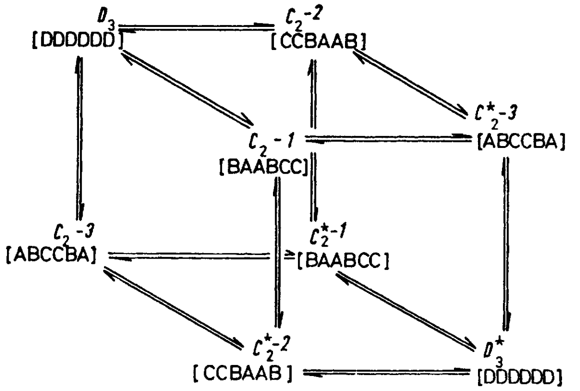
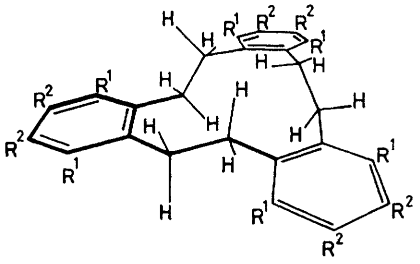
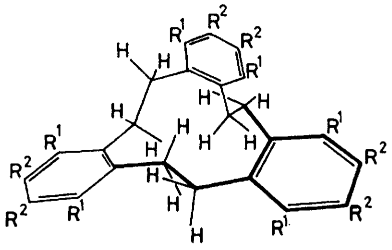


FIGURE 11 Cubic array diagram showing the site exchanges for different nuclei and groups of nuclei involving C_2 (27a), $C_2{}^*$ (27b), D_3 (28a), and $D_3{}^*$ (28b) conformations of compounds (1)—(3). The sites indicated in square brackets read from left to right starting with the lowest and proceeding to the highest numbered nucleus or groups of nuclei in formulae (1)—(3)

In order (i) to assess the relative importance of the D_3 conformations (28a and b; $R^1 = R^2 =$ H) which are not detectable experimentally and (ii) to investigate the nature of the transition state geometry in the $C_2 \rightleftharpoons C_2{}^*$ ring inversion process, strain energy calculations on selected conformations of the tribenzocyclododecene (1) were carried out using a molecular mechanics program (see Experimental section) based on the procedure developed by Allinger *et al.*[19] The results for the ground-state conformations (Figure 9) of the C_2 (27a; $R^1 = R^2 =$ H) and D_3 (28a; $R^1 = R^2 =$ H) type and for the trial transition states (Figure 12) TS ($C_2 \rightleftharpoons C_2{}^*$) (29; $R^1 = R^2 =$ H) to $C_2 \rightleftharpoons C_2{}^*$ ring inversion and TS ($D_3 \rightleftharpoons C_2$) (30; $R^1 = R^2 =$ H) to $D_3 \rightleftharpoons C_2$ ring interconversion are given in Table 3.† In order for a ground-state conformation to reach a transition-state, pedalling of a dimethylene bridge is required until a conformation is attained in which the dimethylene bridge becomes coplanar with one of the aromatic rings (see footnote *g* in Table 3). The data for the individual interactions in each conformation show (Table 3) that the major contributions towards the total strain energies of both transition states arise mainly from angle strain and non-bonded interactions. The angle strain is associated almost entirely with the twelve-membered ring $C\hat{C}C$ angles and the transannular non-bonded interactions are associated with the carbon and hydrogen atoms of the dimethylene groups. Both transition-state



TS ($D_3 \rightleftharpoons C_2$) conformation (29)



TS ($C_2 \rightleftharpoons C_2^*$) conformation (30)

FIGURE 12 The transition state conformations TS ($C_2 \rightleftharpoons C_2{}^*$) (29) and TS ($D_3 \rightleftharpoons C_2$) (30) for ring inversion and interconversion in compounds (1)—(3). For (1), $R^1 = R^2 =$ H; for (2), $R^1 =$ H, $R^2 =$ Me; for (3), $R^1 =$ Me, $R^2 =$ H. The portions of the molecules indicated by thickened bonds are coplanar in each case (see footnote *g* in Table 3)

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† The figures quoted in Table 3 are more refined than those reported previously.[11] The values (kcal mol^{-1}) now gives for the total strain energies E_T for the C_2 and D_3 ground-state conformations are in good agreement [2.36 (2.96 [11]) and 5.96 (5.87 [11])] whereas those for TS ($C_2 \rightleftharpoons C_2{}^*$) and TS ($D \rightleftharpoons D_2{}^*$) are different [11.60 (9.74 [11]) and 19.11 (15.79 [11])].

[27] B. E. Mann, *Progr. NMR Spectroscopy*, 1977, **11**, 95.

conformations show considerable relaxation of non-bonded interactional strain at the expense of increased angle strain. In the case of the ground-state conformations, the D_3 conformation (28a; $R^1 = R^2 = H$) experiences (i) larger non-bonded transannular interactions involving the dimethylene groups and (ii) more angle strain in the twelve-membered ring than does the C_2 conformation (27a; $R^1 = R^2 = H$). These results are consistent with indications from space-filling molecular models of closer packing in the C_2 conformation (27a; $R^1 = R^2 = H$) than in the D_3 conformation (28a; $R^1 = R^2 = H$) of the two sets of three transannularly-interacting hydrogens above and below the mean planes of the twelve-membered rings in both these conformations. The calculated strain energy difference (ΔE_T 3.6 kcal mol^{-1}) between the C_2 (27; $R^1 = R^2 = H$) and D_3 (28; $R^1 = R^2 = H$) conformations (Table 3) is consistent with the failure to observe any D_3 conformational signal in the low temperature broad-band decoupled ^{13}C n.m.r. spectra of the tribenzocyclododecene (1). Entropy differences arising from the different symmetries of the two conformations also favour the C_2 conformation (27a; $R^1 = R^2 = H$). This conformation has a symmetry number of 2 and consequently will be higher in entropy by $R\ln 3$ cal deg^{-1} mol^{-1} than the D_3 conformation (28a; $R^1 = R^2 = H$) which has a symmetry number of 6. If ΔE_T is equated with ΔH, then the entropy difference of $R\ln 3$ means that the free energy difference (ΔG) between the two conformations at room temperature is 4.2 kcal mol^{-1}. This value for ΔG corresponds with *ca.* 0.1% of the D_3 conformations (28a and b; $R^1 = R^2 = H$) in equilibrium with the C_2 conformations (27a and b; $R^1 = R^2 = H$) in solution. Thus, it is not surprising that the D_3 conformations (28a and b; $R^1 = R^2 = H$) of the tribenzocyclododecene (1) are not detected by dynamic ^{13}C n.m.r. spectroscopy. Compared with the C_2 conformations (27a and b; $R^1 = R^2 = H$), the transition state conformation TS ($C_2 \rightleftharpoons C_2^*$) (29; $R^1 = R^2 = H$) is favoured on entropy grounds by $R\ln 2$ cal deg^{-1} mol^{-1} on the basis of symmetry considerations alone. This conclusion can be reached either by (i) noting that the symmetry number is reduced from 2 to 1 on going from the ground state to transition state conformations or (ii) appreciating that a dimethylene group can be pedalled in two energetically equivalent ways during $C_2 \rightleftharpoons C_2^*$ ring inversion. If the difference ($\Delta E_T = 9.24$ kcal mol^{-1}) in the strain energies between the C_2 (27a; $R^1 = R^2 = H$) and the TS ($C_2 \rightleftharpoons C_2^*$) (29; $R^1 = R^2 = H$) conformations is equated with $\Delta H^\ddagger$ then the entropy difference of $R\ln 2$ means that a free energy of activation ($\Delta G^\ddagger$) of 8.8 kcal mol^{-1} can be calculated for $C_2 \rightleftharpoons C_2^*$ ring inversion. The relatively close correspondence between this value and the experimentally determined values (Table 2) of 9.9 and 10.1 kcal mol^{-1} suggests that the selected TS ($C_2 \rightleftharpoons C_2^*$) (29; $R^1 = R^2 = H$) conformation corresponds closely to the actual transition state for $C_2 \rightleftharpoons C_2^*$ ring inversion. This investigation demonstrates that use of molecular mechanics based on strain energy calculations is a reliable complementary procedure with medium-sized ring hydrocarbons for (i) assessing the relative importance of experimentally inaccessible ground-state conformations and (ii) defining the geometry of transition-state conformations.

TABLE 3

Calculated strain energies (E_T/kcal mol^{-1}) of various conformations of 5,6,11,12,17,18-hexahydrotribenzo[*a,e,i*]-cyclododecene (1)

Conformation	E_r [a–c]	E_θ [a–c]	E_ϕ [a–d]	E_δ [a–c,e]	E_{nb} [a–c,f]	E_T
$C_2 \equiv C_2^*$ (27; $R^1 = R^2 = H$)	0.11	2.07	0.28	0.13	−0.23	2.36
$D_3 \equiv D_3^*$ (28; $R^1 = R^2 = H$)	0.25	4.61	0.12	0.10	0.88	5.96
TS($C_2 \rightleftharpoons C_2^*$) (29; $R^1 = R^2 = H$) [g]	0.40	7.69	0.88	0.62	2.01	11.60
TS($D_3 \rightleftharpoons C_2$)(30; $R^1 = R^2 = H$) [g]	0.64	9.72	1.83	0.46	6.46	19.11

[a] The following energy terms (J. F Stoddart, ' Organic Chemistry, Series One, Structure Determination in Organic Chemistry, ed. W. D. Ollis, Butterworths, London, 1973, p. 1) 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 $E_T = E_r + E_\theta + E_\phi + E_\delta + E_{nb}$. [b] Calculations based upon the following force constants. Bond length strain: aromatic k_{CC} 1 102, k_{CH} 729; aliphatic k_{CC} 663. k_{CH} 655 kcal mol^{-1} Å^{-2}. Angle strain : aromatic k_{CCC} 144, k_{CCH} 108; aliphatic k_{CCC} 115, k_{CCH} 94, k_{HCH} 74 kcal mol^{-1} radian^{-2}; all angle strain reduced by a factor of 0.7. [c] Calculations based upon the following equilibrium bond lengths and bond angles: aromatic C–C 1.395, C–H 1.09; aliphatic C–C 1.54, Ar–C 1.50, C–H 1.09 Å. Aromatic $C\hat{C}C$ 120°, $C\hat{C}H$ 120°; aliphatic $C\hat{C}C$ 111.5° $C\hat{C}H$ 109.5°, $H\hat{C}H$ 106°. [d] The torsional strain associated with C–C bonds was treated as a three-fold barrier of height 3.0 kcal mol^{-1}. Aromatic C–C bond twisting was calculated according to Boyd *et al.* (see footnote *e*). [e] Out-of-plane strain associated with aromatic rings was calculated according to Boyd *et al.* (R. H. Boyd, *J. Chem. Phys.*, 1968, **49**, 2574; C. Shieh, D. McNally, and R. H. Boyd, *Tetrahedron*, 1969, **29**, 3653). [f] Non-bonded interactions based upon the Hill equation as summarised in E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, ' Conformational Analysis,' Wiley–Interscience, New York, 1965, ch. 7. [g] Transition-state geometries are defined by holding a CH_2CH_2 unit in the plane of one of the aromatic rings. For the TS ($C_2 \rightleftharpoons C_2^*$) (29; $R^1 = R^2 = H$) conformation, atoms, 5, 4a, 4, 3, 2, 1, 18a, 18, 17, and 16 were ' held ' coplanar. For the TS ($D_3 \rightleftharpoons C_2$) (30; $R^1 = R^2 = H$) conformation, atoms 12, 12a, 13, 14, 15, 16, 16a, 17, 18, and 18a were ' held ' coplanar. See Figure 12.

It was also of interest to ascertain the effect on the conformational behaviour in solution of the twelve-membered ring of introducing six methyl substituents into the *ortho*-positions of the aromatic rings of the hexahydrotribenzocyclodecene (1). Accordingly, we have investigated the temperature dependence of the ^1H n.m.r. spectrum of the 1,4,7,10,13,16-hexamethyl derivative (3). At +20 °C, the spectrum in deuteriochloroform consisted of multiplets for the aromatic and CH_2CH_2 protons, and three singlets for the aryl-methyl protons (see Table 1). Interest was centred on the signal for the aryl-methyl protons since the three singlets observed at room temperature coalesced to give one singlet as the temperature was raised (see Figure 4) to +80 °C. Over this temperature range, the multiplets for the aromatic and CH_2CH_2 protons both coalesced to give singlets However, close inspection of the three singlets for the aryl-methyl substituents at +20 °C indicates that the two singlets located at lower field are slightly broader than the high-field singlet. Two interpretations of this observation may be considered: either (i) the three pairs of diastereotopic methyl protons ($R^1 \equiv \mathrm{Me_A}$, $\mathrm{Me_B}$, or $\mathrm{Me_C}$) of the C_2 and C_2* conformations (27a and b; $R^1 = $ Me, $R^2 = $ H) are exhibiting non-identical relaxation times, or (ii) there is a small amount (<5%) of the D_3 and D_3* conformations (28a and b; $R^1 = $ Me, $R^2 = $ H) whose homotopic methyl protons ($R^1 \equiv \mathrm{Me_D}$) are giving rise to a signal coincident with that of $\mathrm{Me_C}$ in the C_2 conformations (27a and b; $R^1 = $ Me, $R^2 = $ H) and exchanging with $\mathrm{Me_A}$ and $\mathrm{Me_B}$.

TABLE 4

Calculated strain energies (E_T/kcal mol^{-1}) [a] of various conformations of 1,4,7,10,13,16-hexamethyl-5,6,11,12,17,18-hexahydrotribenzo[*a,e,i*]cyclododecene (3)

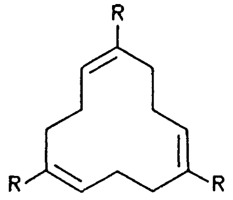
Conformation	E_r	E_θ	E_ϕ	E_δ	E_{nb}	E_T
$C_2 \equiv C_2$* (27; $R^1 = $ Me, $R^2 = $ H)	0.35	2.71	0.76	0.24	0.05	4.11 [c]
$D_3 \equiv D_3$* (28; $R^1 = $ Me, $R^2 = $ H)	0.31	2.47	1.53	0.65	0.00	4.96 [c]
TS($C_2 \rightleftharpoons C_2$*) (29; $R^1 = $ Me, $R^2 = $ H) [b]	0.87	15.29	1.43	0.76	2.44	20.79 [d]
TS($D_3 \rightleftharpoons C_2$) (30; $R^1 = $ Me, $R^2 = $ H) [b]	0.96	12.99	1.87	0.98	5.05	21.85

[a] See footnotes *a*–*f* in Table 3. [b] Transition-state geometries are defined by holding a CH_2CH_2 unit in the plane of one of the aromatic rings. For the TS ($C_2 \rightleftharpoons C_2$*) (29; $R^1 = $ Me, $R^2 = $ H) conformation, atoms 5, 4a, 4, 3, 2, 1, 18a, 18, 17, and 16 were 'held' coplanar. For the TS($D_3 \rightleftharpoons C_2$) (30; $R^1 = $ Me, $R^2 = $ H) conformation, atoms 12, 12a, 13, 14, 15, 16, 16a, 17, 18, and 18a were 'held' coplanar. See Figure 12. [c] The C_2 conformation (27a; $R^1 = $ Me, $R^2 = $ H) is also favoured by entropy. On the basis of symmetry considerations alone, the C_2 conformation (27a; $R^1 = $ Me, $R^2 = $ H), which has a symmetry number of 2, will be Rln 3 cal deg^{-1} mol^{-1} higher in entropy than the D_3 conformation (28a; $R^1 = $ Me, $R^2 = $ H) which has a symmetry number of 6. If the difference in strain energies (ΔE_T 0.85 kcal mol^{-1}) between the two ground-state conformations is equated with ΔH, then the entropy difference of Rln 3 means that the free energy difference ($\Delta G_{\text{calc.}}$) between the two conformations is *ca.* 1.5 kcal mol^{-1}. [d] If the difference in strain energies ($\Delta E_T^\ddagger$ 16.68 kcal mol^{-1}) between the C_2 conformation (27a; $R^1 = $ Me, $R^2 = $ H) and the transition state TS ($C_2 \rightleftharpoons C_2$*) (29; $R^1 = $ Me, $R^2 = $ H) is equated with $\Delta H^\ddagger$ then an approximate estimate for $\Delta G^\ddagger_{\text{calc.}}$ of 16.3 kcal mol^{-1} follows from recognising that the transition state is favoured on entropy grounds by Rln 2 cal deg^{-1} mol^{-1} (*i.e.* the CH_2CH_2 unit can be pedalled in two energetically equivalent ways during $C_2 \rightleftharpoons C_2$* ring inversion).

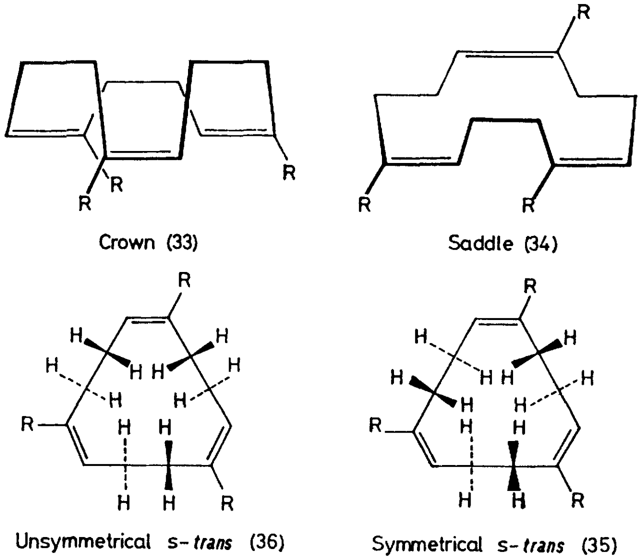
Strain energy calculations have been performed on the ground-state conformations (27a and b; $R^1 = $ Me, $R^2 = $ H) and (28a and b; $R^1 = $ Me, $R^2 = $ H) and on the probable transition states (see Figure 2) TS ($C_2 \rightleftharpoons C_2$*) (29; $R^1 = $ Me, $R^2 = $ H) for $C_2 \rightleftharpoons C_2$* ring inversion and TS ($D_3 \rightleftharpoons C_2$) (30; $R^1 = $ Me, $R^2 = $ H) for $D_3 \rightleftharpoons C_2$ ring interconversion. The results (Table 4) agree with the conclusion that the C_2 conformation (27a; $R^1 = $ Me, $R^2 = $ H) is more stable ($\Delta G_{\text{calc.}} = $ *ca.* 1.5 kcal mol^{-1}) than the D_3 conformation (28a; $R^1 = $ Me, $R^2 = $ H) but suggest that the latter may contribute slightly to the conformational equilibrium. If this is the case, then the fact that the calculated energy barriers [$\Delta E_T^\ddagger{}_{(D_3 \longrightarrow C_2)}$ 16.89, $\Delta E_T^\ddagger{}_{(C_2 \longrightarrow D_3)}$ 17.74 kcal mol^{-1}] for $D_3 \rightleftharpoons C_2$ ring interconversion are of the same order of magnitude as the $C_2 \rightleftharpoons C_2$* ring inversion barrier ($\Delta E_T^\ddagger$ 16.68 kcal mol^{-1}) suggests that an exchange process involving a fourth site might be occurring in the temperature range +20 to +80 °C. This possibility [*i.e.* interpretation (ii) above] was explored by generating theoretical spectra using line-shape equations based on a four-site exchange process (method III in the Experimental section) amongst $\mathrm{Me_A}$, $\mathrm{Me_B}$, $\mathrm{Me_C}$, and $\mathrm{Me_D}$ with the chemical shifts of $\mathrm{Me_C}$ and $\mathrm{Me_D}$ being made coincident. It was found that the line-shapes were insensitive to the magnitude of the rate constants for $D_3 \rightleftharpoons C_2$ ring interconversion. However, in view of the results of the strain energy calculations, the values employed for these rate constants were the same as those established simultaneously for $C_2 \rightleftharpoons C_2$* ring inversion (see below). Good matches were obtained (see Figure 4) between theoretical and experimental spectra provided the contribution from the D_3 conformations (28a and b; $R^1 = $ Me, $R^2 = $ H) was not allowed to exceed 0.8%. Rate constants for the $C_2 \rightleftharpoons C_2$* ring inversion process at various temperatures were determined and the average value for $\Delta G^\ddagger$ ($C_2 \rightleftharpoons C_2$*) was found to be 17.5 kcal mol^{-1}. However, after this detailed consideration, interpretation (ii) discussed in the preceding paragraph was effectively ruled out by the observation that there were no significant changes in the room temperature line-shape for the aryl-methyl protons down to −40 °C. By implication, interpretation (i) must provide the answer to the problem. Comparison (see Figure 4) of the experimental ^{1}H n.m.r. spectra for the aryl-methyl protons with theoretical spectra generated by line-shape equations based upon a three-site exchange process [method II in the Experimental section] amongst $\mathrm{Me_A}$, $\mathrm{Me_B}$, and $\mathrm{Me_C}$ gave a value for $\Delta G^\ddagger$ of 17.4 kcal mol^{-1} for $C_2 \rightleftharpoons C_2$* ring inversion. There is encouraging agreement between this value and the $\Delta G^\ddagger_{\text{calc.}}$ value of 16.3 kcal mol^{-1} determined from strain energy calculations (see Table 4) assuming that the transition state for $C_2 \rightleftharpoons C_2$* ring inversion corresponds to TS ($C_2 \rightleftharpoons C_2$*) (29; $R^1 = $ Me, $R^2 = $ H).

A comparison (Table 2) between the $\Delta G^\ddagger$ ($C_2 \rightleftharpoons C_2$*) values for the hexahydrotribenzocyclododecene (1) and its 2,3,8,9,14,15- (2) and 1,4,7,10,13,16- (3) hexamethyl derivatives shows that approximately the same barrier is associated with $C_2 \rightleftharpoons C_2$* ring inversion in compounds (1) and (2) whereas a much higher barrier (plus *ca.* 7 kcal mol^{-1}) is associated with the same ring inversion process in compound (3). This observation leads to the conclusion that the presence of aryl-methyl substituents in the *meta*-positions with respect to the dimethylene bridges does not contribute towards an increase in the energy barrier associated with $C_2 \rightleftharpoons C_2$* ring inversion. Thus, the assumption that the 2,3,8,9,14,15-hexamethyl derivative (2) is a good model for the parent hydrocarbon (1) is vindicated. In contrast, the presence of aryl-methyl substituents in the *ortho*-positions with respect to the dimethylene bridges increases significantly the energy barrier associated with $C_2 \rightleftharpoons C_2^*$ ring inversion as a result of (i) nonbonded interactions between the methyl groups and adjacent dimethylene bridges, and (ii) nonbonded interactions between juxtaposed methyl groups. By way of comparison, it is interesting that the activation parameters for the conformational changes in the trisalicylides (4)—(6), for which analogous transition states have been proposed,[4] were found [4] to correlate in a similarly predictable manner with the varying steric demands of the alkyl substituents occupying the *ortho*-positions. Thus, the free energies of activation 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) prefer to adopt the less symmetrical C_2 conformation (27) in solution, both helical (C_1) and propeller (C_3) conformations are present in solutions of the trisalicylides (4)—(6) with the more symmetrical propeller always preferred.

Finally, in this discussion on the conformational behaviour of twelve-membered ring hydrocarbons, it is worth reflecting upon the pioneering work of Baker *et al.*[2] In fact, the C_2 conformation (27a; $R^1 = R^2 = H$), established by dynamic n.m.r. spectroscopy and strain energy calculations in the present investigation to be the most stable ground-state conformation, corresponds with form (1b) in Figure 1. This is (i) one of four forms [(1a—d) in Figure 1] proposed as a 'strainless phase' of hexahydrotribenzocyclododecene (1) by Baker *et al.*[2] and (ii) one of the two forms [(1b and c) in Figure 1] which satisfies the preliminary *X*-ray crystallographic evidence [2] (see the introductory section) that (1) lacks trigonal symmetry, at least in the crystal. To our knowledge, the only other related investigations in more recent times are those describing the conformational behaviour of the all-*cis*-1,5,9-cyclododecatriene (31) [28] and its 1,5,9-tribromo-derivative (32).[29] The crown (33), saddle (34), symmetrical s-*trans*-(35), and unsymmetrical s-*trans*-(36) conformations shown in Figure 13 were all considered as possibilities by Untch *et al.*[28,29] for compounds (31) and (32) in solution. On the basis of (i) u.v. spectroscopy of (31), (ii) dipole moment measurements on (32), and (iii) the magnitudes of the vicinal coupling constants for the CH_2CH_2 protons of (32), the presence of crown (33) and saddle (34) conformations in significant amounts was excluded. From examination of molecular models it was deduced that the unsymmetrical s-*trans*-(35) is less strained than the symmetrical s-*trans*-(36) conformation because intra-annular hydrogen repulsions are less in (36) than in (35). Thus, it was concluded that the unsymmetrical s-*trans*-conformation (36) is of lower energy and would be the most populated in solution. Since the unsymmetrical s-*trans*-conformation (36) of compounds (31) and (32) is stereochemically analogous to the C_2 conformations (27) of compounds (1)—(3), there is close correspondence between the conformational behaviour of the hexahydrotribenzocyclododecenes (1)—(3) and the *cis*,*cis*,*cis*-1,5,9-cyclododecatrienes (31) and (32) in solution.



(31) R = H
(32) R = Br



Crown (33) Saddle (34)

Unsymmetrical s-*trans* (36) Symmetrical s-*trans* (35)

FIGURE 13 Possible ground-state conformations [crown (33), saddle (34), symmetrical s-*trans* (35), and unsymmetrical s-*trans* (36)] for *cis*,*cis*,*cis*-cyclododeca-1,5,9-triene (31) and its tribromo-derivative (32) proposed by Untch *et al.*[28,29] For (31), R = H; for (32), R = Br

The Temperature-dependent ^{1}H *N.m.r. Spectra and Conformational Properties of* 2,3,8,9- (15) *and* 1,4,7,10- (16) *Tetramethyl*-5,6,11,12-*tetrahydrodibenzo*[a,e]*cyclooctene*.—The availability of the 1,4,7,10-tetramethyl derivative (16) of tetrahydrodibenzocyclo-octene (14) provided an opportunity to study the effect on the conformational behaviour in solution of the eight-membered ring of introducing four *ortho*-methyl substituents into the aromatic rings. The low temperature ^{1}H n.m.r. spectrum of (16) shows two sets of signals which could be easily assigned to two differently populated diastereoisomeric conformations. Each of these two ground-state conformations was associated with sets of signals provided by (i) four homotopic aromatic protons, (ii) four homotopic aromatic methyl substituents, and (iii) a pair of CH_2CH_2 groups. The corresponding changes observable in the ^{1}H n.m.r. spectra of (16) in carbon disulphide are (*cf.* Table 5) as follows: (i) the

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[28] K. G. Untch and D. J. Martin, *J. Amer. Chem. Soc.*, 1965, **87**, 3518.

[29] S. Castellano and K. G. Untch, *J. Amer. Chem. Soc.*, 1966, **88**, 4238.

singlet (τ 3.47; +30 °C) broadened at lower temperatures eventually giving at −61 °C, two sharp singlets (τ 3.25 and 3.50; relative intensities 12 : 88), (ii) the singlet (τ_{Me} 7.87; +30 °C) gave two sharp singlets at −61° (τ_{Me} 7.70 and 7.88, relative intensities 12 : 88) and (iii) the singlet (τ 7.01) observed at +30 °C for the CH_2CH_2 protons broadened considerably as the temperature was lowered and then sharpened again at −20 °C, giving eventually at −61 °C a major signal (singlet A_4, τ 6.97; relative intensity *ca.* 85) and a minor signal (unresolved AA′BB′ system, τ_A 6.76, τ_B 6.88; relative intensity *ca.* 15). The characteristics of the signals associated with (iii) are such that the A_4 system must be assigned to the major conformation (molar population 0.88 at −61 °C in CS_2 solution) which is one of a family of flexible Boat * conformations.[10,11] Similarly, the AA′BB′ system must be associated with the minor conformation (molar population 0.12 at −61 °C in CS_2 solution) which corresponds to a rigid Chair * conformation. Line-shape analyses employing a program (see method I in the Experimental section) for two-site exchange processes were carried out (see Figure 3) for (i) and (ii) described above. They each gave a $\Delta G^‡$ value of 12.1 kcal mol^{-1} for C ⟶ Boat interconversion (see Table 6). Strain energy calculations have been performed on selected conformations of the 1,4,7,10-tetramethyl derivative (16). The results (Table 7) characterise (i) the two ground-state conformations (see Figure 14) as the C conformation (37; R^1 = Me, R^2 = H) and a minimum energy boat (MEB) conformation (38; R^1 = Me, R^2 = H) with torsion angles of *ca.* 26° about the 5,6- and 11,12-bonds and (ii) the transition-state conformations (see Figure 15) as the TS1 (39; R^1 = Me, R^2 = H) and TS2 conformations. The MEB conformation (38; R^1 = Me, R^2 = H) is predicted to be more stable (ΔE_T 1.34 kcal mol^{-1}) than the C conformation (37; R^1 = Me, R^2 = H) which is in accord with experimental observation (see Table 6) and the strain energy difference ($\Delta E_T^‡$ 13.23 kcal mol^{-1}) between the TS1 (39; R^1 = Me, R^2 = H) and C (37; R^1 = Me, R^2 = H) conformations is in satisfying agreement with the observed $\Delta G^‡$ value of 12.1 kcal mol^{-1} for C ⟶ Boat interconversion. This value is *ca.* 2 kcal mol^{-1} higher than the reported values [$\Delta G^‡_{C \longrightarrow Boat}$ = 10.2 (refs. 10—12) 10.0 (ref. 13) kcal mol^{-1}] for tetrahydrodibenzocyclo-octene (14). Clearly, the presence of four *ortho*-methyl substituents on the aromatic rings serves to destabilise the TS1 conformation (39; R^1 = Me, R^2 = H) relative to the C conformation (37; R^1 = Me, R^2 = H) in the 1,4,7,10-tetramethyl derivative (16).

TABLE 5

Temperature-dependent ^1H n.m.r. spectral parameters (100 MHz) for compounds (15) and (16)

Compound	Solvent	Temp. (°C)	Group	τ [a]
(15)	$CDCl_3$–CS_2 (2 : 1)	−71	C_6H_2	2.98 (s) (A), 3.34 (s) (B)
			CH_2CH_2 [b]	6.95 (s), 6.97 (AA′), 7.40 (BB′)
			CH_3	7.76 (s) (A), 7.94 (s) (B)
		+20	C_6H_2	3.31 (s) (AB)
			CH_2CH_2 [b]	7.09 (s) [b]
			CH_3	7.91 (s) (AB)
(16)	CS_2	−61	C_6H_2	3.25 (s) (A), 3.50 (s) (B)
			CH_2CH_2 [b]	6.97 (s), 6.76 (AA′), 6.88 (BB′) [b]
			CH_3	7.70 (s) (A), 7.88 (s) (B)
		+30	C_6H_2	3.47 (s) (AB)
			CH_2CH_2 [b]	7.01 (s) [b]
			CH_3	7.87 (s) (AB)

[a] Sites are designated A and B for the two-site systems. Sites that represent two time-averaged signals are designated AB. [b] The CH_2CH_2 group gives an AA′BB′ system for the chair conformation and a time-averaged singlet for the boat conformation, which coalesce to a single singlet at higher temperatures.

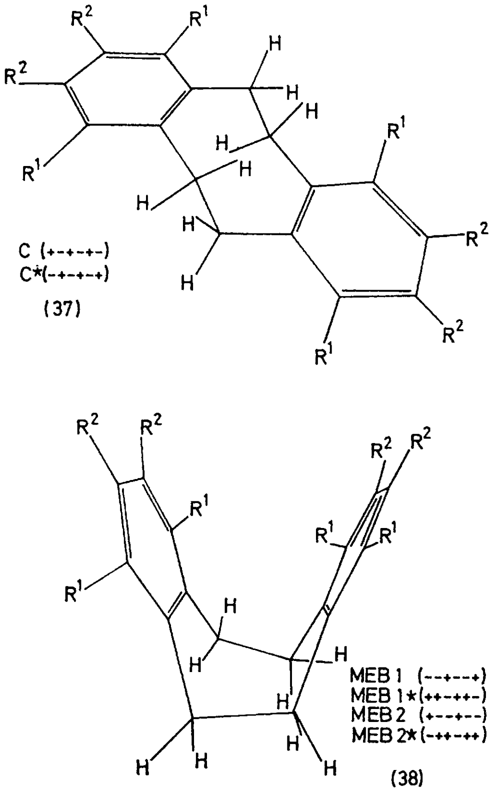

FIGURE 14 The ground-state C (37) and MEB (38) conformations of compounds (15) and (16). The notation for the torsional angles is defined in refs. 10 and 11 and refers in turn to the 4a,5-, 5,6-, 6,6a-, 10a,11-, 11,12-, and 12,12a-bonds. The descriptors C and C* refer to degenerate conformations; the descriptors MEB 1 and MEB 1* refer to enantiomeric conformations; further degenerate analogues are the MEB 2 and MEB 2* conformations. See refs. 10 and 11 for a full discussion of the conformational itinerary of these ‘ 6,8,6 ’ systems

The availability of the 2,3,8,9-tetramethyl derivative (15) as a suitable model for tetrahydrodibenzocyclo-

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* The description ‘ Boat ’ is non-specific and refers to any of the infinite number of conformations lying on the pseudorotational itinerary B $\rightleftharpoons$ TB $\rightleftharpoons$ B* $\rightleftharpoons$ TB* $\rightleftharpoons$ B (see refs. 10 and 11 for a definition of the descriptors B, B*, TB, and TB*). Similarly, the description ‘ Chair ’ refers to both the degenerate conformations (C and C*) of the rigid chair type.

octene (14) provided a means of assessing the reported[10–13] values (see above) for the free energy of activation associated with C ⟶ Boat interconversion in (14). Potentially, good ^{1}H n.m.r. probes are present in compound (15) in the form of (i) the four homotopic aromatic protons and (ii) the four homotopic aromatic methyl substituents. The ^{1}H n.m.r. spectral data for (15) in deuteriochloroform–carbon disulphide (2 : 1) at (i) +20 °C and (ii) −70 °C indicate (see Table 5) that the signals for the aromatic protons are the most suitable for line-shape analysis (see Figure 2) employing the two-site exchange program (see method I in the Experimental section) over the temperature range −52 to −71 °C. The results of this analysis (Table 6) show that the C (37; $R^1 = H$, $R^2 = Me$) and MEB (38; $R^1 = H$, $R^2 = Me$) conformations (see Figure 14) of (15) are populated to the extent of C : MEB ≃ 60 : 40 in $CDCl_3$–CS_2 (2 : 1) at −71 °C and that the free energy of activation is 10.5 kcal mol^{-1} for C ⟶ Boat interconversion in close agreement with the values of 10.2 (refs. 10—12) and 10.0 (ref. 13) reported for tetrahydrodibenzocyclo-octene (14). This correspondence in conformational behaviour between (14) and (15), together with strain energy calculations discussed previously[10,11] for (14), suggest that (i) the 2,3,8,9-tetramethyl derivative (15) is a suitable model for tetrahydrodibenzocyclo-octene (14) and (ii) C ⟶ Boat interconversion in the 2,3,8,9-tetramethyl derivative (15) involves a transition-state conformation (see Figure 15) of the TS1 (39; $R^1 = H$, $R^2 = Me$) type.

TABLE 6

Site exchanges and thermodynamic parameters associated with the Chair ⟶ Boat ring interconversion process in compounds (15) and (16)

Compound	R^1	R^2	Site exchanges [a]	p_A	p_B	ΔG/kcal mol^{-1}	$\Delta G^‡$/kcal mol^{-1}
(15)	H	Me	A ⟶ B	60	40	+0.16 (−71 °C)	10.5 ± 0.2
(16)	Me	H	A ⟶ B	12	88	−0.83 (−64 °C)	12.1 ± 0.5 [b]

[a] Details of the chemical shifts are given in Table 5. For the 2,3,8,9-tetramethyl derivative (15), a full line-shape analysis was carried out (see Figure 2) on the ^{1}H n.m.r. spectra for the aromatic protons. For the 1,4,7,10-tetramethyl derivative (16), a full line-shape analysis was carried out (see Figure 3) on the ^{1}H n.m.r. spectra for (i) the aromatic protons and (ii) the methyl protons. [b] Identical values for $\Delta G^‡$ were obtained from line-shape analysis of the ^{1}H n.m.r. spectra for (i) the aromatic protons and (ii) the methyl protons.

TABLE 7

Calculated strain energies (E_T/kcal mol^{-1}) [a] of various conformations [b] of 1,4,7,10-tetramethyl-5,6,11,12-tetrahydrodibenzo[*a,e*]cyclo-octene (16)

Conformation	E_r	E_θ	E_ϕ	E_δ	E_{nb}	E_T
C ≡ C* (37)	0.05	1.18	5.95	0.13	0.00	7.31
B ≡ B* [b]	0.11	1.66	6.00	0.15	0.04	7.96
TB ≡ TB* [b]	0.20	1.86	6.10	0.07	1.03	9.26
MEB (38)	0.08	1.62	4.05	0.22	0.00	5.97
TS1 ≡ TS1* ≡ TS2 ≡ TS2* (39)	0.87	16.88	0.93	1.05	0.81	20.54

[a] See footnotes *a*—*f* in Table 3. [b] These conformations have been defined in Part 1[10] and in a recent review.[11]

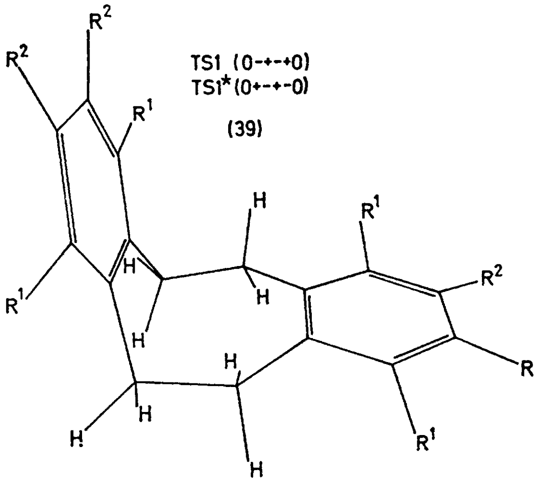

FIGURE 15 The transition-state conformation TS1 (39) for C ⟶ Boat interconversion in compounds (15) and (16). The notation for the torsional angles is defined in refs. 10 and 11 and refers in turn to the 4a,5-, 5,6-, 6,6a-, 10a,11-, 11,12-, and 12,12a-bonds. The descriptors TS1 and TS1* refer to degenerate conformations defined by coplanarity of atoms 11, 12, 12a, 4a, 5, and 6. Further degenerate analogues are the TS2 and TS2* conformations (see refs. 10 and 11) defined by coplanarity of atoms 5, 6, 6a, 10a, 11, and 12

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