Force Field Calculations on Cyclophanes with Unsaturated Bridges

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Force field calculations using the Allinger MMP2 program have been carried out on unsaturated cyclophanes with extensive π-systems. The cyclophanes are found to show bond alternation. The benzene rings are twisted out of the average molecular planes resulting in loss of cyclic conjugation. The calculated conformations of some cage cyclophanes have central cavities large enough for the inclusion of guest ions or molecules. The relative energy for some hypothetical planar conformations of the unsaturated cyclophanes has been calculated and is discussed in connection with dynamic processes in neutral cyclophanes and induced ring current effects in dianionic species. The planar conformations have significantly higher energy (15–189 kcal mol^{-1}) than the most stable conformations.

Macrocyclic compounds with conjugated ring peripheries have long attracted the interest of organic chemists from both a theoretical as well as synthetic point of view. Annulenes and bridged annulenes have served as probes for investigation of concepts and properties such as aromaticity and ring currents, bond alternation, homoaromaticity and topology, anion and cation formation, etc.[1-3]

We have described a convenient one-pot synthesis of unsaturated cyclophanes using multiple Wittig reactions.[4] The neutral compounds can be regarded as normal aromatic species and show no peripheral ring current effects.[5-8] However, the neutral cyclophanes with a formal 4N π-electron periphery undergo a completely reversible two-electron reduction to their dianions.[9] The dianions show the characteristics of the annulenes.[10,11] An investigation of the aromaticity of cyclophanes with unsaturated bridges by resonance energy calculations shows that both neutral and dianionic compounds are aromatic but for different reasons. The neutral cyclophanes are aromatic because of the incorporated benzene rings while the dianions are aromatic not only because of the benzene rings present but also partly because of the (4N + 2) π-electron perimeter.[12]

On irradiation these cyclophanes show a marked shift of the emission spectrum as compared with the absorption spectrum.[13] Often cis–trans isomerization occurs readily whereas the intramolecular photocyclization to a dehydrophenanthrene rarely happens.[13,14]

In order to further investigate the properties of these macrocyclic compounds we have performed force field (molecular mechanics) calculations of the Allinger type. The results are used in connection with questions of the electronic properties on excitation, to understand the dynamic processes in the neutral cyclophanes,

TABLE I: Minimized Energy Values and Heats of Formation of Cyclophanes 1, 5–14

compd	steric energy, kcal mol^{-1}	strain energy, kcal mol^{-1}	heat of formation, kcal mol^{-1}
1a	−14.30	13.47	152.26
1b	115.99	129.38	
5a	−14.16	14.39	166.47
5b	66.23	87.61	
6a	−18.51	10.84	176.15
6b	35.33	60.43	
6c	−14.31	15.02	179.26
7a	−20.72	9.40	188.02
7b	8.33	36.61	
8a	−25.99	4.90	196.77
8b	−10.63	19.35	
9a	−17.56	20.39	192.49
9b	107.91	130.68	
10a	−20.32	19.61	200.84
10b	93.03	122.13	
11a	67.36	108.64	315.53
11b	67.86	109.15	316.10
11c	73.59	115.04	322.04
11d	256.80	292.39	
11e	257.63	292.89	
12	−13.03	25.59	215.96
13	−11.68	27.14	217.49
14	17.67	54.56	230.42

TABLE II: Average and Individual Twist (in Degrees) of the Benzene Rings in Compounds 1a, 5a–11a from the Average Molecular Plane

ring	1a	5a	6a	7a	8a	9a	10a	11a
I	35.3	31.5	26.8	25.8	4.1			
II		38.6	40.5	40.7	41.0			
III		34.6	34.7	17.5				
IV		35.3		38.5				
av	35	35	34	31	23	37	32	37

and to find the lowest energy conformations.

Will molecular mechanics calculations show any effects of the cyclic conjugation, i.e., will 4N and (4N + 2) peripheral π-systems be geometrically different as far as bond lengths are concerned?

Method of Calculation

We have used the force field of Allinger et al. with provision for conjugated systems using a quantum mechanical π-electron calculation (the MMP2 program).[15] The minimized geometries were obtained by full relaxation of several trial structures. The latter were generated by using the perception routines of the LHASA program.[16] The calculations on planar geometries of the cy-

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(2) Vogel, E. *Isr. J. Chem.* **1980**, *20*, 215.
(3) Boekelheide, V. *Pure Appl. Chem.* **1975**, *44*, 750.
(4) Norinder, U.; Tanner, D.; Wennerström, O. *Croat. Chem. Acta* **1983**, *56*, 269 and references therein.
(5) Thulin, B. *J. Chem. Soc., Perkin Trans. 1* **1981**, 664.
(6) Tanner, D.; Thulin, B.; Wennerström, O. *Acta Chem. Scand., Ser. B* **1979**, *B33*, 443.
(7) Raston, I.; Wennerström, O. *Acta Chem. Scand., Ser. B* **1982**, *B36*, 655.
(8) Höglund, H.-E.; Wennerström, O. *Acta Chem. Scand., Ser. B* **1982**, *B36*, 636.
(9) Ankner, K.; Lamm, B.; Thulin, B.; Wennerström, O. *Acta Chem. Scand. Ser. B* **1978**, *B32*, 155; *J. Chem. Soc., Perkin Trans. 1* **1980**, 1301.
(10) Huber, W.; Müllen, K.; Wennerström, O. *Angew. Chem.* **1980**, *92*, 636.
(11) Müllen, K.; Unterberg, H.; Huber, W.; Wennerström, O.; Norinder, U.; Tanner, D.; Thulin, B. *J. Am. Chem. Soc.* **1984**, *106*, 7514.
(12) Norinder, U.; Wennerström, O. *Acta Chem. Scand., Ser. A* **1983**, *A37*, 431.
(13) Norinder, U.; Sandros, K.; Wennerström, O. *Acta Chem. Scand., Ser. B* **1984**, *B38*, 597.
(14) Norinder, U.; Tanner, D.; Wennerström, O. *Tetrahedron Lett.* **1983**, 5411.

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TABLE III: Bond Lengths (in Å) of Compounds 1a, 6a, 8a–11a, 12–14

bond	1a	6a	8a	9a	10a	11a	12	13	14
1–2	1.47	1.47	1.48	1.47	1.47	1.47	1.47	1.49	1.49
2–3	1.35	1.35	1.35	1.35	1.35	1.35	1.35	1.35	1.34
3–4		1.47	1.47	1.48	1.47	1.47	1.48	1.47	
4–5			1.36						
5–6		1.47	1.47		1.49	1.47			
6–7		1.35				1.36			
7–8		1.47				1.47			
8–9		1.35							
9–10		1.48				1.47			
10–11						1.35			
11–12						1.47			

clophanes were performed by relaxation of planar trial structures with and without restricted motion conditions, and in all cases the energy minimized geometry of the two methods were identical. The final energies and heats of formation are presented in Table I.

Results and Discussion

[2.2.2.2]Paracyclophanetetraene (1). Liljefors and Wennerström have previously reported the energy minimized geometry of 1 using the Allinger MMP1 program.[17] We have

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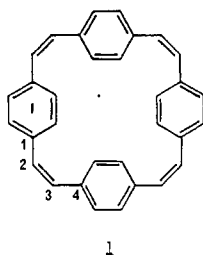
recalculated the geometry with the revised Allinger force field program MMP2. The two resulting geometries are, within the computational limits, identical as far as geometrical features, i.e., bond lengths, bond angles, and torsional angles, are concerned. Thus the compound has D_{2d} symmetry with the benzene rings tilted ca. 35° out of the average molecular plane (Table II). This is in good agreement with the X-ray structure of 1.[18] Bond alternation is pronounced with normal bond lengths for the bridging vinylene groups and normal delocalized bonds in the benzene rings (Table III). In order to investigate the energy requirements for increased planarity we have calculated the minimum energy of a completely planar conformation, 1b. The planar form is calculated to be 130 kcal mol⁻¹ higher in energy than the nonplanar one, 1a. The geometry of 1b is highly unfavorable which results in considerable deformation of bond angles and bond lengths. Both single and double bonds in 1b are somewhat stretched. The major increase in energy, however, stems from increased bending energy. The benzene rings have been elongated along the axes of connections and the angles at the bridging groups are also enlarged. The inner protons in 1 also have to be considered. In 1b these protons are forced against each other closer than the sum of the van der Waals radii. In 1a the distance between the inner protons is 2.95 Å while in 1b the distance is only 1.59 Å. The attached carbon atoms are 3.15 Å apart in 1a and 3.28 Å in 1b.

The large difference in energy between the planar and nonplanar conformations should be remembered when discussing the geometry of the dianion of 1 which shows a large diamagnetic perimeter ring current.[10] Although the bond lengths in 1 must be slightly changed on reduction to 1^{2-} the latter must still be nonplanar with a certain twist of the benzene rings from the molecular plane. The rotation of these benzene rings is fast on the NMR time scale at room temperature in 1, and no barrier to the rotation has been measured so far.[19] In the anion radical, however, the rotation

is slower and a barrier of 7 kcal mol⁻¹ has been found.[20] The barrier to rotation or flipping is even more pronounced in the corresponding dianion, 1^{2-}, where the barrier is calculated to ca. 15 kcal mol⁻¹ from line-shape analysis of the temperature-dependent ¹H NMR spectra.[11]

We have also found previously that the introduction of methyl and ethyl substituents on the benzene rings in the proper positions changes the geometry and the barrier to interconversion of conformers. In the tetramethyl derivative, 2, the barrier to rotation of the substituted benzene rings is 15 kcal mol⁻¹.[19] In the oc-

2 R = H
3 R = Me
4 R = Et
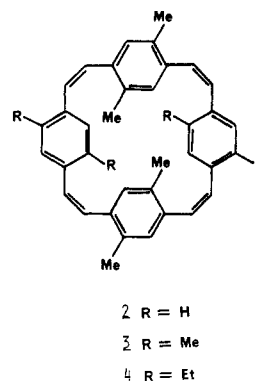
tamethyl derivative, 3, the barrier to flipping of the benzene rings is 10 kcal mol⁻¹.[21] In the tetramethyl tetraethyl derivative, 4, the two dynamic processes can be observed separately. The higher one involves rotation and the lower one flipping of the benzene rings. The calculated barriers are 15 and 10 kcal mol⁻¹, respectively, from line-shape analysis of the temperature-dependent ¹H NMR spectra.[21,22]

[2.2.2.4]Paracyclophanepentaene (5). [2.2.2.4]Paracyclophanepentaene (5) has an additional double bond in one of the bridges as compared to 1. The symmetry of the cyclophane 5

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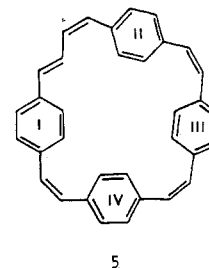
is thereby lowered. The increase in size reduces the energy difference between the planar and nonplanar conformations, 5b and 5a, respectively, to 80 kcal mol⁻¹. The bond lengths in 5a are essentially the same as in 1a. The enlargement of the ring causes a slight increase of the bond angles at the bridging groups, ca.

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(21) Norinder, U.; Wennerström, O. *Tetrahedron Lett.*, 1984, 4787.
(22) Norinder, U.; Raston, I.; Wennerström, O., to be published.

TABLE IV: Bond Angles (in Degrees) of Compounds 1a, 6a, 8a–11a, 12–14

angle	1a	6a	8a	9a	10a	11a	12	13	14
1-2-3	128.4	130.3	127.9	127.6	129.0	127.3	129.6	125.9	120.1
2-3-4		130.2	126.4	128.3	129.6	127.5	131.2	127.0	
3-4-5			120.6						
4-5-6			126.5						
5-6-7		125.7				125.9			
6-7-8		121.2				125.3			
7-8-9		124.9							
8-9-10		125.4							
9-10-11						127.5			
10-11-12						127.2			

2°. The mean deviation from planarity of the benzene rings is practically the same as in 1a (Table II). The butadiene group is relatively strain free with bond angles of ca. 123° and torsional angles of the S-trans bond and the trans double bond of 172° and 178°, respectively. The cis double bonds in 5a are only slightly perturbed, ca. 10°, which is the same as in 1a.

[2.2.4.4]Paracyclophanehexaene (6). There are two interesting conformations of cyclophane 6 with adjacent butadiene bridges.
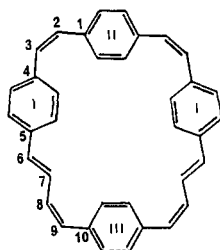
6A

One of them has S-trans orientation at the butadiene bridges, 6a, and the other has S-cis orientation, 6c. Calculations predict 6a to be more stable than 6c by 4.2 kcal mol⁻¹ which supports the
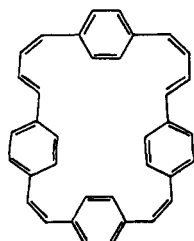

6c

assignment made from vicinal proton–proton coupling constants.[5] The minimized geometry of 6a shows normal bond lengths with bond alternation at the bridging units and normal benzene rings (Table III). The bond angles in the butadiene parts are only slightly different from standard values. The vinylene bridging groups have somewhat widened bond angles (Table IV). The torsional angles of both the butadiene (the cis part) and the vinylene groups are essentially as in 1a, viz., 9.8°, 10.9°, and 10.8°. The S-trans bond is slightly twisted out of planarity with an angle of 172.5° while the trans double bond is twisted only 3°. In 6a there are three types of benzene ring, I, II, and III. Rings I in 6a are twisted 27° from the average molecular plane while II is twisted 35°. Somewhat surprisingly, ring III is twisted more, 40.5°, apparently due to the interaction between the inner olefinic protons and the inner protons on ring III.

The main reason for the higher energy of 6c over 6a stems from the torsional strain at the butadiene bridges. The torsional angle of the cis double bond is almost the same as that in 6a, 10.8° and 9.8°, respectively. The S-cis bond, however, has a much larger torsional angle 41.4°. Even the trans double bond is more twisted in 6c than in 6a, 10.7° and 2.9°, respectively. The benzene rings in 6c are, however, less twisted from the average molecular plane than in 6a, 24° and 34°, respectively.

The completely planar form, 6b, has 54 kcal mol⁻¹ higher energy than 6a.

[2.4.4.4]Paracyclophaneheptaene (7). The vinylogous cyclophane with three butadiene bridges, 7, is another unsymmetrical
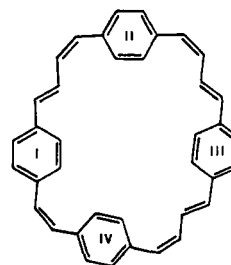
7

molecule with four nonequivalent benzene rings and bridges. As a consequence of the ring enlargement the calculated difference between the nonplanar (7a) and the planar (7b) conformation has decreased to 29 kcal mol⁻¹. The average twist of the benzene rings is almost the same as in 1a (Table II) due to the interaction between inner olefinic and aromatic protons.

[4.4.4.4]Paracyclophaneoctaene (8). The calculated difference in energy between the nonplanar (8a) and the planar (8b) minimized geometry of cyclophane 8 is only 15 kcal mol⁻¹. The two
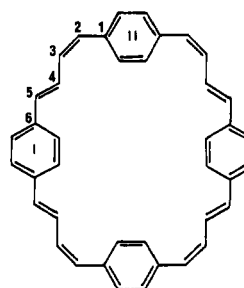
8

different types of benzene rings in 8, I and II, are tilted 4° and 41°, respectively, from the average molecular plane (see also Table II). The reason is the same as discussed earlier for cyclophanes 6 and 7. The torsional angles of the trans double bond and the S-trans single bond are 177° and 179°, respectively. The torsional angle of the cis double bond is 18°. As for the other cyclophanes, 1, 5, 6, and 7, the nonplanar conformation of 8 shows bond alternation of the bridging groups and quite normal benzene rings (Table III).

[2](1,4)Naphthaleno[2]paracyclo[2](1,4)naphthaleno[2]paracyclophanetetraene (9). Substitution of two of the benzene rings in cyclophane 1 by two naphthalene rings connected in the 1- and 4-positions generates the cyclophane 9. The calculated geometry
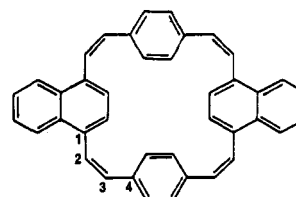
9

of the nonplanar conformation resembles that of **1a**. The molecule has C_{2v} symmetry. The completely planar form (**9b**) is 125 kcal mol^{-1} higher in energy than the nonplanar form (**9a**). The naphthalene rings show the characteristic bond alternation which is also present in the bridging groups. The torsional angle of the vinylene groups and the twist of the benzene rings from the average molecular plane are also the same as in **1a** but the naphthalene rings are tilted slightly more, ca. 40°.

[*2.2.0.2.2.0*]*Paracyclophanetetraene* (**10**). The introduction of two biphenyl units into the ring periphery of **1** to give **10** does

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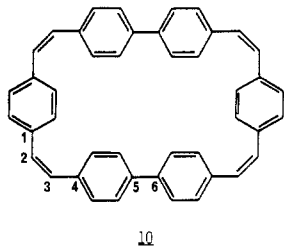
not change the bond lengths or bond angles of the nonplanar conformation **10a** as compared with **1a** but the inner protons are pushed somewhat closer together, 2.28 and 2.95 Å, respectively (Tables III and IV). The remaining benzene rings are tilted 38° in **10a** while the biphenyl groups are tilted 25°. The torsional angle between the two benzene rings in the biphenyl groups is 67°. The four bridging double bonds are almost planar with a small (8°) torsional angle. The hypothetical planar conformer **10b** is highly strained (Table I).

[*2.2.2.2.2.2*]*Paracyclophanehexaene* (**11**). Of the many different configurational isomers of [2.2.2.2.2.2]paracyclophanehex-aene, the cis,cis,trans,cis,cis,trans isomer **11** is discussed here. It


11
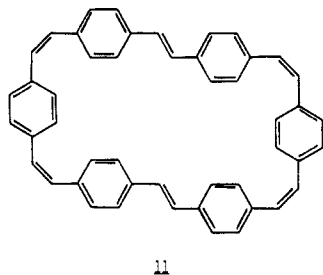
can adopt several conformations in which essentially only the orientation of the *trans*-stilbene unit differs. The π-system of the *trans*-stilbene unit can be kept relatively planar as in **11a** or **11b** or alternatively can be twisted as in **11c**. The *trans*-stilbene moieties may be kept parallel (**11b** and **11c**) or not (**11a**). The calculations predict **11a** to be the most stable conformation followed by **11b** (+0.5 kcal mol^{-1}) and **11c** (+6.2 kcal mol^{-1}). The conformation **11a** might be viewed as a two-step ladder with C_2 symmetry which apparently is slightly more favored than the twisted conformer **11b**. The latter shows a small amount of bending and torsional strain. Conformer **11c**, which also is similar to a two-step ladder, suffers from the loss of conjugation caused by the twisted *trans*-stilbene units. The two benzene rings in the *trans*-stilbene moiety are almost orthogonal but retain conjugation via the connecting double bond. The torsional angles of the latter with respect to the benzene rings are 40.5° and 36.7°, respectively. Bond lengths in **11a**, and **11c** are similar to those of **1a**. The benzene rings in **11a** are somewhat more twisted out of the average molecular plane than the benzene rings in **1a** (Table II). The *trans*-stilbene fragments of **11a** are almost planar; a small twist angle of 3° was found by the calculations.

Two planar conformations of **11** (**11d** and **11e**) were found to be highly strained (Table I).

Not only cyclophanes but also bicyclophanes[8] can be prepared by one-pot multiple Wittig reactions albeit in low yields. Bicyclophanes such as **12** and **13** are potentially interesting as host molecules for small guests if they can adopt a reasonably rigid conformation with a central cavity.


11A

11B

11C
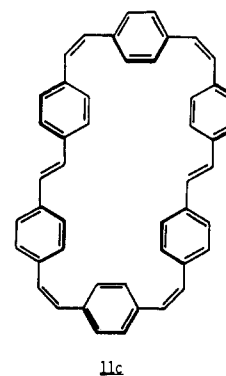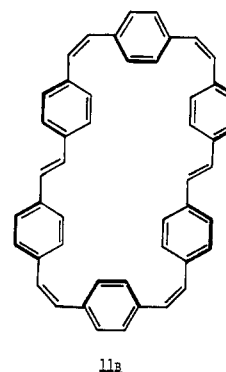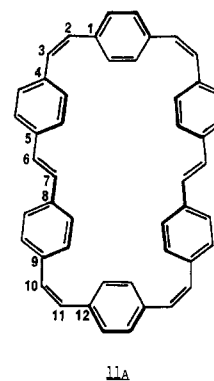
[*2.2.2.2.2.2*]*(1,3,5)$_2$(1,3)$_3$Bicyclophanehexaene* (**12**). Molecular models and ^{1}H NMR data have been used to deduce a low energy conformation of **12** with D_3 symmetry and a minimal cavity in


12
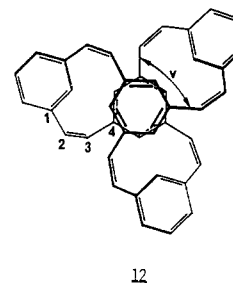
the center.[8] Force field calculations on this cage cyclophane lend support to this suggested structure. Cyclophane **12** should have D_3 symmetry. The calculated twist angle, i.e., the angle between the points of attachment by the bridges on the tri-substituted benzene rings when the molecule is viewed along the C_3 axis, is 87° (see scheme of **12**) which is smaller than the previously suggested value (110°). The distance between the tri-substituted benzene rings is 4.47 Å. The bond lengths and bond angles of **12** are normal and show no additional strain effects (Table IV). The molecule has considerable π-electron overlap despite the layered structure. The torsional angle of the cis double bonds is only 7° and the torsional angles between the vinylene groups and the tri- and meta-substituted benzene rings are also small, 37° and 23°, respectively.

[2.2.2.2.2.2]($1,3,5$)$_2$($1,4$)$_3$Bicyclophanehexaene (**13**). If the meta-substituted benzene rings in **12** are exchanged for para-substituted rings another cage cyclophane, **13**, results. This bi-

13
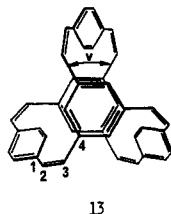
cyclophane is also of D_3 symmetry with a calculated twist angle of 65° which is somewhat larger than in the previously suggested conformation (50°). The distance between the two trisubstituted benzene rings is 6.93 Å. Compound **13** shows normal bond lengths (Table III). Bond angles in the tri-substituted rings are normal whereas the para-substituted rings are slightly elongated. The π-electron overlap in **13** is smaller than in **12**. The torsional angle of the vinylene groups is still small, ca. 9°, but the torsional angles between them and the para- and tri-substituted benzene rings are larger, 55° and 25°, respectively, as compared with **12**.

[2.2.2.2.2.2]($1,3,5$)$_4$Tricyclophanehexaene (**14**). The fascinating tricyclophane **14** or [2.2.2.2.2.2]tetrahedrophane with unsaturated bridges has yet to be synthesized. This cage cy-

14
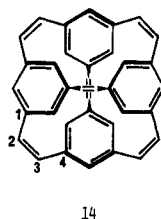
clophane consists of four identical tri-substituted benzene rings joined by six vinylene groups. The molecule is relatively strain free (Table I) with normal bond lengths and bond angles (Table III and IV). The torsional angle at the cis double bonds is small, ca. 5°. The benzene rings and the double bonds are almost orthogonal (100°), and the overall π-electron overlap is therefore small. The molecule is of T symmetry.

In all of the cage cyclophanes, **12**, **13**, and **14**, there exists a central cavity. The framework of **14** is more rigid than those of **12** and **13**. The two latter compounds are flexible cage cyclophanes. The central cavities in the minimum energy geometries are small in **12** and **13** whereas the cavity in **14** has an interesting size (50 Å^3 if the molecule is approximated as a sphere and normal van der Waals radii are assumed). Thus the cavity in **14** could possibly accommodate a guest ion or molecule of proper size whereas the bicyclophanes **12** and **13** must undergo conformational changes before complexation with guest molecules. This could

occur by reduction of the twist angle and, in the case of **13**, also by rotation of the para-substituted rings. However, the energy cost of such conformational changes can be substantial.

One particularly interesting aspect of the calculated conformations of these cage cyclophanes concerns their symmetry. New symmetry elements can only appear at maxima or minima on the total energy surface.[23] The highest possible symmetry of **12**, **13**, and **14** is D_{3h}, D_{3h}, and T_d, respectively. However, π-electron overlap between bridges and benzene rings is minimized in these conformations and thus to increase this overlap in the energy-minimized structures the symmetries are reduced to D_3, D_3, and T, respectively. Even for compound **14** a small twist resulting in loss of the mirror plane symmetry element is energetically favorable. However, the barrier to interconversion of the two mirror image forms of **14** should be small.

Conclusions

Method of Calculation. The molecular mechanics program employed in this work (MMP2) performs without difficulty on large conjugated π-systems of the kind discussed here. The computational time may in some cases tend to become rather long. The block diagonal Newton–Raphson technique works well and the convergence toward the minimized structures is reasonably rapid. The SCF π-electron module is, however, slow when dealing with such extensive π-systems.

Results. The force field calculations give no indication that effects due to perimeter conjugation are important. On the contrary, the neutral cyclophanes with unsaturated bridges all show bond alternation in the bridges and normal benzene rings. There is no alternating behavior in the series of cyclophanes 1, 5, 6, 7, and 8. Thus there is no geometrical reason for the alternating behavior in the same series on electrochemical reduction, which then has to be due to the electronic properties of the products from the reduction, i.e., the dianions.

The calculated minimum energy geometries of the cage cyclophanes **12**, **13**, and **14** are all chiral (D_3 symmetry for **12** and **13**, and T symmetry for **14**) due to the distortion of the more symmetrical conformations by increased π-electron overlap upon twist of the molecules.

(23) Pearson, R. G. "Symmetry Rules for Chemical Reactions"; Wiley: New York, 1976.