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# Structures and strain energies of small [*n*]metacyclophanes

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***Received (in Cambridge, UK) 30th September 1999, Accepted 12th January 2000***
***Published on the Web 7th March 2000***

The structures and strain energies of various derivatives of [5]- and [6]metacyclophanes have been computed by employing the density functional method (ADF). They showed a good agreement with the few available X-ray crystal structures. The structure of 9,12-dichloro[6]metacyclophane was experimentally determined at 200/233 K. Contrary to intuition, the incorporation of sp$^2$-hybridised carbon atoms in the oligomethylene chain was found to have a minor influence only on the structure and strain energy of these compounds. It is concluded that small metacyclophanes with potentially interesting interactions between unsaturated fragments in the bridge and the aromatic ring or between two aromatic rings, *e.g.* the so far elusive [1.1]metacyclophane, are realistic synthetic targets.

## Introduction

Although small [*n*]metacyclophanes ($n = 5$, 6) have been the subject of extensive research during the past three decades, accurate values of their strain energies are still not available.[1] Whenever experimental data are lacking calculations may be called upon. However, in contrast to the [*n*]paracyclophanes for which extensive high-level calculations have been reported,[2] this is not the case for the [*n*]metacyclophane series. Both molecular mechanics (MM2)[3] and semi-empirical (MNDO)[4] techniques have been applied to calculate the structures and strain energies of small [*n*]metacyclophanes ($n = 5$, 6, 7), but it was evident that both methods strongly overestimate the out of plane bending of the aromatic ring. So far, *ab initio* calculations have only been reported by Grimme *et al.*[5] on dithia[6]metacyclophanes, and by Jenneskens *et al.*[6] on [5]metacyclophane. In the latter case, the optimised structure seemed much more realistic than the MNDO structure, although the STO-3G minimal basis SCF method was employed. Therefore, a reinvestigation of the small [*n*]metacyclophanes by more sophisticated calculational methods seemed desirable. In addition, two recent developments inspired us to undertake this study. In the first place, the evolution of computational chemistry, which has been spurred by the development of ever more powerful CPU's in conjunction with the development of less time demanding calculational methods, like the DF methods, nowadays allows the calculation of large systems using fairly extended basis sets. Secondly, the recent synthesis of derivatives of [5]metacyclophane with sp$^2$-hybridised carbon atoms in the bridge[7,8] prompted us to investigate the influence of unsaturation in the bridge on the structure and strain energy of these compounds. In this way calculations may help to predict whether it is worth pursuing the synthesis of so far elusive compounds such as [1.1]metacyclophane.[9]

## Experimental

### Calculational details

All calculations presented in this paper were performed using the Amsterdam-Density-Functional (ADF) programme package.[10–12] Using PM3 structures as starting geometries, all structures were optimised without imposing symmetry constraints. The molecular orbitals were expanded in an uncontracted set of Slater-type orbitals (STO's) containing diffuse functions. The basis is of triple-$\zeta$ quality, augmented with one polarisation function: 2p on H; 3d on C, O, and Cl. The cores (C, O, 1s; Cl, 1s-2p) were treated by the frozen-core approximation.[10] The numerical integration was performed using the procedure developed by Baerends *et al.*[13,14] Energies were evaluated using the local density approximation, LDA, characterised by the electron gas exchange (Slater's potential[15] $X\alpha$ with $\alpha = 2/3$)[16] plus Becke's[17] nonlocal corrections to the exchange energy, together with the Vosko–Wilk–Nusair (VWN)[18] parametrisation with Perdew's[19] nonlocal correction to the correlation energy.

### X-Ray crystal structure determination of 9,12-dichloro[6]-metacyclophane (2b) †

As **2b** melts below room temperature, a special technique to crystallise it *in situ*, *i.e.* on the diffractometer, was applied.[20] A focused CO$_2$ laser beam was directed onto the capillary, which contained the neat sample, being flushed by cold nitrogen. Thus a molten zone was produced and moving this under computer control along the capillary, a cylindrical single crystal was produced. The data collection of the triclinic system was performed at 233 K up to $2\theta = 45°$, but when we started to collect further data at higher $2\theta$ angles, a failure of the low temperature device caused the sample to melt. Attempts to grow a new crystal under the same conditions again failed; instead we accomplished another polymorphic form with a monoclinic cell. This crystal was measured at 200 K.

In the triclinic cell (space group $P\bar{1}$) we found four molecules, *i.e.* two independent molecules in the asymmetric unit (**2ba**, **2bb**), both enantiomorphic to each other. The monoclinic cell (space group $P2_1/n$) contains four formula units, *i.e.* one independent molecule (**2bc**). Thus we have three molecules (Fig. 1) with slightly different geometries, determined by two independent experiments. Comparison of the three molecules reveals the main differences in the torsion angles of the bridges, having some effects also on the bond distances within

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† CCDC reference number 188/219. See http://www.rsc.org/suppdata/p2/a9/a907863k/ for crystallographic files in .cif format.

DOI: 10.1039/a907863k

**Table 1** Bond lengths of **2ba**, **2bb**, and **2bc**[a]

| | C11–C1 | C1–C2 | C2–C3 | C3–C4 | C4–C5 | C5–C6 | C6–C7 |
|---|---|---|---|---|---|---|---|
| **2ba** | 1.502(4) | 1.552(4) | 1.541(4) | 1.535(4) | 1.524(4) | 1.544(4) | 1.502(3) |
| **2bb** | 1.501(3) | 1.564(3) | 1.548(3) | 1.563(3) | 1.543(4) | 1.548(4) | 1.508(3) |
| **2bc** | 1.495(2) | 1.554(2) | 1.549(2) | 1.551(2) | 1.540(2) | 1.545(2) | 1.495(2) |
| Mean[b] | 1.499(3) | 1.557(4) | 1.546(3) | 1.550(7) | 1.536(5) | 1.546(2) | 1.502(3) |

[a] X-Ray crystal structure. [b] The esd's of the mean values were calculated according to common error propagation programmes.

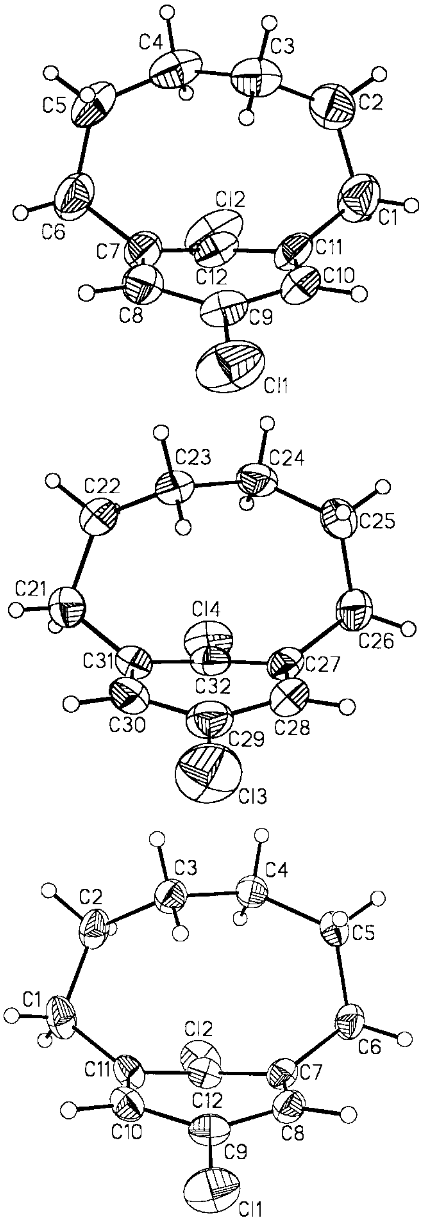

**Fig. 1** Molecular ellipsoid plots (50% probability) of the polymorphic forms of **2b** (top to bottom): **2ba**, **2bb** (the two independent molecules), and **2bc**. In this Figure, the IUPAC numbering is used.

the benzene rings. In all three molecules we found rather short distances within the benzene rings (**2ba**: 1.371–1.392 Å, **2bb**: 1.374–1.395, **2bc**: 1.374–1.393 Å, esd's for **2ba**, **2bb** 0.003 and for **2bc** 0.002 Å); in none of the cases an alternation of the bond distances within the benzene rings can be discerned. The bond distances and angles within the bridges are listed in Tables 1 and 2, together with the mean values which will be compared to the *ab initio* calculated data; Table 3 presents the angles *α*, *β*, and *γ* which describe the bending of the aromatic ring (*cf.* Fig. 2).

**2b(a,b).** $C_{12}H_{14}Cl_2$, crystal cylindric, diameter 0.3 mm, measured on a Siemens R3 diffractometer with Mo-Kα-radiation. $T = 233$ K. Cell dimensions $a = 8.9226(14)$, $b = 11.207(2)$, $c = 12.067(2)$ Å, $\alpha = 111.422(14)$, $\beta = 92.306(14)°$, $\gamma = 95.988(14)$, $V = 1113.2(3)$ Å$^3$, triclinic crystal system, $Z = 4$, $d_{calc} = 1.367$ g cm$^{-3}$, $\mu = 0.540$ mm$^{-1}$, space group $P\bar{1}$, data collection of 3042 intensities ($1.18° \le \theta \le 22.49°$), 2874 independent ($R_{merg} = 0.0419$), 2536 observed [$F_o \ge 4\sigma(F)$], empirical extinction correction parameter 0.002(2); structure solution with direct methods (Siemens-SHELXS Vers. 5.03) and refinement on $F^2$ (Siemens-SHELXL-97) (254 parameters), the hydrogen atom positions were calculated and refined as riding groups with the 1.2 fold isotropic $U$ value of the corresponding C-atoms. $R_1 = 0.0349$, $wR_2$ (all data) = 0.0898, GoF = 1.039, $w^{-1} = \sigma^2(F_o^2) + (0.002P)^2$, where $P = [\max(F_o^2) + (2F_c^2)]/3$, maximum residual electron density 0.359 e Å$^{-3}$.

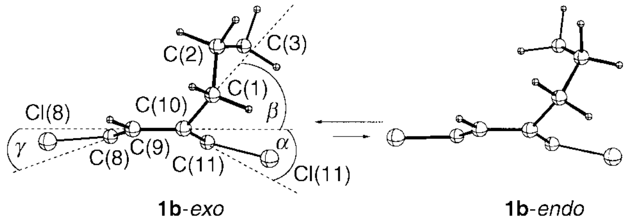

**Fig. 2** Equilibrium between the *exo*- and *endo*-conformer of **1b**. In this Figure, the IUPAC numbering is used.

**2bc.** $C_{12}H_{14}Cl_2$, crystal cylindric, diameter 0.3 mm, measured on a Siemens R3 diffractometer with Mo-Kα-radiation. $T = 200$ K. Cell dimensions $a = 9.0585(14)$, $b = 8.2339(14)$, $c = 14.660(3)$ Å, $\beta = 99.398(14)°$, $V = 1078.8(3)$ Å$^3$, monoclinic crystal system, $Z = 4$, $d_{calc} = 1.411$ g cm$^{-3}$, $\mu = 0.557$ mm$^{-1}$, space group $P2_1/n$, data collection of 1966 intensities ($2.48° \le \theta \le 24.96°$), 1884 independent ($R_{merg} = 0.0228$), 1624 observed [$F_o \ge 4\sigma(F)$], structure solution with direct methods (Siemens-SHELXS Vers. 5.03) and refinement on $F^2$ (Siemens-SHELXL-97) (127 parameters), the hydrogen atom positions were calculated and refined as riding groups with the 1.2 fold isotropic $U$ value of the corresponding C-atoms. $R_1 = 0.0314$, $wR_2$ (all data) = 0.0911, GoF = 1.068, $w^{-1} = \sigma^2(F_o^2) + (0.051P)^2 + 0.287P$ where $P = [\max(F_o^2) + (2F_c^2)]/3$, maximum residual electron density 0.406 e Å$^{-3}$.

## Results and discussion

The compounds under investigation in this study are shown. Of these, **1a**, **1b**, **2a**, **2b**, **3b**, **4b**[8] and **8**[9] have been synthesised.‡

### X-Ray crystal structures

Before discussing the calculational results, it should be pointed out that in order to check the reliability of the calculations, comparison with experimental data is essential. X-Ray crystal structures have only been determined for **1b**[24] and **3b**.[21] Surprisingly, in the case of the [6]metacyclophanes, only the X-ray crystal structure of a derivative with a $CH_2O(CH_2)_4$ bridge (**10**) is available.[22] It was for this reason that the X-ray crystal

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‡ In order to facilitate the comparison of equivalent positions in structurally different cyclophanes, a numbering scheme different from that according to IUPAC nomenclature rules has been adopted.

**Table 2** Bond angles of **2ba**, **2bb**, and **2bc**[a]

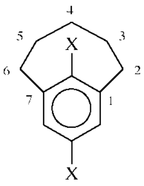
| | C11–C1–C2 | C1–C2–C3 | C2–C3–C4 | C3–C4–C5 | C4–C5–C6 | C5–C6–C7 |
|---|---|---|---|---|---|---|
| **2ba** | 109.6(2) | 120.0(2) | 118.1(2) | 120.0(2) | 120.3(2) | 108.0(2) |
| **2bb** | 109.5(2) | 118.6(2) | 117.1(2) | 119.1(2) | 118.3(2) | 107.5(2) |
| **2bc** | 110.3(1) | 117.1(1) | 115.9(2) | 119.0(1) | 118.3(1) | 108.1(1) |
| Mean[b] | 109.8(2) | 118.6(7) | 117.0(5) | 119.4(3) | 119.0(6) | 107.9(2) |

[a] X-Ray crystal structure. [b] The esd's of the mean values were calculated according to common error propagation programmes.

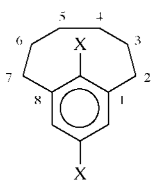
**Table 3** Deformation angles of the aromatic ring of **2ba**, **2bb**, and **2bc**[a]

| | $\alpha$ | $\beta$ | $\gamma$ |
|---|---|---|---|
| **2ba** | 19.9 | 39.9 | 8.2 |
| **2bb** | 18.2 | 40.0 | 7.4 |
| **2bc** | 20.2 | 39.2 | 9.7 |
| Mean[b] | 19.4 | 39.7 | 8.4 |

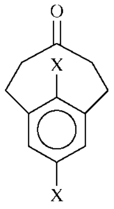
[a] X-Ray crystal structure. [b] The esd's of the mean values were calculated according to common error propagation programmes.



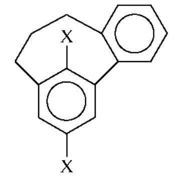
**1a** : X = H
**1b** : X = Cl



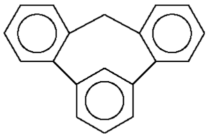
**2a** : X = H
**2b** : X = Cl



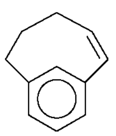
**3a** : X = H
**3b** : X = Cl



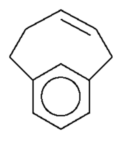
**4a** : X = H
**4b** : X = Cl



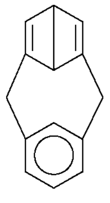
**5**



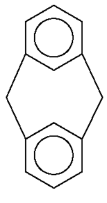
**6**



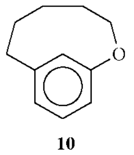
**7**



**8**



**9**



**10**

structure of **2b** was determined in order to compare it with those of **1b** and **3b** and to search for trends and sequences. The data for **2b** are presented in Fig. 1 and Tables 1, 2, and 3; the definition of the bending angles $\alpha$, $\beta$, and $\gamma$ of the aromatic ring is illustrated for **1b** in Fig. 2. An unexpected but interesting outcome of this structure determination of **2b** was its polymorphy; three polymorphic molecules **2ba**, **2bb**, and **2bc** were found in two types of crystals, but this aspect will not be further discussed in the present paper. However, as the structural data of the three polymorphs are very similar, their average values will be used for comparison with the calculational results.

Inspection of the X-ray data of **2b** reveals an important anomaly. All bond lengths appear to be rather short. This is most evident in the aromatic bond lengths (1.370–1.390 Å); all are shorter than in benzene. However, it should be pointed out that there is no indication for bond alternation. One of the most important geometrical features of a small cyclophane concerns the out of plane bending of the aromatic ring, represented by the angles $\alpha$ and $\gamma$ (Fig. 2). The mean deformation angle $\alpha$ of **2b** ($\alpha = 19.4°$) is only slightly larger than for the [6]metacyclophane derivative **10** ($\alpha = 17°$).[22] This difference seems to result largely from the chloro-substitution rather than from the differences between the bridges. The deformation of the aromatic ring is also reflected in the projected angle $\beta$ of the benzylic carbon–carbon bonds in **2b** (39.7°). Noteworthy are also the large bond angles in the bridge, implying a considerable amount of angular strain at the sp$^3$-hybridised carbon atoms.

## Calculated structures

As it has been established by $^1$H NMR spectroscopy that for many [5]metacyclophanes a conformational equilibrium between the *exo*-conformer and the *endo*-conformer exists[23] (Fig. 2), the structures of both conformers have been optimised for most compounds under investigation in this study. In order to facilitate the comparison of structural parameters, the numbering scheme shown above is adopted, although it is not in line with IUPAC nomenclature rules; note that for **3**–**9** the numbering is as shown for **1**.

Comparison of the DF optimised geometrical parameters of **1b** and **3b**, listed in Tables 4, 5, and 6, with the experimental data shows a very good agreement. All calculated bond lengths differ less than 0.02 Å from the X-ray data, whereas the difference for the bond angles is less than 2°. Even more important is the fact that the DF method is capable of predicting the deformation angles with great accuracy; all deviations are below 1°. The largest discrepancies between the calculated and experimentally determined structure are found in the case of **2b**. Although the deformation angles $\alpha$, $\beta$, and $\gamma$ agree very well, the bond lengths and bond angles differ up to 0.04 Å, and 2°, respectively. The fact that we found **2b** in two polymorphs with bond distances differing by more than 0.01 Å indicates a crucial influence of crystal packing on the geometries; this might explain the differences between the mean value of the experimental and the calculated structures (maximum deviation: 0.033 Å for the C(2)–C(3) bond). If thermal librational corrections are considered, which expand the intramolecular distances for **2ba**, **2bb**, and **2bc** by 0.009, 0.007, and 0.004 Å, respectively, the discrepancies approach the normal range for the different methodologies of structure determination.

A more detailed analysis of the calculated structures reveals several important features. In the first place, dichloro-substitution results in an increase of the deformation angles $\alpha$ and $\gamma$ (*vide infra*). In the second place, the benzene ring appears to be less bent in the *endo*-conformer. In particular in the case of **5**, these differences are fairly large ($\Delta\alpha = 4.6°$, $\Delta\beta = 5.9°$, $\Delta\gamma = 1.0°$). This was contrary to our expectation, as experiments have indicated that for most cyclophanes, with the exception of **4** and **8**, the *exo*-conformer is favoured. However, taking **1a** as an example, a decrease of the deformation of the benzene ring in the *endo* conformation appears to be accompanied by an increase of the strain in the bridge, as signalled by the slightly more elongated bond lengths. This problem will be further dealt

**Table 4** Selected bond lengths (Å) of small metacyclophanes

| | Bond length/Å | | | | | | |
|---|---|---|---|---|---|---|---|
| Compound | C1–C2 | C2–C3 | C3–C4 | C4–C5 | C5–C6 | C6–C7 | C7–C8 |
| **1a**-*exo* | 1.512 | 1.573 | 1.576 | 1.576 | 1.573 | 1.512 | — |
| **1a**-*endo* | 1.513 | 1.591 | 1.579 | 1.579 | 1.591 | 1.513 | — |
| **1b**-*exo* | 1.511 | 1.576 | 1.574 | 1.574 | 1.576 | 1.511 | — |
| **1b**-*endo* | 1.510 | 1.591 | 1.577 | 1.577 | 1.591 | 1.510 | — |
| **1b**-*exo*[a,b] | 1.506 | 1.569 | 1.566 | 1.566 | 1.569 | 1.506 | — |
| **2a** | 1.509 | 1.590 | 1.564 | 1.572 | 1.558 | 1.564 | 1.509 |
| **2b** | 1.506 | 1.590 | 1.565 | 1.571 | 1.558 | 1.567 | 1.507 |
| **2b**[a,c,d] | 1.499 | 1.557 | 1.546 | 1.550 | 1.536 | 1.546 | 1.502 |
| **3a**-*exo* | 1.519 | 1.573 | 1.563 | 1.563 | 1.573 | 1.519 | — |
| **3a**-*endo* | 1.522 | 1.587 | 1.570 | 1.570 | 1.587 | 1.522 | — |
| **3b**-*exo* | 1.516 | 1.577 | 1.566 | 1.566 | 1.577 | 1.516 | — |
| **3b**-*endo* | 1.517 | 1.590 | 1.566 | 1.566 | 1.590 | 1.517 | — |
| **3b**-*endo*[a,e] | 1.516 | 1.578 | 1.547 | 1.547 | 1.578 | 1.516 | — |
| **4a**-*exo* | 1.483 | 1.438 | 1.566 | 1.579 | 1.575 | 1.513 | — |
| **4a**-*endo* | 1.491 | 1.436 | 1.553 | 1.585 | 1.585 | 1.519 | — |
| **4b**-*exo* | 1.482 | 1.436 | 1.557 | 1.577 | 1.575 | 1.514 | — |
| **4b**-*endo* | 1.492 | 1.434 | 1.550 | 1.581 | 1.584 | 1.516 | — |
| **4b**-*endo*[a,f] | 1.498 | 1.421 | 1.549 | 1.583 | 1.578 | 1.511 | — |
| **5**-*exo* | 1.485 | 1.441 | 1.569 | 1.569 | 1.441 | 1.485 | — |
| **5**-*endo* | 1.493 | 1.435 | 1.554 | 1.554 | 1.435 | 1.493 | — |
| **6**-*exo* | 1.472 | 1.362 | 1.551 | 1.581 | 1.576 | 1.514 | — |
| **6**-*endo* | 1.483 | 1.361 | 1.550 | 1.585 | 1.583 | 1.522 | — |
| **7**-*exo* | 1.517 | 1.542 | 1.360 | 1.544 | 1.590 | 1.516 | — |
| **7**-*endo* | 1.521 | 1.552 | 1.361 | 1.545 | 1.581 | 1.521 | — |
| **8** | 1.525 | 1.533 | 1.557 | 1.557 | 1.533 | 1.525 | — |
| **9** | 1.563 | 1.563 | 1.409 | 1.409 | 1.563 | 1.563 | — |

[a] X-Ray crystal structure. [b] Ref. 24. [c] Mean values. [d] This work. [e] Ref. 21. [f] Ref. 31.

**Table 5** Selected bond angles of small metacyclophanes

| | Bond angle (deg) | | | | | |
|---|---|---|---|---|---|---|
| Compound | C1–C2–C3 | C2–C3–C4 | C3–C4–C5 | C4–C5–C6 | C5–C6–C7 | C6–C7–C8 |
| **1a**-*exo* | 106.8 | 121.1 | 122.5 | 121.1 | 106.8 | — |
| **1a**-*endo* | 108.8 | 120.3 | 119.9 | 120.3 | 108.8 | — |
| **1b**-*exo* | 106.0 | 121.4 | 122.8 | 121.4 | 106.0 | — |
| **1b**-*endo* | 109.0 | 120.4 | 120.4 | 120.4 | 109.0 | — |
| **1b**-*exo*[a,b] | 104.7 | 121.9 | 122.2 | 121.9 | 104.7 | — |
| **2a** | 110.6 | 118.6 | 117.3 | 118.5 | 117.6 | 109.0 |
| **2b** | 109.8 | 118.6 | 117.0 | 119.4 | 119.0 | 107.9 |
| **2b**[a,c,d] | 109.6 | 120.0 | 118.0 | 119.9 | 120.3 | 108.0 |
| **3a**-*exo* | 105.3 | 115.6 | 122.5 | 115.6 | 105.3 | — |
| **3a**-*endo* | 108.0 | 115.9 | 120.9 | 115.9 | 108.0 | — |
| **3b**-*exo* | 105.4 | 118.8 | 122.3 | 118.8 | 105.4 | — |
| **3b**-*endo* | 108.1 | 116.1 | 121.1 | 116.1 | 108.1 | — |
| **3b**-*endo*[a,e] | 107.3 | 115.7 | 120.7 | 115.7 | 107.3 | — |
| **4a**-*exo* | 117.6 | 129.7 | 128.0 | 119.7 | 104.9 | — |
| **4a**-*endo* | 113.5 | 124.3 | 122.0 | 118.1 | 108.9 | — |
| **4b**-*exo* | 117.6 | 129.7 | 127.9 | 120.3 | 104.8 | — |
| **4b**-*endo* | 113.5 | 124.5 | 121.9 | 118.5 | 109.2 | — |
| **4b**-*endo*[a,f] | 112.6 | 124.2 | 121.0 | 118.5 | 108.5 | — |
| **5**-*exo* | 117.9 | 130.0 | 132.3 | 130.0 | 117.9 | — |
| **5**-*endo* | 113.2 | 123.2 | 124.9 | 123.2 | 113.2 | — |
| **6**-*exo* | 119.7 | 134.4 | 127.6 | 121.5 | 105.8 | — |
| **6**-*endo* | 115.4 | 127.6 | 123.5 | 117.8 | 109.8 | — |
| **7**-*exo* | 111.5 | 134.9 | 136.8 | 121.8 | 104.2 | — |
| **7**-*endo* | 105.6 | 133.8 | 136.6 | 120.2 | 109.1 | — |
| **8** | 105.4 | 130.3 | 118.3 | 130.3 | 105.4 | — |
| **9** | 104.8 | 114.2 | 119.3 | 114.2 | 104.8 | — |

[a] X-Ray crystal structure. [b] Ref. 24. [c] Mean values. [d] This work. [e] Ref. 21. [f] Ref. 31.

with in the discussion of the strain energy of these compounds. In order to address the question how incorporation of one or more sp$^2$-hybridised carbon atoms in the bridge influences the structure of a cyclophane, the most important features of all structures will be briefly reviewed. Kinetic experiments have shown that **3b** is considerably less reactive than **1b** in Diels–Alder reactions,[21] yet the benzene rings are almost equally deformed (**3b**-*exo*: $\alpha + \gamma = 38°$ *versus* **1b**-*exo*: 38.5°). Apparently, the influence of the incorporation of an sp$^2$-hybridised carbon atom on the bending of the benzene ring is negligible. In the case of **4b**, NMR experiments have shown that it exists exclusively in the *endo*-conformation.[8] Comparison of the structures of **4b**-*endo* and **1b**-*exo* reveals that benzoannelation results in a minor increase of total bending (**4b**-*endo*: $\alpha + \gamma = 40.9°$ *versus* **1b**-*exo*: 40.1° (exptl 38.8°)[24]). Nevertheless, **4b**-*endo* turned out to be approximately 10 times more reactive

**Table 6** Deformation angles of small cyclophanes

| Compound | Deformation angle (°) $\alpha$ | $\beta$ | $\gamma$ |
|---|---|---|---|
| **1a**-*exo* | 23.2 | 42.7 | 10.2 |
| **1a**-*endo* | 21.5 | 43.0 | 8.9 |
| **1b**-*exo* | 28.0 | 47.4 | 12.0 |
| **1b**-*endo* | 27.2 | 45.8 | 10.9 |
| **1b**-*exo*[a,b] | 26.8 | 48.0 | 12.0 |
| **2a** | 14.7 | 34.2 | 6.3 |
| **2b** | 19.5 | 39.3 | 8.0 |
| **2b**[a,c,d] | 19.4 | 39.7 | 8.4 |
| **3a**-*exo* | 22.4 | 43.2 | 9.7 |
| **3a**-*endo* | 21.3 | 41.9 | 8.9 |
| **3b**-*exo* | 27.3 | 47.7 | 11.5 |
| **3b**-*endo* | 26.6 | 46.5 | 11.2 |
| **3b**-*endo*[a,e] | 26.6 | 46.3 | 11.9 |
| **4a**-*exo* | 23.9 | 44.5 | 10.0 |
| **4a**-*endo* | 22.3 | 42.1 | 9.5 |
| **4b**-*exo* | 29.8 | 47.9 | 12.5 |
| **4b**-*endo* | 28.2 | 45.5 | 12.4 |
| **4b**-*endo*[a,f] | 26.8 | 45.2 | 12.1 |
| **5**-*exo* | 27.2 | 46.0 | 10.9 |
| **5**-*endo* | 22.7 | 40.1 | 10.0 |
| **6**-*exo* | 25.1 | 42.1 | 10.1 |
| **6**-*endo* | 23.5 | 41.0 | 9.7 |
| **7**-*exo* | 24.6 | 43.5 | 10.9 |
| **7**-*endo* | 24.5 | 44.1 | 10.5 |
| **8** | 20.2 | 41.0 | 9.2 |
| **9** | 25.4 | 47.6 | 13.5 |

[a] X-Ray crystal structure. [b] Ref. 24. [c] Mean values. [d] This work. [e] Ref. 21. [f] Ref. 31.

than **1b**-*exo*. Thus, we are forced to abandon our earlier hypothesis[4] that the reactivity of a [5]metacyclophane is related exclusively to the deformation of its benzene ring.

Another important question is whether a relationship exists between the total bridge length and the bending of the benzene ring. Intuitively, one would assume that as the incorporation of an unsaturated segment in the bridge leads to a shortening of that bridge, this would result in an increase of the deformation of the benzene ring. At first glance this seems indeed to be the case. From **1a**-*endo via* **4a**-*endo* to **5a**-*endo*, the bridge length ($\Sigma d$(C–C)) gradually decreases from 9.25 Å to 8.98 Å while at the same time, the total bending increases from 30.1° to 32.6°. However, cyclophanes **6**-*exo* ($\Sigma d$(C–C) = 9.056 Å) and **7**-*exo* ($\Sigma d$(C–C) = 9.069 Å) do not fit into this picture. Clearly, the idea that the bending of the benzene ring correlates with the bridge length is an oversimplification; we will show in a later part of this paper that the strain introduced by a shortening of the bridge is in part compensated by a reduction of the angular strain. Furthermore, these systems respond by elongating the $sp^2$–$sp^2$ bond which is part of the bridge. As anticipated, the softer aromatic bonds in **4** and **5** are more apt to adjust themselves to the strained situation than the localised double bonds in **6** and **7**. Remarkably, the strongly elongated bonds in **4** and **5** (up to 1.44 Å) do not affect the other aromatic bonds which have normal values (1.395–1.402 Å).

Next we consider the occurrence of conjugation in **4**, **5**, and **6**, taking **4b** as an example. Interestingly, the dihedral angles between the aromatic rings, which determine the extent to which conjugation may occur, differ considerably for both conformations. In the *exo*-conformation of **4b**, these angles amount to 37.1°, −150.8°, −118.3° and 53.9°, compared to 48.9°, −129.1°, 103.6° and 78.4° in the *endo*-conformation. Hence, conjugation is expected to be stronger in the *exo*-conformation. It should be pointed out that from the UV-spectrum of **4b**-*endo*, it was concluded that there was little biphenyl-type conjugation.[8]

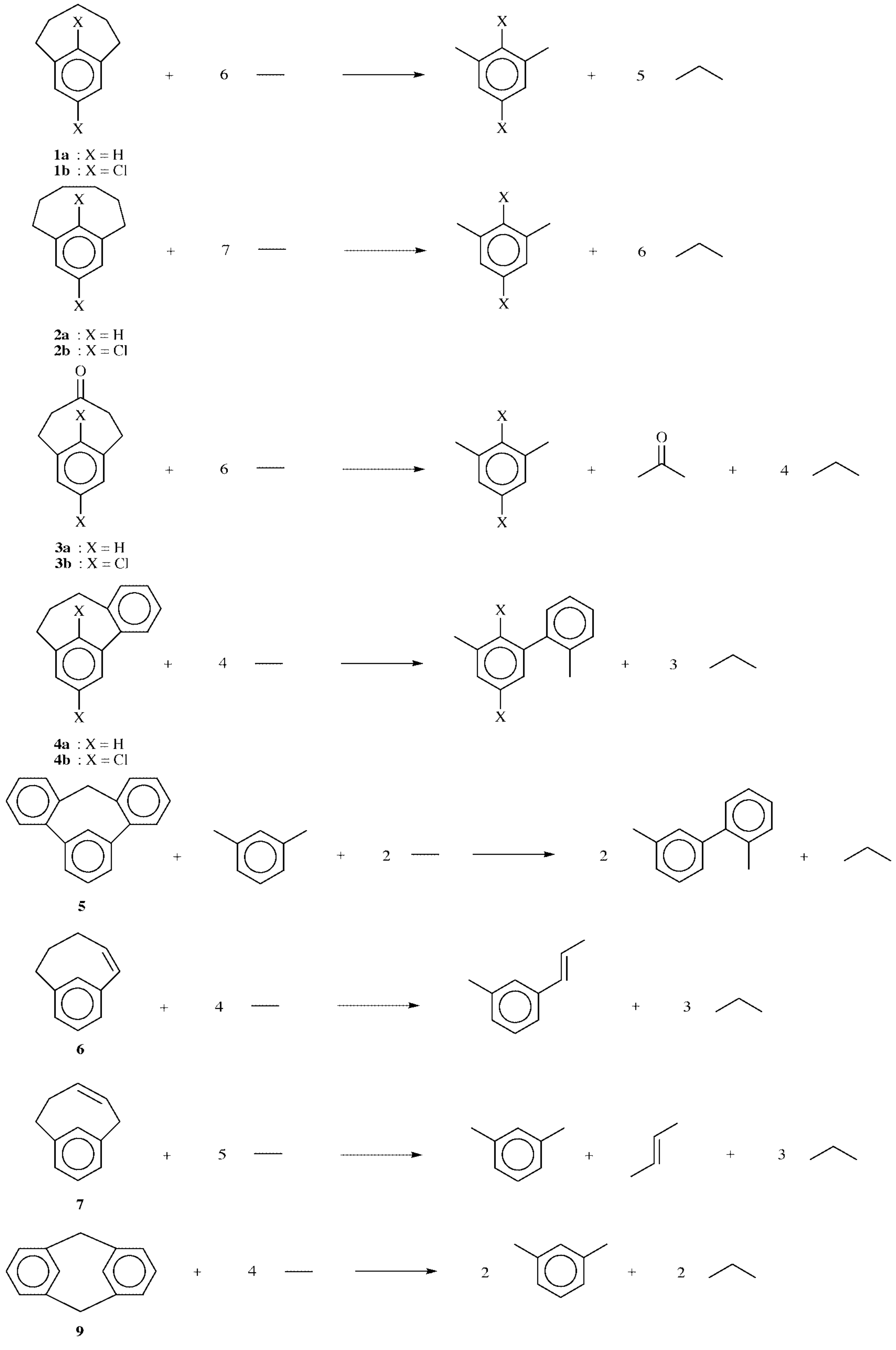
Finally, a brief description of compounds **8** and **9** is presented. For both compounds only the much more stable *endo*-conformation has been computed. Remarkably, **8** is less bent than the parent compound **1a** ($\alpha = 20.2°$, $\gamma = 9.2°$). Another important feature is the short interannular distance $d$ (2.78 Å); in **9**, this distance is even shorter (2.47 Å). This is considerably less than the corresponding distance in [2.2]metacyclophane (2.63 Å).[25] In an attempt to diminish the undoubtedly strong repulsive interannular interaction, compound **9** responds by a further bending of the benzene ring ($\alpha = 25.4°$) and a lengthening of the bridging bonds (1.563 Å).

## Conformational equilibria

NMR experiments have indicated that the parent compound **1a** exclusively exists in the *exo*-conformation.[1] In the case of **1b**, also the less stable *endo*-conformer is observed in minor quantities (*exo*:*endo* = 80:20).[23] From the temperature dependence of the $^1$H NMR spectra, the thermodynamic equilibrium parameters were deduced ($\Delta\Delta H = 3.1$ kJ mol$^{-1}$, $\Delta\Delta S = 2.1$ J mol$^{-1}$ K$^{-1}$).[21] It is gratifying that the relative stabilities of the conformers of **1a** are well described by the DFT calculations of the homodesmotic reactions depicted in Scheme 1 ($\Delta\Delta E = 16.1$ kJ mol$^{-1}$; Table 7). In addition, the influence of chlorine substituents on the conformer stabilities in **1b** is well reproduced. From **1a** to **1b**, the energy difference between the *exo*- and *endo*-conformer decreases from 16.1 to 7.3 kJ mol$^{-1}$. The latter value and the experimental one ($\Delta\Delta H = 3.1$ kJ mol$^{-1}$) are in satisfactory agreement; it is evident that chlorine substituents destabilise the *exo*-conformer more than the *endo*-conformer (*vide infra*). The same holds for all other cyclophanes investigated here. However, subtle differences are observed. For instance, in the case of **3a** and **3b**, the energy differences between the conformers amount to 20.2 and 5.8 kJ mol$^{-1}$, respectively. Hence, the chlorine substituents destabilise the *exo*-conformer by 14.4 kJ mol$^{-1}$ relative to the *endo*-conformer. Even more important is the observation that the calculations correctly predict the *endo*-conformers of **4a** and **4b** to be more stable than the *exo*-conformers. In the case of **4b**, an NMR study confirmed that it occurs exclusively as the *endo*-conformer.[8] Again the *exo*-conformer is destabilised by chlorine substituents more strongly (**4a**: $\Delta\Delta E = 9.7$ kJ mol$^{-1}$; **4b**: $\Delta\Delta E = 14.2$ kJ mol$^{-1}$). For **5**, the energy difference between both conformers increases up to 45 kJ mol$^{-1}$ in favour of the *endo*-isomer. The origin of this phenomenon may be found in the bond angles of the bridge. In particular the angle C3–C4–C5, which is forced to open up from 124.9° in **5**-*endo* to 132.3° in **5**-*exo*, seems to be responsible for the instability of the latter. Although the smaller dihedral angles between the aromatic rings in the *exo*-conformers of **4** and **5** allow better conjugation, the concomitant energy gain appears to be too small to overcome the additional angle strain. Somewhat surprisingly, the *exo*-conformer of **6** is found to be slightly lower in energy than the *endo*-conformer. A detailed analysis of the geometrical parameters revealed only minor differences and thus did not provide an explanation for this observation. In the case of **8** and **9**, only the *endo*-conformers have been considered, as preliminary PM3 calculations indicated that their *exo*-conformers were much higher in energy.

## Homodesmotic strain energies

As mentioned before, experimental data on the strain energies (SE) of [5]- and [6]metacyclophanes are lacking. Thus, calculations constitute the only source of information. Over the years, various methods have been employed. MM2 calculations, which define the SE of a compound as the energy difference between the calculated heat of formation and that obtained by strain-free group increments, provided values of 184 and 117 kJ mol$^{-1}$ for **1a** and **2a**, respectively.[3] In the case of MNDO calculations, the SE's have been evaluated by several approaches. Comparison of the calculated heat of formation with those derived from Benson's group increments yielded a value of 192.9 kJ mol$^{-1}$ for **1a**.[4] A comparable SE was obtained by



**1a** : X = H
**1b** : X = Cl

**2a** : X = H
**2b** : X = Cl

**3a** : X = H
**3b** : X = Cl

**4a** : X = H
**4b** : X = Cl

**5**

**6**

**7**

**9**

**Scheme 1** Homodesmotic reaction schemes.

defining the strain energy as the energy difference between [5]metacyclophane and its ortho isomer benzocycloheptene.[26] However, the SE's thus obtained are considerably lower than those derived from STO-3G calculations *via* the homodesmotic reaction scheme depicted in Scheme 1. In this case, the SE is defined as the enthalpy of a reaction in which the strained compound is converted to products which are strain-free, while the term homodesmotic denotes that both reactants and products contain the same number of each type of carbon–carbon bond ($C_{sp^3}$–$C_{sp^3}$; $C_{sp^3}$–$C_{sp^2}$; *etc.*) as well as the same number of each type of carbon atom. In the latter case the term "type" denotes (carbon) atoms with the same hybridisation state and the same number of hydrogen atoms attached to them. Because the homodesmotic reaction scheme has gained wide acceptance for evaluating SE's, we have constructed the following homodesmotic reactions (Scheme 1).

From the results summarised in Table 7, it is obvious that the differences in SE between the various [5]metacyclophanes are

**Table 7** Strain energies (SE/kJ $mol^{-1}$) and partitioning into the different components

| Compound | SE (HD)/ kJ $mol^{-1}$ | SE (sum)/ kJ $mol^{-1}$ | SE (rep)/ kJ $mol^{-1}$ | SE (bb)/ kJ $mol^{-1}$ | SE (br)/ kJ $mol^{-1}$ | SE (bb)/ SE (sum) |
|---|---|---|---|---|---|---|
| **1a**-*exo* | 174.2 | 163.8 | 10.4 | 118.8 | 44.9 | 0.726 |
| **1a**-*endo* | 190.2 | 166.1 | 24.1 | 105.8 | 60.3 | 0.637 |
| **1b**-*exo* | 182.4 | 181.0 | 1.4 | 135.2 | 45.8 | 0.747 |
| **1b**-*endo* | 189.7 | 177.7 | 11.9 | 117.5 | 60.2 | 0.661 |
| **2a** | 121.1 | 104.2 | 16.9 | 50.6 | 53.5 | 0.486 |
| **2b** | 128.1 | 119.1 | 9.0 | 64.6 | 54.5 | 0.542 |
| **3a**-*exo* | 167.0 | 150.8 | 16.1 | 116.6 | 34.3 | 0.773 |
| **3a**-*endo* | 187.2 | 151.3 | 35.9 | 101.2 | 50.1 | 0.669 |
| **3b**-*exo* | 186.3 | 171.6 | 14.7 | 130.8 | 40.7 | 0.763 |
| **3b**-*endo* | 192.1 | 167.6 | 24.6 | 116.7 | 50.9 | 0.696 |
| **4a**-*exo* | 186.8 | 176.0 | 10.8 | 126.8 | 49.2 | 0.720 |
| **4a**-*endo* | 177.1 | 152.9 | 24.2 | 115.9 | 37.0 | 0.758 |
| **4b**-*exo* | 194.8 | 195.0 | −0.2 | 147.1 | 47.9 | 0.754 |
| **4b**-*endo* | 180.6 | 167.1 | 13.5 | 131.3 | 35.8 | 0.786 |
| **5**-*exo* | 217.2 | 213.4 | 3.8 | 143.2 | 70.3 | 0.671 |
| **5**-*endo* | 172.2 | 157.6 | 14.6 | 124.6 | 33.0 | 0.791 |
| **6**-*exo* | 200.6 | 182.4 | 18.2 | 131.6 | 50.8 | 0.721 |
| **6**-*endo* | 204.0 | 169.5 | 34.5 | 120.4 | 49.1 | 0.710 |
| **7**-*exo* | 202.1 | 179.6 | 22.5 | 130.2 | 49.3 | 0.725 |
| **7**-*endo* | 211.1 | 182.2 | 28.9 | 131.3 | 50.9 | 0.720 |
| **8** | 457.5 | — | — | 97.8 | — | — |
| **9** | 354.9 | — | — | 130.4 | — | — |

small. SE's fall in the range of 167–202 kJ $mol^{-1}$. For **1a**-*exo*, a SE of 174 kJ $mol^{-1}$ is obtained which is in close agreement with the previously reported MM2 and semi-empirical values.[3,4] The same holds for **2a** for which a value of 121 kJ $mol^{-1}$ was derived. Although experimental studies have indicated that chlorine substituents increase the thermal stability of a cyclophane and diminish its reactivity, these calculations show that chlorines lead to an increase of the SE which probably originates mainly from a repulsion between the chlorine atom attached to C11 and methylene groups in the bridge. Apparently, there is no simple direct relationship between the SE of a [5]metacyclophane and its reactivity. The increase of the SE brought about by chlorine substituents amounts to 8.3 kJ $mol^{-1}$ and 7.0 kJ $mol^{-1}$ for **1a**-*exo*→**1b**-*exo* and **2a**→**2b**, respectively. Against this background, the increase in SE from **3a**-*exo*→**3b**-*exo* seems to be exceptionally large (19.3 kJ $mol^{-1}$). This is probably caused by a repulsion between the lone pairs on chlorine and oxygen. The strain of **3a**-*exo* is slightly less than that of **1a**-*exo*. This confirms our earlier perception that the incorporation of a carbonyl group in the bridge lowers the SE of a [5]metacyclophane. Although the slightly decreased bridge length tends to increase the SE, this is overcompensated by the inherently larger angle around the $sp^2$-hybridised carbon atom in the bridge. However, the calculated SE of **3b**-*exo*, which is *higher* than that of **1b**-*exo*, shows that the relationship between the reactivity and the homodesmotic SE is more intricate as **3b** is *less* reactive than **1b**. For the benzo-annelated cyclophanes **4a**-*endo* and **4b**-*endo*, strain energies of 177.1 and 180.6 kJ $mol^{-1}$, respectively, were found. This is to be contrasted with semi-empirical PM3 calculations which predicted an increase of the SE of about 18 kJ $mol^{-1}$.[8] The SE of **4b**-*endo* is even smaller than that of **1b**-*endo* by 9.1 kJ $mol^{-1}$. This may be explained by invoking the same factors as in the case of **3**: the serious angle strain in the five-membered bridge as well as transannular repulsions are relieved by incorporation of (2!) $sp^2$-hybridised carbon atoms; apparently, this overcompensates the shortening of the bridge-length caused by replacing a unit (3 $sp^3$–$sp^3$-bonds) by an aromatic ring (one $sp^2$–$sp^2$-bond and 2 $sp^2$–$sp^3$-bonds). The influence of a second benzo-annelation on the SE also turns out to be negligible. The cyclophanes **6** and **7** behave differently: incorporation of a single aliphatic double bond in the bridge increases SE by about 25 kJ $mol^{-1}$. Apparently, the decrease of the angular strain cannot counterbalance the increase of SE arising from the shorter bridge length. One should keep in mind that the double bond in **6** and **7** is less apt to elongate than the aromatic double bond in **4** and **5** (*vide supra*).

Finally, the cyclophanes **8** and **9** will be discussed briefly. As shown in Table 7, the SE of **9** (355 kJ $mol^{-1}$) is about twice that of **1a**. Even more important is the observation that **8**, which has been synthesised,[9] is about 103 kJ $mol^{-1}$ higher in energy than **9**. This indicates that it is worth pursuing the synthesis of **9**, although undoubtedly many experimental difficulties will have to be overcome during this work. In principle, **8** should be convertible into **9** by heat or irradiation, by analogy to the methodology applied for small paracyclophanes.[1,27]

## Partitioning of the strain energy

One of the disadvantages of the above-mentioned approach is that the SE(HD) obtained from homodesmotic reactions includes the strain energy which arises from deformations in the bond lengths and angles as well as that from non-bonded interactions. Clearly, this confuses the analysis of the influence of $sp^2$-hybridised carbon atoms in the bridge on the SE of a small metacyclophane. In order to circumvent this problem, we have disconnected the bridge and the benzene ring of a cyclophane while maintaining the original geometry. Hydrogen atoms were then placed at the resulting free valencies at a distance of 1.092 Å ($C_{sp^2}$–H) and 1.102 Å ($C_{sp^3}$–H), respectively. Separate single point calculations were performed on both the bridge and the benzene ring frozen in the conformation calculated for the corresponding cyclophane. Comparison of the energies obtained in this way with the energies of fully optimised strain-free reference compounds, *e.g.* pentane or benzene, provides both the SE of the bridge (SE(br)) and of the bent benzene ring (SE(bb)). The sum of the strain energy of the two components (SE(br) + SE(bb)) is denoted as SE(sum). The validity of this approach may be assessed by comparison of SE(sum) with the homodesmotic strain energy SE(HD). If the former method is warranted, both SE's should have roughly comparable values. It is reassuring to find that this is indeed the case. Thus, a SE(sum) of 163.8 kJ $mol^{-1}$ was derived for **1a**-*exo* compared to a SE(HD) of 174.2 kJ $mol^{-1}$. As anticipated, the SE(sum) is slightly lower than SE(HD) as the interaction between the bridge and the benzene ring, which is usually of a repulsive nature, is neglected in the former. This repulsion energy, denoted as SE(rep), may be derived by subtracting SE(sum) from SE(HD).

From the results summarised in Table 7, it also becomes clear that the SE largely resides in the benzene ring (118.8 *versus* 44.9 kJ mol$^{-1}$). This affirms our earlier hypothesis that in a simple mechanical picture, the benzene ring acts as a soft spring absorbing a larger fraction of the energy by out of plane bending, while the bridge may be considered as a more rigid clamp.[4] A useful parameter to interpret the distribution of the SE is the ratio between SE(bb) and SE(sum). In the case of **1a**-*exo*, this ratio is about 0.726, in close agreement with the STO-3G value of 0.69,[6] despite the quantitative difference in SE(sum). For **1a**-*endo*, the value of SE(bb) (105.8 kJ mol$^{-1}$) is lower which confirms what the geometrical parameters ($\alpha$ and $\gamma$) had already suggested (*vide supra*; Table 6). However, this decrease of SE(bb) is almost counterbalanced by an increase of the SE(br) (**1a**-*exo*: 44.9; **1a**-*endo*: 60.3 kJ mol$^{-1}$). The SE(sum) signals that in the absence of SE(rep), the *exo*-conformer would be favoured by only 2.3 kJ mol$^{-1}$. Perhaps not surprisingly, the decisive factor turns out to be SE(rep) (13.7 kJ mol$^{-1}$) which accounts almost completely for the difference in SE(sum). This energy difference arises from the strong repulsion, in the *endo* conformation, between the aromatic ring and the methylene groups in the bridge.

Next we consider the influence of chlorine substituents. Introducing chlorine atoms tends to increase the SE(bb), whereas SE(br) is hardly affected. Surprisingly, at the same time SE(rep) drops. The same effect is observed for all other cyclophanes in this study. Focusing our attention on **2b**, we notice that the values of SE(bb) and SE(br) confirm what we already guessed from the geometrical features of the X-ray crystal structure; the bridge of **2b** contains a relatively larger part of the total SE than in **1b**. The small ratio of 0.486 between SE(bb) and SE(sum) demonstrates that the SE is almost equally divided between the bridge and the benzene ring. The difference between the energy distribution in **1** and **2** may find its origin in the increased eclipsing strain of the 9-membered ring in the latter. In line with this, the value of SE(br) (53.5 kJ mol$^{-1}$) is even larger than that of **1a**-*exo* (44.9 kJ mol$^{-1}$).

The ketocyclophane **3a**-*exo* displays several important features. First, we notice that the SE(br) is indeed lowered by the incorporation of an sp$^2$-hybridised carbon atom (34.3 *versus* 44.9 kJ mol$^{-1}$). It is worth mentioning that the repulsive term SE(rep) is exceptionally large in the *endo*-conformer. Chlorine substituents change this picture only slightly. Just like in the case of **3a**-*exo*, the SE(sum) of **3b**-*exo* turns out to be smaller than for **1b**-*exo*. However, when SE(rep) is taken into account, the order of stability reverses. Therefore, one may conclude that SE(sum) probably gives a more accurate picture of the inherent influence of an sp$^2$-carbon atom in the bridge. Finally, it should be pointed out that the increased rigidity of the bridge results in a shift of SE from the bridge to the benzene ring. This is indicated by the fraction of SE located in the benzene ring which increases from 0.726 for **1a** to 0.773 for **3a**.

Focusing our attention on the most stable conformers of **4**, we notice that SE(sum) for **4a**-*endo* is considerably lower than for **1a**-*exo* (152.9 *versus* 163.8 kJ mol$^{-1}$). On the other hand the SE(sum) of **4a**-*exo* is considerably larger (176 kJ mol$^{-1}$) as in this case both SE(br) and SE(bb) are increased. Although the repulsion term is smaller, this is insufficient to compensate for the increased SE(sum). Similarly, in the chlorinated series, **4b**-*endo* is less strained than **1b**-*exo*. This intriguing outcome seems to contradict the observation that **4b**-*endo* is about 10 times more reactive in Diels–Alder reaction than **1b**-*exo*. In addition, it should be pointed out that we have previously demonstrated that, with regard to the differences in reactivity, electronic effects must be ruled out.[8] At present, we are therefore inclined to believe that the differences in reactivity are related to the overall energy gained in the reaction which will have a strong influence on the activation barrier. In order to substantiate this proposition, the energies of the Diels–Alder adducts would have to be evaluated which is at present beyond our computational possibilities.

The trends described above persist in the case of **5**. A second benzo-annelation reduces the SE(br) in **5**-*endo* to 33 kJ mol$^{-1}$. At the same time, the SE(bb) increases to 124.6 kJ mol$^{-1}$. The net outcome of the second benzo-annelation is an SE(sum) of 157.6 kJ mol$^{-1}$. A comparison of the ratios between SE(bb) and SE(tot) seems to suggest a relationship between the rigidity of the bridge and the distribution of the SE. This may be illustrated by the following series: from **1a** to **5**, the ratio SE(bb): SE(sum) monotonously increases from 0.726 to 0.791. This again gives support to the hypothesis that the benzene ring acts as a softer spring which absorbs more energy than the bridge.

Unlike the compounds described so far, the incorporation of an aliphatic double bond in the bridge increases the SE substantially. As described in the previous section, the SE(HD) of **6**-*exo* was calculated to amount to 200.6 kJ mol$^{-1}$. The SE(sum) of 182 kJ mol$^{-1}$ which is about 19 kJ mol$^{-1}$ higher than for **1a**-*exo* nicely fits into this picture. The increase of the SE(bb) comprises the major part of this increase. Although SE(sum) is much smaller in the *exo*-conformer, the large value of SE(rep) again proves to be the decisive factor. The situation is similar for **7**; again the *exo*-conformer is favoured as a result of the lower SE(rep). However, the differences between the conformers are less pronounced.

## Resonance energy of bent benzene rings

One of the key issues in the investigation of small cyclophanes has been whether the aromatic ring could be forced to give up its bond delocalisation on bending. Current knowledge suggests that [5]metacyclophanes are fully delocalised.[1,24] From our calculations it is clear that **1a** is fully delocalised without bond alternation. This is in agreement with the X-ray crystal structure of **1b**.[24] In addition, NMR studies on the anisotropy of the magnetic susceptibility suggest that according to this criterion, **1a** is possibly even slightly more aromatic than benzene itself.[28] On the other hand, [5]metacyclophanes show a high reactivity, unprecedented for normal aromatics. Although this behaviour was at first considered to be the consequence of a Kékulé-type cyclohexatriene-like bond fixation of **1a**, it has since been recognised to result mainly from the high ground-state energy of the compound.[1] The seemingly paradoxical observation that the strain energy of **1a** (about 180 kJ mol$^{-1}$) exceeds the aromatic resonance energy (84–151 kJ mol$^{-1}$) has led to vigorous controversy. However, it should be kept in mind that if bond localisation would occur in **1a**, resulting in a bridged cyclohexa-1,3,5-triene, this would still contain a strained *trans* double bond which violates Bredt's rule. Therefore, it is more appropriate to employ an analysis first applied by Baird and Dewar to planar benzene,[29] in which the loss of resonance energy is evaluated by comparing the energy of a bent benzene ring with that of a correspondingly bent, but localised cyclohexa-1,3,5-triene. For this purpose, single point calculations were carried out for cyclohexa-1,3,5-triene with $d(\text{C=C}) = 1.337$ Å and $d(\text{C–C}) = 1.483$ Å. For benzene, an additional resonance energy for the delocalised species of 39.7 kJ mol$^{-1}$ was obtained in accord with the previously reported value.[29] For [6]metacyclophane (**2a**) and [5]metacyclophane (**1a**), this value decreases negligibly to 38.4 and 36.9 kJ mol$^{-1}$, respectively.

These results imply that even strongly bent benzene rings are delocalised to almost the same extent as benzene itself. Although this observation seems surprising at first, several arguments can be put forth to explain them. First, as mentioned above, if a bent benzene ring were to localise, this would result in the formation of cyclohexa-1,3,5-triene which still contains a strained bridgehead double bond violating Bredt's rule; consequently the energetic situation will hardly improve. Secondly, as first pointed out by Shaik and Hiberty *et al.*,[30] the σ-frame is the dominant energetic factor in determining the delocalisation of benzene rather than the π-system. Our previous results[1,4] and those described above support this view.

## Conclusions

We have demonstrated that the DF-method is able to provide accurate geometries for highly bent cyclophanes. Homodesmotic reaction schemes have been constructed in order to evaluate the strain energies (SE) of various cyclophanes with and without $sp^2$-hybridised carbon atoms in the bridge. These results indicate that the influence of one or more $sp^2$-hybridised atoms is small because an increase of the SE due to the shorter bridge length is in most cases counterbalanced by a reduction of the angular strain as a result of the larger natural bond angle of an $sp^2$-hybridised atom. The only exception is the incorporation of an aliphatic CH=CH double bond, which, for unknown reasons, leads to a substantial increase of the SE of about 25 kJ $mol^{-1}$.

Furthermore, it is concluded that there exists no clear-cut relationship between the SE of a [5]metacyclophane and the bending of the benzene ring, nor does the SE directly relate to the reactivity in Diels–Alder reactions. Instead, it is suggested that the reactivity predominantly depends on the release of strain energy in the transition state and thus, in part, in the Diels–Alder adducts. The important observation was made that **8**, the known mono-Dewar benzene isomer of [1.1]metacyclophane (**9**) is 103 kJ $mol^{-1}$ higher in energy than the so far elusive **9** itself. This encourages us to continue our experimental efforts to synthesise the latter compound. Finally, it was confirmed that even highly bent benzene rings (certainly up to $\alpha = 30°$) almost fully retain their delocalisation. Even in the case of [5]metacyclophane (**1a**), delocalisation is favoured over localisation to the corresponding cyclohexa-1,3,5-triene by 36.9 kJ $mol^{-1}$.

## Acknowledgements

The authors wish to thank the Section of Theoretical Chemistry of the Vrije Universiteit in Amsterdam for the use of computing facilities. This investigation was supported by the Council of Chemical Sciences (G. C. W.) with financial aid from the Netherlands Organization for Scientific Research (N. W. O.).

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*Paper a907863k*