Force Field Calculations on Molecular Belts built from Cyclohexa-1,4-diene Rings

Roger W. Alder* and Richard B. Sessions
School of Chemistry, University of Bristol, Bristol BS8 1TS

Calculations using the MM2 program are reported on a series of hydrocarbons constructed by lateral fusion of *n* cyclohexa-1,4-diene rings, the [*n*]beltenes. Strain energy per macro-ring unit $(-CH_2-C{=}C-CH_2-)$ decreases monotonically from [3]beltene to [12]beltene. The beltenes have the shape of a semi-rigid molecular torus, the larger beltenes containing a substantial cavity. Encapsulation of acetylene becomes favourable with [8]beltene. The encapsulation of some other small molecules has been examined. The shape and strain energy of selected hydrogenated beltenes is discussed.

Cyclohex-1,4-diene is planar,[1] but undergoes wide-amplitude bending[2] about an axis joining the methylene carbon atoms, thus acting as molecular hinge (Figure 1). An interesting set of hypothetical molecules can be constructed by lateral fusion of cyclohexa-1,4-diene rings and linkage into a macrocyclic belt-like assembly as shown in the general formula (**1**). We shall refer† to these compounds as [*n*]beltenes for simplicity; thus Figure 2 shows [4]beltene. Perspective drawings of the larger beltenes become very confused, so we shall use plan (top) views as shown for [4]beltene with the conventions shown in Figure 2.

Molecular models suggest that the strain energy of the beltenes is not excessively large for [5]beltene and beyond. These systems are roughly circular and beyond about [6]beltene should possess a substantial cavity which might encapsulate other molecules or ions. Models again suggest that the shape and size of the cavity can be dramatically altered by hydrogenation of selected ring junctions. During the current intense activity in host–guest chemistry, a remarkably diverse range of molecules have been examined as potential cavity-based hosts. The choice of molecular system has been largely based on synthetic expediency. We believe the beltene architecture has much to recommend it as a fundamental skeleton for molecular hosts. Since the preparation of beltenes will require a major synthetic effort, it seemed desirable to probe the properties of these molecules by calculation. In this paper we report force-field calculations on beltenes and some prototype host–guest complexes. The MM2 program which we use has been shown to give a good account of the structure and energy of cyclohexa-1,4-diene itself.[3–5]

The beltenes may be regarded as the parents of numerous related systems. The conjugated systems (**2**) and (**3**) are of current theoretical interest.[6] Systems with alternating benzo rings (**4**) should have much in common with the beltenes and might well be a more practical target for synthesis. In this context, the recent preparation of (**5**)[7] and (**6**)[8] is of interest, and the calixarenes[9,10] represent other incompletely cyclised analogues. The incorporation of quinone rings in a beltene structure could lead to novel electron-transfer chemistry on encapsulated species.‡ The macrocyclic compounds (**7**)[11] and (**8**)[12] containing π-bonds built from radially oriented *p*-orbitals have some features in common with beltenes.§

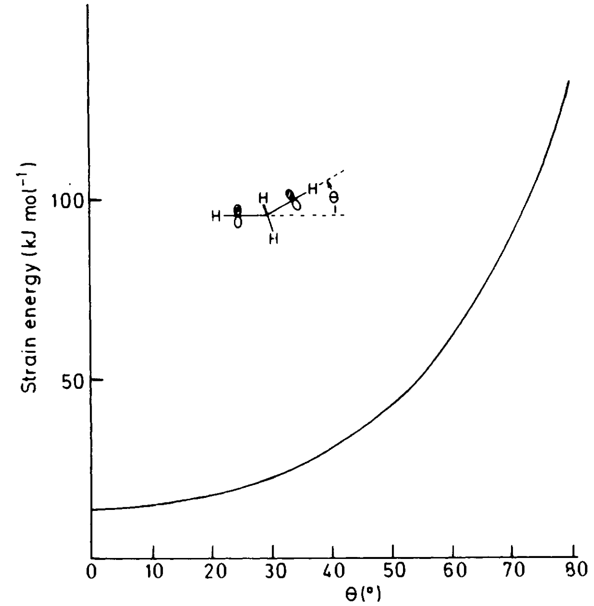
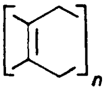


Figure 1. Flexing of cyclohexa-1,4-diene from MM2 calculations; see also ref. 4



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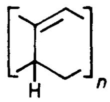

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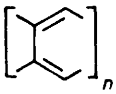

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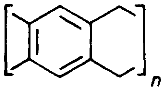

(**4**)

Our version of MM2 could not handle conjugated systems, so we have confined our attention to the beltenes as defined above and to hydrogenated analogues. We believe this paper presents the first systematic study of host–guest complexation by molecular mechanics, although Miller and Whitlock[13a] have calculated the decrease in steric energy for complexation of benzene in a boxlike host which they prepared, and calculations

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† Trivial nomenclature is traditionally the prerogative of the first workers to *synthesize* a novel molecular system; we have no desire to usurp that privilege.

‡ Most studies on host–guest chemistry have concentrated on acid–base and related even-electron processes; the redox chemistry of guest species has been rather neglected.

§ Since submission of this paper several molecules with a complete belt-like structure have been reported. Boekelheide and co-workers have prepared $[2_6](1,2,4,5)$cyclophane or deltaphane which has alternating benzenoid and cyclo-octadiene rings (H. C. Kang, A. W. Hanson, B. Eaton, and V. Boekelheide, *J. Am. Chem. Soc.*, 1985, **107**, 1979). Cram *et al.* have prepared several cavitands with alternating aromatic and eight-membered rings in a belt and show that these cavitands complex the linear molecules CS_2, $CH_3C{\equiv}CH$, and O_2; the CS_2 complex has a structure which closely resembles that calculated for [8]beltene with acetylene in this paper (D. J. Cram, K. D. Stewart, I. Goldberg, and K. N. Trueblood, *J. Am. Chem. Soc.*, 1985, **107**, 2574).

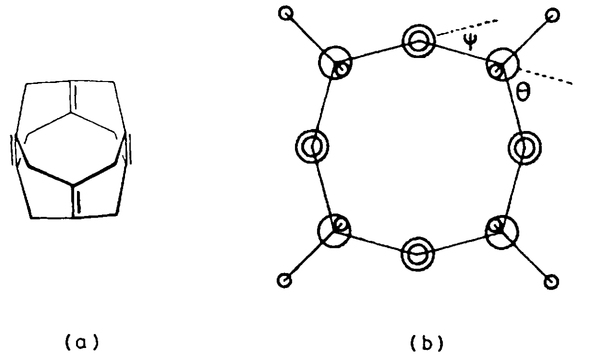
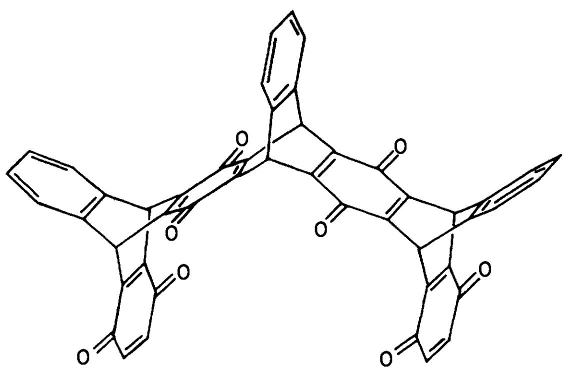


Figure 2. [4]Beltene, (a) perspective drawing, (b) plan view as calculated by MM2; double circle, double bonded bridgehead carbon; circle, methylene carbon; small circle, hydrogen. For θ and ψ see Table 1



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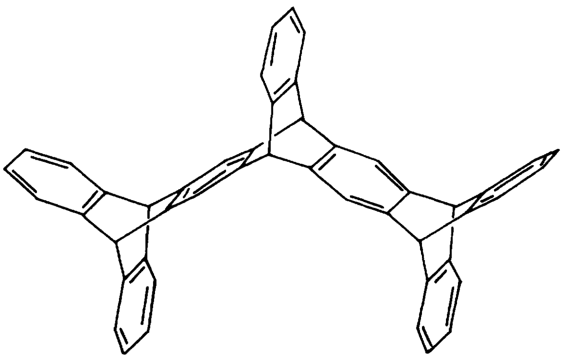


(6)

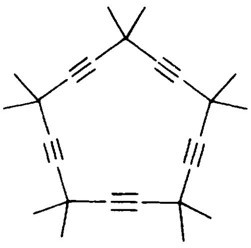
on alkali cation complexes of 18-crown-6 and anisole spherands have been reported recently.[13b]

Results and Discussion

[n]*Beltenes*.—The [n]beltenes from $n = 3$ to 12 gave minimum-energy structures with D_{nh} symmetry. It can be confidently asserted that no other conformational minima exist for these molecules. This arises from the shape of the strain energy/θ curve for cyclohexa-1,4-diene (Figure 1).[4] The second derivative $d^2E/d\theta^2$ is always positive and so extra flexing of some cyclohexa-1,4-diene units in order to flatten others will always increase the strain energy. However, because of the 'soft' character of the potential in Figure 1, the large beltenes should be quite flexible—the molecular equivalent of a rubber ring or torus. Figure 2 shows the calculated structure for [4]beltene and Figures 3(a) and (b) illustrate [8]beltene. As shown in Figure 3(b), the torus has a van der Waals thickness of *ca.* 4 Å, a depth of 7—8 Å, and a principal radius r which is given by equation (1). This means that the larger beltenes have a cylindrical cavity

$$r = \tfrac{1}{2}\{[2.6/\sin(360/2n)]^2 - 2.6^2\}^{\frac{1}{2}} \qquad (1)$$

of diameter $2r$ − 3.88 Å and depth 7—8 Å (see also Table 1). In very large beltenes, the structure might collapse so as to bring some of the opposite walls into favourable van der Waals contact, but this would be too costly in energy terms for the beltenes considered here.



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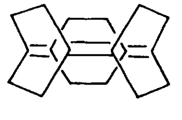


(8)

The strain energy of the beltenes per $-CH_2\text{–}C{=}C\text{–}CH_2-$ unit [see (**1**)] is plotted in Figure 4, and the contributing factors to the strain energy are listed in Table 1. The strain energy–ring size curve for the beltenes is much simpler than for the cycloalkanes themselves. There is no medium-ring anomaly because (i) there is no dihedral angle crisis and (ii) transannular interactions are unimportant. For the larger beltenes ($n > 6$), the strain energy is almost entirely derived from flexing the cyclohexa-1,4-diene molecular hinge, so that strain energy per ring unit is almost equal to that of a similarly bent cyclohexa-1,4-diene (see Table 1). The small beltenes have substantial olefinic torsional strain,[14] reminiscent of that in alkanes like (**9**).[15]

For comparison with the beltenes, we made calculations on the series of molecules (**10**). We considered it possible that the inner rings of these compounds might be puckered, and a variety of input geometries were tried for (**10**), but only flat structures emerged as energy minima from MM2. This simplifies the discussion of strain energies which were 27.1, 39.9, and 52.7 kJ mol^{-1} for $n = 1$, 2, and 3 respectively. The constant increment of 12.8 kJ mol^{-1} can be taken as the strain energy of an inner C_4H_4 unit and thus as the strain energy *per unit* of an infinite beltene.

Before leaving the parent beltenes, the question of the interaction of the π-bonds in beltenes deserves comment. Through-bond and through-space interactions in cyclohexa-1,4-diene and related molecules is well known and has been thoroughly studied by photoelectron spectroscopy.[16] Interaction between the π-bonds in (**7**) and (**8**) has been observed by photoelectron spectroscopy and for (**7**) may well involve the in-plane as well as the out-of-plane π-bonds. Interactions between the π-bonds in beltenes must be expected to occur and their photoelectron spectra would be interesting. Would these interactions seriously alter the energy and geometry of beltenes, perhaps in ways not allowed for by MM2? In general these interactions have much more effect on orbital energies (some rise, some fall) than on total energies. However, Ermer, Bödecker, and Preut[17] recently noted substantial discrepancies between the calculated structure for (**11**) and the observed structure for (**12**), and ascribed this to orbital symmetry effects. As we noted earlier, MM2 gives a good account of the geometry of cyclohexa-1,4-diene itself and we believe any problems in the calculations are likely to be due to more distant π-bonds experiencing face-to-face contact. Except in the smallest beltenes the distances involved are rather larger than for (**11**)

Table 1. Geometry and energy (kJ mol^{-1}) for the [*n*]beltenes[a]

n	3	4	5	6	7	8	9	10	11	12
θ } see Figure 2(b)	68.4	59.7	54.6	50.6	46.9	43.4	39.7	36	32.7	30
ψ	51.6	30.3	17.4	9.4	4.5	1.6	0.3	0	0	0
Cavity diameter (Å)	0	0	0	0.6	1.5	2.4	3.3	4.1	5.0	5.8
Heat of formation	524	456	452	465	484	508	535	564	597	630
Strain energy (per C_4H_4 unit)	141	81.0	57.9	45.4	37.3	31.7	27.8	25.0	22.9	21.2
Compression	7.4	2.7	1.5	1.2	1.0	0.9	0.8	0.8	0.7	0.7
Bending	21.7	12.0	8.5	5.5	3.5	2.3	1.6	1.3	1.2	1.2
van der Waals, 1,4-	26.9	17.9	15.2	13.7	12.6	11.8	11.2	10.8	10.4	10.1
van der Waals, other	5.5	−2.3	−5.3	−5.4	−4.9	−4.4	−4.1	−4.0	−3.9	−3.9
Torsion	79.5	47.5	34.1	26.2	20.8	16.9	14.1	11.9	10.2	8.9
Olefinic torsion	76.8	31.8	10.9	3.2	0.8	0	0	0	0	0
Strain energy of cyclohexa-1,4-diene at same θ	84.9	59.4	49.4	42.7	38.1	33.9	29.7	26.4	23.8	22.2

[a] Lists of *x*, *y*, *z* co-ordinates for energy-minimised structures are available as Supplementary Publication No. SUP 56329 (45 pp.). For details of Supplementary Publications see Instructions for Authors, *J. Chem. Soc., Perkin Trans. 2*, 1985, Issue 1.

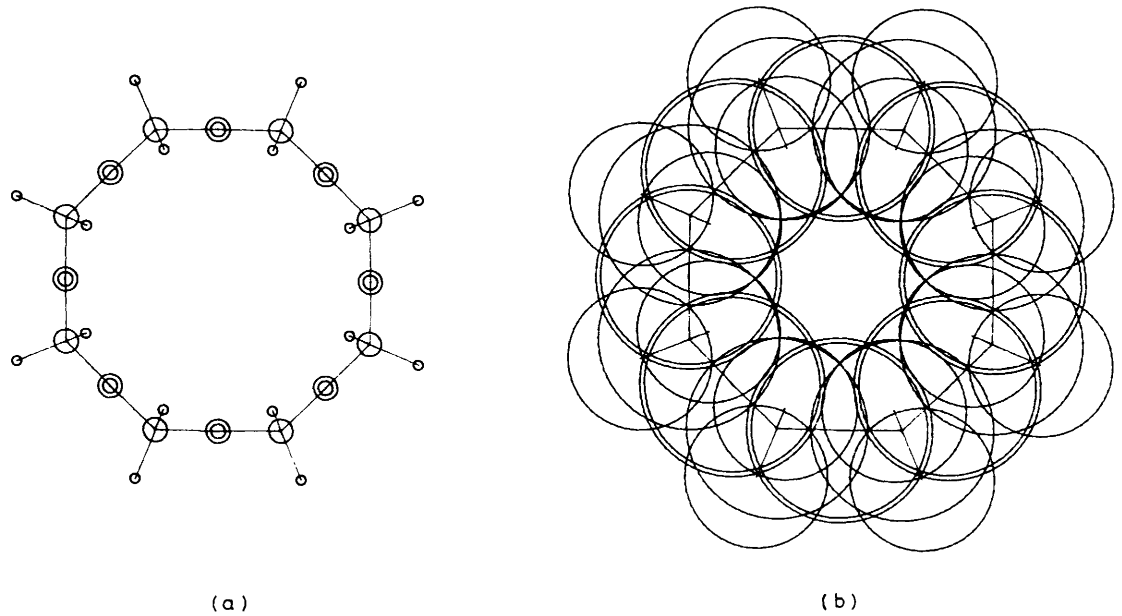

(a) (b)

Figure 3. (a) Plan view of [8]beltene using the conventions in Figure 2; (b) plan view of [8]beltene, showing van der Waals radii; van der Waals radii of doubly bonded carbons are shown as double circles

and (**12**), so we do not believe there are serious problems for our calculations.

Hydrogenated Beltenes.—We have made calculations (see Table 2) on some beltenes to which 2, 3, and 4 pairs of hydrogen atoms have been added from the outside to selected ring junction double bonds (inside addition of hydrogen is possible with larger beltenes). As detailed in Table 2 and illustrated for the doubly hydrogenated [8]beltene in Figure 5, we have confined our attention to the systems of highest symmetry. The interest of these systems is twofold: (i) synthetic routes to beltenes are likely to produce hydrogenated beltenes as intermediates, *e.g.* through Diels–Alder reactions; (ii) models suggest dramatic changes in the shape and size of cavities on hydrogenation.

Perhydrogenation of [3]beltene gives the known hydrocarbon tetracyclo[5.3.1.1^{2,6}.0^{4,9}]dodecane (iceane)[18] and is accompanied by an enormous relief of strain. The MM2 strain energy is a little higher than that calculated by MM1 (94) or the Engler force field (105 kJ mol^{-1}).[19] Addition of 2 × H_2 to opposite ring junctions of [4]beltene also leads to decreased strain, but perhydrogenation now gives rise to an increase in strain. In the perhydro compound, the cyclohexane rings are flattened boats, unable to twist. With [6]beltene, strain energy begins to rise with the addition of 3 × H_2. Fully hydrogenated [6]beltene, which we might call [6]beltane, might however adopt an all-chair conformation at the expense of severe interactions among the 'inside' CH_2 groups. Replacing these by NH or oxygens would give extremely interesting derivatives of 18-crown-6, *e.g.* (**13**).

The larger partially hydrogenated beltenes have several structures which are energy minima; we have no means of ensuring we have located them all and thus found the lowest-energy structure. They are also quite floppy, so energy does not vary strongly with some deformations. Force-field calculations can therefore converge on energy minima quite slowly. Thus we started the calculation of the doubly hydrogenated [8]beltene at the geometry of [8]beltene with the hydrogens appended to the

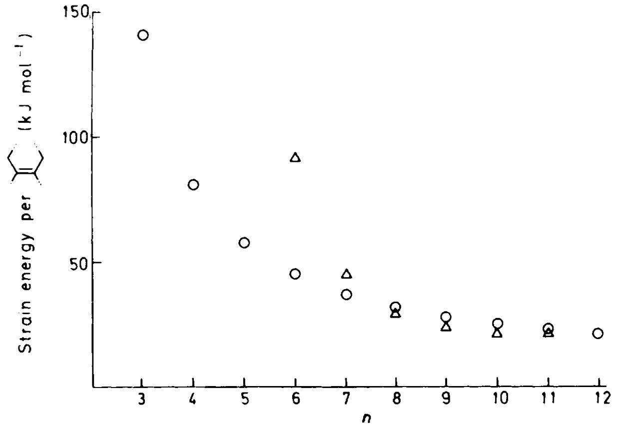
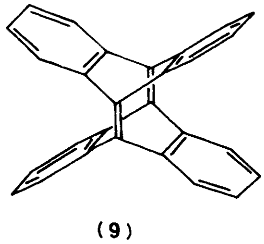


Figure 4. Strain energy of the [*n*]beltenes as a function of *n*; Δ points are the strain energies for the acetylene complexes.



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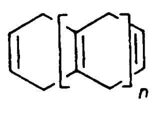

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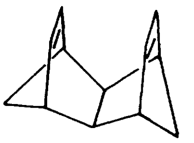

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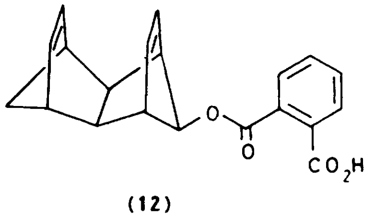


(12)

structure. After 50 iterations, the strain energy was 299 kJ mol^{-1}; after 156 iterations, the minimisation was complete with quite substantial changes of geometry, but only a small decrease in strain energy (to 277). The calculated structure was quite open. When, on the other hand we imposed symmetry restrictions on the methylene adjacent to the $>$CH–CH$<$, a much more stable structure (ΔH_f 242; strain energy 187) was located. This structure has *no cavity* (Figure 5); the opposite sides of the ring are in favourable van der Waals contact. Similar results were obtained with the doubly hydrogenated [10]beltene. These are probably the most stable structures. For the triply hydrogenated [9]beltene, the most stable structure located had threefold symmetry, but it still possessed a cavity (probably inevitable), and we feel less certain that it is the global energy minimum.

Beltene Complexes.—Miller and Whitlock,[13a] following up Cram's ideas on enforced cavities,[13c] suggest two generally useful principles in designing cavity-based hosts:

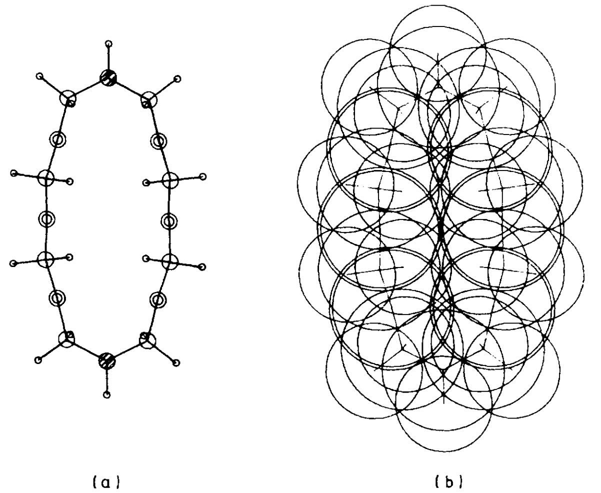
(i) A conformationally flexible (*i.e.* collapsible) host will collapse with loss of complexation ability *unless* suitable intercavity attractive interactions are present. Collapsible hosts must be 'guest sticky'.

(ii) Hosts with functionally neutral cavities will accept guests *if* the cavity is maintained rigidly. Rigid hosts need not be guest sticky.

The parent beltenes are semi-rigid and should fall in category (ii); complexes relying solely on van der Waals forces should be possible for molecules of the correct size and shape.

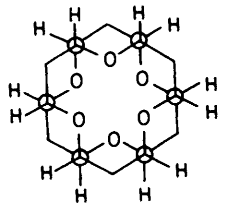
Table 2. Strain energies of hydrogenated [*n*]beltenes (kJ mol^{-1})

n	3	4	6	8	9	10
Parent [*n*]beltene	423	326	272	254	250	250
[*n*]Beltene with two opposed bridgehead double bonds hydrogenated (D_{2h})		194	183	187		198
[*n*]Beltene with three symmetrically placed hydrogenated bridgehead double bonds (D_{3h})	116		241		292	
[*n*]Beltene with four hydrogenated bridgehead double bonds (D_{4h})		224				



(a) (b)

Figure 5. (a) Plan view of doubly hydrogenated [8]beltene; the methine carbons at the hydrogenated bridgeheads are shown hatched; (b) van der Waals radii for doubly hydrogenated [8]beltene



(13)

The sizes of the cavities within various beltenes are listed in Table 1. We have found it possible to make standard MM2 calculations on a beltene with an acetylene molecule inside for [6]- to [11]-beltene (the [12]beltene–acetylene complex exceeded the capacity of our program). Normal minimisation occurred even for the [6]- and [7]-beltene complexes which are calculated to be unstable with respect to their component. Symmetry constraints were not imposed, so that it appears that there may be a barrier to dissociation, however small.

The energy changes on complex formation with acetylene were: [6]beltene +275 (unfavourable), [7]beltene +52, [8]-beltene −20, [9]beltene −32, [10]beltene −27, [11]beltene- −20 kJ mol^{-1}. Except for the case of the highly strained [6]beltene complex, the energy changes were almost completely

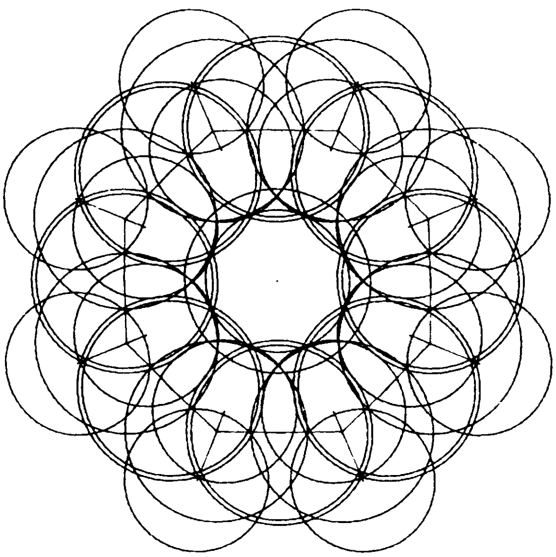


Figure 6. Plan view of the [8]beltene–acetylene complex; the central circles show the van der Waals radii for the carbon and hydrogen atoms of acetylene

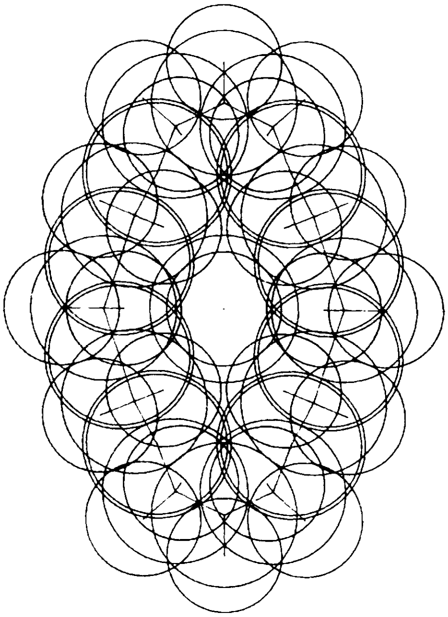


Figure 7. Plan view of the complex of acetylene with doubly hydrogenated [10]beltene

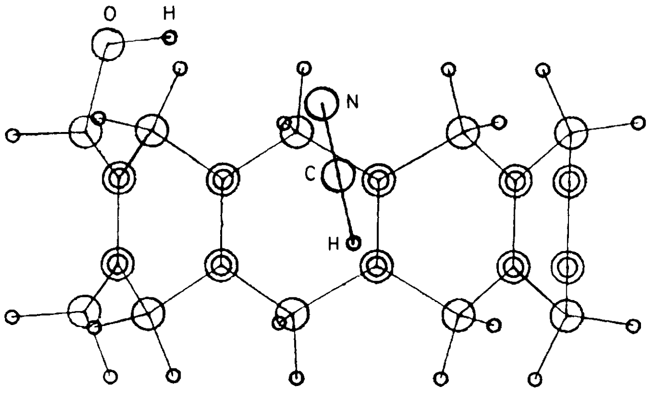


Figure 8. Side view of the complex of hydroxylated [9]beltene with HCN

due to van der Waals interactions, as expected. Figure 6 shows a picture of the [8]beltene–acetylene complex—the cavity is still slightly too small and the best complexation occurs with [9]beltene. With [10]- and [11]-beltene, the cavity is too large and the acetylene was asymmetrically placed to maximise the favourable van der Walls forces. For comparison [8]beltene with an acetylene on the outside gave a complexation energy of -8 kJ mol^{-1}. The strain energies of the beltene–acetylene complexes are plotted on Figure 2.

We also calculated the complexes of the doubly hydrogenated [8]- and [10]-beltene with acetylene (see Figure 7). These are unstable with respect to their components by 104 and 33 kJ mol^{-1}, respectively. However, when we calculated the doubly hydrogenated [10]beltene *at the geometry of its acetylene complex*, the extra strain energy was 44 kJ mol^{-1}. Thus formation of the complex from the beltene in this geometry is favourable by 11 kJ mol^{-1}. Thus our calculations give support to Miller and Whitlock's principles—these hydrogenated beltenes are conformationally flexible and collapsible.

Since the cavity which can be created inside doubly hydrogenated [10]beltene is not cylindrical, we made calculations on a non-cylindrical host, ethylene. With the π-bond perpendicular to the horizontal plane of the beltenes (as for acetylene) we fixed the ethylene plane parallel and perpendicular to the longer axis of the beltene. These gave strain energies of 230 and 266 kJ mol^{-1}, respectively. The less stable complex collapsed to the more stable complex when symmetry constraints were removed. Of course, even the more stable complex is unstable with respect to ethylene and the (collapsed) host.

Finally we have explored the possibility of modelling more specific host–guest interactions (hydrogen bonding) by MM2 calculations. We replaced an *endo*-CH_2 proton in [9]beltene with an OH group and calculated its complex with HCN. Figure 8 shows the most stable orientation with the HCN tipped towards the OH and a clear indication of an $O{-}H \cdots N{\equiv}C{-}H$ hydrogen bond ($H \cdots N$ distance 2.58 Å). However, the energy change on complex formation (-38) is only marginally more favourable than for the HCN complex with [9]beltene itself (-34 kJ mol^{-1}). Essentially identical results were obtained with CH_3CN with regard to both geometry and energy changes. When HCN was oriented the 'wrong way round' in the hydroxylated [9]beltene (*i.e.* with its hydrogen near the OH) the energy change on complexation was reduced to -32 and a slightly more stable complex (heat of complexation -34 kJ mol^{-1}) was obtained by rotation about the C–O through 120° so that the hydroxy proton pointed out of the cage.

We think these results indicate that MM2 can give a reasonable picture of weak electrostatic interactions in these complexes. In the complexes we have studied there is a conflict between the orientation demands of the [9]beltene cage and those of the hydrogen bond, which would presumably be strongest in a linear $O{-}H \cdots N{\equiv}C{-}H$ orientation, so that the very small energy advantage provided by the hydrogen bond is not difficult to understand. The MM2 method has been shown to give a reasonably good account of simple examples of hydrogen bonding (*e.g.* RCO_2H dimers).[3,20]

Acknowledgements

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