Some Investigations on [6]Metacyclophanes

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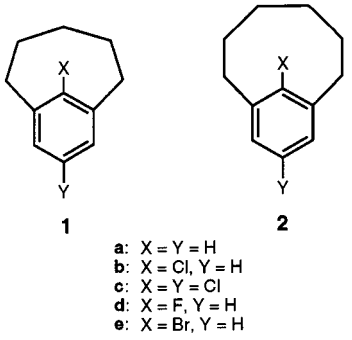
[6]Metacyclophanes **2** with chlorine or fluorine substituents have been synthesized by a novel, convenient version of the base-catalyzed double elimination of hydrogen chloride from the corresponding halopropellanes **7**. Conformational analysis by ^{1}H and ^{13}C NMR spectroscopy revealed remarkable analogies of certain partial structures of the hexamethylene bridge of **2** with the known *exo* and *endo* conformers of [5]metacyclophanes **1**. The Diels–Alder reactivity of **2** towards tetracyanoethene was investigated in order to clarify seemingly contradictory reports in the literature. As anticipated, it was observed that the reactivity of **2** is strongly reduced compared to that of the more strained lower homologues **1**, but there is a subtle fine tuning: While the unsubstituted parent compound **2a** still forms adducts with strong dienophiles, chlorine substitution at the aromatic ring completely blocks the Diels–Alder reactions.

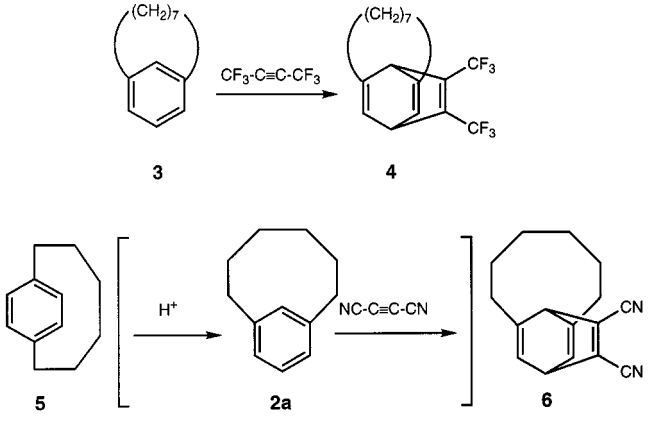
Introduction

The chemistry of small cyclophanes[1−3] is of interest for a number of reasons, most of which stem from the fact that a short bridge distorts the aromatic ring from its preferred planarity. Not surprisingly, this bending enhances the reactivity, and in some cases it does so to a considerable extent.[3] Thus, [5]metacyclophanes (**1**, Scheme 1), which are the smallest metacyclophanes viable at room temperature, react with dienophiles in Diels−Alder reactions at a rate that approaches and sometimes surpasses that of ordinary 1,3-dienes. However, this is *not* due to a localized cyclohexatriene structure, as physical data obtained from X-ray crystal structures,[4] NMR spectroscopy,[5] heats of hydrogenation,[6] and theoretical calculations[6,7] indicate that the benzene ring of **1** is fully delocalized and aromatic. Thus, their high reactivity is not a consequence of bond fixation,[8] but of the high strain present both in the bent aromatic rings and in the distorted bridges, which is released on reaction with dienophiles,[3] electrophiles,[3] phosphinidenes,[9] or carbenes.[10]

Because of their extremely high reactivity, [5]metacyclophanes **1** have so far attracted most of our attention, but it seemed desirable to compare them with their next higher homologues, the less bent and less strained [6]metacyclophanes **2**. In particular, our interest was roused by some seemingly contradictory reports in the literature concerning the Diels−Alder reactivity of **2**. Thus, Hirano et al. reported that "attempted cycloaddition of dienophiles on [6]metacyclophanes failed",[11] and we found that the 9,12-dichloro derivative **2c** did not react with tetracyanoethene at 60 °C.[12] On the other hand, the less strained higher homologue [7]metacyclophane (**3**) did undergo a Diels−Alder reaction with hexafluoro-2-butyne at 150 °C to furnish **4**.[13] More recently, **2a**, inadvertently formed in situ from [6]paracyclophane (**5**), was shown to react with dicyanoacetylene with formation of the adduct **6** in 6% yield[14] (Scheme 2).



Scheme 1



Scheme 2

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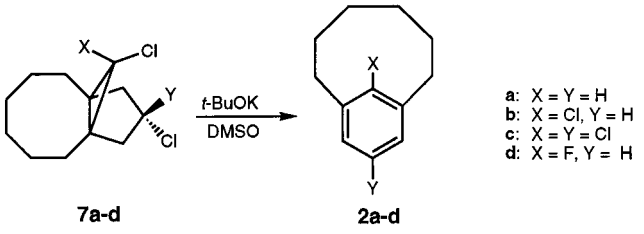
Synthesis

The synthesis of [6]metacyclophane (**2a**) was first reported by Hirano et al. in 1975.[11] Our approach to small [*n*]metacyclophanes follows a different strategy, initially developed for the preparation of the more strained lower homologues **1**.[3] As illustrated for the synthesis of four [6]metacyclophanes **2** in Scheme 3, this comprises double elimination of hydrogen halide from an appropriately substituted halopropellane **7** in the final step. Presumably because of the milder reaction conditions, the yields of **2** were two to four times higher than those obtained by the method of Hirano.[11]



Scheme 3

The synthesis of the parent compound **2a** by a special variation of our general approach has recently been reported.[6] For the halogen-substituted derivatives of **2**, two methods have been successful. In the past, it was a problem that the normally successful base-induced elimination of hydrogen halide by addition of **7** to a solution of *t*BuOK in DMSO gave inferior results, and therefore we had previously performed this elimination with the aid of Ag^+/lutidine.[3,15−18] Recently, we observed that, if performed according to a special methodology − namely, slow addition of solid *t*BuOK to a solution of **7** in DMSO − good yields of **2** are obtained in most cases and, as the workup is convenient, this is now our preferred procedure. Thus, **2b** (45%), **2c** (83%), and **2d** (50%) were obtained without optimization of the yields. However, this method is not suitable for the preparation of **2** when X or Y is Br (**2e**, for example), because reductive replacement of Br by H is the predominant reaction in this case.[6,18]

Conformational Analysis

The conformational analysis of [6]metacyclophane (**2a**) and of its 12-bromo derivative **2e** has already been investigated by Hirano et al. in 1975.[11] With the improved NMR equipment and techniques currently available, we felt that a reinvestigation was desirable in order to study the geometry of the bridge in more detail. At room temperature, the NMR spectrum clearly shows the nonequivalence of the benzylic protons, indicating that the hexamethylene chain resides at one side of the aromatic ring; no ring flip to the other side occurs. In the case of **2a**, however, Hirano et al. observed that this ring flip does take place at higher temperatures (115 °C).[11] This is impossible for the lower homologue [5]metacyclophane (**1a**) and its derivatives, because the bridge is too short to swing around to the other side.[17]

At room temperature, [6]metacyclophanes undergo a second conformational movement, a pseudorotation of the hexamethylene bridge on the same side of the ring[11] (Figure 1). This dynamic process can be frozen on the NMR time scale, and we have determined the energy barrier from variable-temperature ^{13}C NMR measurements and lineshape analysis. For the dichloro[6]metacyclophane (**2c**), the parameters are $\Delta H^{\ddagger} = 10.9$ kcal·mol^{-1} and $\Delta S^{\ddagger} = -5$ cal·mol^{-1}·K^{-1} ($CDCl_3$); this is in good agreement with previously determined data for three derivatives of **2** [$\Delta G^{\ddagger} = 11.1-12.7$ kcal·mol^{-1} ($CFCl_3$, $T_c = -31.5$ to -1.0 °C)].[11] A related conformational motion, the *exo*−*endo* change (cf. Figure 2), occurs in [5]metacyclophanes, and the activation parameters for **1c** ($\Delta H^{\ddagger} = 11.6$ kcal·mol^{-1} and $\Delta S^{\ddagger} = -5.5$ cal·mol^{-1}·K^{-1})[17] are remarkably similar to those of **2c**.

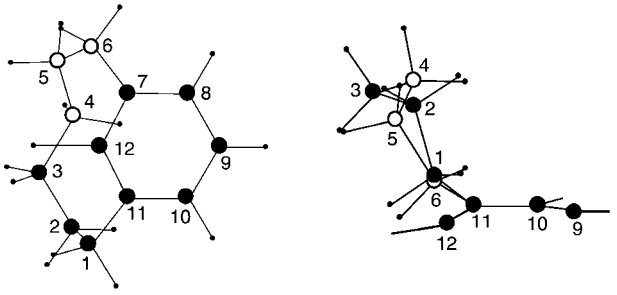


Figure 1. Top and side view of **2a** (MNDO,[23] see text)

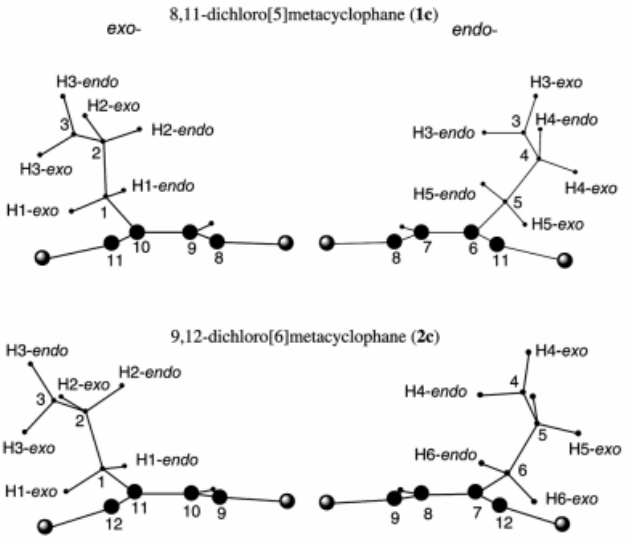


Figure 2. The *exo* and *endo* conformations of 8,11-dichloro[5]metacyclophane (**1c**) and the corresponding positions in 9,12-dichloro-[6]metacyclophane (**2c**) (MNDO[23])

Whereas a plane of symmetry is present in **1**, this is not the case in **2**; this makes the low-temperature ^1H NMR spectra difficult to disentangle, but it was possible to assign them with the aid of HH-COSY, CH correlation, and NOE techniques. The ^1H chemical shifts of **2a**, **2b**, and **2c** are

listed in Table 1 and the coupling constants in Table 2, while the ^{13}C NMR chemical shifts of **2b** and **2c** are presented in Table 3.

Table 1. ^{1}H chemical shifts of **2**

H atom	**2a**[a][b]	**2b**[a][c]	**2c**[a] [c]
H(1)*exo*	2.46	3.27	3.26
H(1)*endo*	2.61	2.58	2.54
H(2)*exo*	1.83	1.86	1.85
H(2)*endo*	0.52	0.56	0.63
H(3)*exo*	0.91	1.35	1.32
H(3)*endo*	1.90	1.66	1.70
H(4)*exo*	1.26	1.24	1.35
H(4)*endo*	−1.46	−1.75	−1.56
H(5)*exo*	1.63	1.95	1.95
H(5)*endo*	1.92	1.86	1.85
H(6)*exo*	3.07	3.36	3.32
H(6)*endo*	2.19	2.30	2.28

[a] $T = 213$ K. − [b] $CDCl_3$. − [c] CD_2Cl_2.

Table 2. Coupling constants J(H,H) [Hz] in the hexamethylene bridge of **2**; for conditions see Table 1

J(H,H)	**2a**[a]	**2b**[a]	**2c**[a]
H(1)*exo*-H(1)*endo*	−12.4	−12.6	−12.5
H(1)*exo*-H(2)*exo*	3.8	4.3	4.3
H(1)*exo*-H(2)*endo*	12.5	13.0	12.7
H(1)*endo*-H(2)*exo*	3.3	2.9	3.0
H(1)*endo*-H(2)*endo*	3.3	4.0	4.0
H(2)*exo*-H(2)*endo*	−12.4	−12.7	−13.5
H(2)*exo*-H(3)*exo*	[b]	[b]	[b]
H(2)*exo*-H(3)*endo*	7	6.1	
H(2)*endo*-H(3)*exo*	12.4	12.0	12.0
H(2)*endo*-H(3)*endo*	[b]	[b]	[b]
H(3)*exo*-H(4)*exo*		3.8	
H(3)*exo*-H(4)*endo*		5.1	
H(3)*endo*-H(4)*exo*		8.0	
H(3)*endo*-H(4)*endo*		3.7	
H(4)*exo*-H(4)*endo*	−13	−12.6	
H(4)*exo*-H(5)*exo*	[b]	1.4	
H(4)*exo*-H(5)*endo*	8	6.9	
H(4)*endo*-H(5)*exo*	9	9.2	
H(4)*endo*-H(5)*endo*	[b]	1.4	
H(5)*exo*-H(5)*endo*	−13.8	−12.6	
H(5)*exo*-H(6)*exo*	9.5	9.6	8.8
H(5)*exo*-H(6)*endo*	8.7	10.2	10
H(5)*endo*-H(6)*exo*	[b]	[b]	[b]
H(5)*endo*-H(6)*endo*	8.7	7.2	7
H(6)*exo*-H(6)*endo*	−14.3	−13.7	−13.9

[a] Values not given could not be determined. − [b] $J < 1$ Hz.

Certain ^{13}C signals of **2** show analogies with those of the *exo* and *endo* conformers of [5]metacyclophanes **1**. In the *exo* conformer of **1c**, the three bridge signals are δ = 40.5 (C1), 41.6 (C2), and 25.1 (C3), and in the *endo* conformer they are δ = 34.9 (C1), 34.5 (C2), and 21.2 (C3).[19] Qualitatively, the same order is observed in **2c**; in particular, the pronounced shift difference Δδ(C3 − C4) = 4.1 of **2c** is nearly identical to the corresponding Δδ(*exo*-C3 − *endo*-C3) = 3.9 of **1c**. These analogies arise from the fact that the geometry of the bridge of **2** shows certain features

Table 3. ^{13}C Chemical shifts and ^{1}J(C,H) [Hz] of **2**; for conditions see Table 1

C atom	**2b**	J(CH)	**2c**	J(CH)
C1	34.4	131	34.4	131
C2	35.5	125	35.3	127
C3 (out; *exo*)	27.6	127	27.5	125
C4 (above; *endo*)	23.2	125	23.4	124
C5	27.5	127	27.3	128
C6	30.8	131	30.8	131
C7	143.3	s	144.5	s
C8	127.0	161.8[a]	126.5	167.3[b]
C9	125.7	161.5	131.0	s
C10	124.4	161.2[c]	123.8	166.4[d]
C11	142.2	s	143.3	s
C12	136.4	s	135.1	s

[a] Long range J(CH) = 8.8, 5.9, 5.9 Hz. − [b] Long range J(CH) = 6.1, 6.1, 6.1 Hz. − [c] Long range J(CH) = 8.1, 8.0, 4.1 Hz. − [d] Long range J(CH) = 6.7, 6.7, 4.1 Hz.

which resemble either those of the *exo* or the *endo* conformer of [5]metacyclophanes **1**. In Figure 1, this is indicated with black atoms (quasi-*exo*) and white ones (quasi-*endo*) of the bridge; in Figure 2, the *exo* and *endo* conformations of **1** are compared with those of the corresponding halves of the bridge of **2** (quasi-*exo* and quasi-*endo*). As indicated in Figure 1, during pseudorotation of the bridge of **2**, the methylene group of C3, pointing away from the aromatic ring (quasi-*exo*) moves to a position above the aromatic ring (quasi-*endo*), equivalent to that originally occupied by C4, and vice versa. Thus, the black atoms become white and vice versa. Simultaneously, the *endo*-protons at C3 and C4 move in and out of the shielding cone of the aromatic ring; hence the difference in their chemical shifts is considerable for **2b**: δ(H3-*endo*) = 1.66 and δ(H4-*endo*) = −1.75. This effect is also observed in **1**; in **1b**, δ(H3-*endo*) of the *exo* conformer is δ = 1.36, while in the *endo* conformer, it is δ = −1.20.[20] The corresponding H3-*exo* and H4-*exo* protons in **2b** could also be assigned unambiguously by CH-correlation: δ(H3-*exo*) = 1.35 and δ(H4-*exo*) = 1.24.

Let us first consider the quasi-*exo* part of the bridge of **2b**. The two benzylic signals are observed at δ = 3.27 (H1-*exo*) and δ = 2.58 (H1-*endo*), with Δδ = 0.69. The H2 protons resonate at δ = 1.86 (H2-*exo*) and δ = 0.56 (H2-*endo*); the latter is rather shielded due to its closeness to the shielding cone. The same effect is observed for H2-*endo* in the *exo* conformer of **1b** (δ = 0.33).[20]

For the quasi-*endo* part of the bridge of **2b**, the benzylic protons are found at δ = 3.36 (H6-*exo*) and δ = 2.30 (H6-*endo*); Δδ = 1.16. The H5 protons are the least informative as both resonate at δ = 1.9. The same is observed for the H2 protons in the *endo* conformer of **1b**; they appear at δ = 1.55 and 2.18. In **1b**, the benzylic protons in the *endo* conformer have Δδ = 1.67, and in the *exo* conformer Δδ = 1.21. The same trend is observed in the hexamethylene bridge of **2b**, where Δδ = 1.06 in the quasi-*endo* part and 0.69 in the quasi-*exo* part. In addition, the coupling patterns for H1 and H2 are almost the same as those of the *exo*

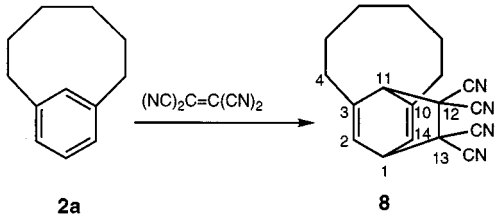
conformer of **1a** {*J*[H(1)*exo*-H(2)*exo*] = 3.0 Hz, *J*[H(1)*exo*-H(2)*endo*] = 12.5 Hz, *J*[H(1)*endo*-H(2)*exo*] = 3.3 Hz, *J*[H(1)*endo*-H(2)*endo*] = 3.3 Hz}, and the same holds for H5 and H6 of the quasi-*endo* conformer.[17]

Remarkable is the long-range *J*(CH) coupling [presumably ^3J(CH), cf. Table 3, footnotes] of the aromatic carbon atoms C8 and C10 (see Figure 2). A possible explanation may be the slightly different pyramidalization angles of those atoms, which are in turn caused by the different benzylic environments of the quasi-*exo* and *endo* conformers. Thus, the [6]metacyclophanes **2** display interesting NMR behavior, and the geometry of the bridge corresponds to that observed in the *exo* and *endo* conformers of [5]metacyclophanes **1**.

Diels−Alder Reactivity of [6]Metacyclophanes (2)

As indicated in the Introduction, the seemingly contradictory reports on the propensity of **2** to undergo Diels−Alder reactions was one of the starting points for our investigation. We therefore investigated the reactivity of **2a** towards the powerful dienophile tetracyanoethene.

When tetracyanoethene was added to a solution of **2a** in $CDCl_3$, the solution turned intensely red, indicating the formation of a charge transfer complex.[21] After 2 h at room temperature, the solution became almost colorless again. A ^{1}H NMR spectrum indicated that **2a** had been completely consumed and that a new compound had been formed; it was identified as the Diels−Alder adduct **8** by its characteristic NMR spectra (Scheme 4). Only 11 ^{13}C signals were present, indicating C_s symmetry in **8**. In the ^{1}H NMR spectrum, only one olefinic signal was observed [δ = 6.30 (d, ^3J = 6.0 Hz, with further small couplings, 2-,14-H)], and two double allylic bridgehead protons (1-,11-H) which by chance nearly coincide [δ = 4.46 (t, ^4J = 1.7 Hz, 11-H) and 4.45 (t, ^3J = 6.0 Hz, 1-H)]. HR-MS confirmed the composition of **8**. This result is in line with the report by Tobe et al.[14] (cf. **6**, Scheme 2): **2a** does indeed undergo Diels−Alder reactions. As expected, the reactivity of **2a** is intermediate between that of **1a**[3] and **3**.[13]



Scheme 4

When, however, **2b** − the 12-chloro derivative of **2a** − was treated with tetracyanoethene, no adduct was formed, not even after longer reaction times and at elevated temperatures. Finally, in an attempt to force adduct formation, the NMR tube containing **2b** and tetracyanoethene in $CDCl_3$ was sealed under vacuum and heated for 3 d at 100 °C. The solution turned black, but no adduct could be detected in the ^{1}H NMR spectrum, while **2b** was still present in practically undiminished amounts and had apparently survived the drastic conditions.

Thus, even monochloro substitution retards the rate of product formation considerably. This is paralleled by the behavior of **1** and its derivatives, in which chloro substitution was found to retard the reaction, although the reactivity was not suppressed completely in this case.[3] One may therefore extrapolate that the 9,12-dichloro derivative **2c** should be even less reactive than **2b**, and **2c** has indeed been reported to be unreactive.[12] In conclusion, our recent results confirm that certain [6]metacyclophanes **2** do undergo Diels−Alder reactions, but their occurrence strongly depends on the substitution pattern of the benzene ring.

Experimental Section

General: ^{1}H NMR and ^{13}C NMR were recorded with Bruker AC-200 or MSL-400 spectrometers. Almost all NMR samples were measured in $CDCl_3$ and chemical shifts are reported relative to $CHCl_3$ [δ(^{1}H) = 7.27] or $^{13}CDCl_3$ (δ = 77.0). [6]Metacyclophane (**2a**) was measured in CD_2Cl_2 relative to $CHDCl_2$ [δ(^{1}H) = 5.32] or $^{13}CD_2Cl_2$ (δ = 53.8). The assignment of signals is based on several 2D NMR techniques (CH correlation, HH-COSY, sometimes NOE and 1D-INADEQUATE experiments. − High-resolution mass spectra (HR-MS) were measured with a Finnigan MAT 90 spectrometer operating at an ionization potential of 70 eV.

10-Chlorobicyclo[6.3.0]undec-1(8)-ene (9): A mixture of 10,10-dichlorobicyclo[6.3.0]undec-1(8)-ene[12] (0.493 g, 2.25 mmol) and triphenyltin hydride (0.806 g, 2.3 mmol) was heated to 100 °C for 5 h. After the mixture had cooled to room temp., pentane was added, whereupon a white precipitate formed. This was filtered off and washed with several portions of pentane. The combined pentane layers were concentrated under reduced pressure and the resulting slurry was purified by column chromatography (Al_2O_3/pentane). After evaporation of the pentane eluate, **9** was obtained as a colorless oil (crude yield about 60−80%) which was directly used for the synthesis of **7b** and **7d**. − **9**: ^{1}H NMR (200 MHz): δ = 4.45 [tt, ^3J = 6.9, ^3J = 3.6 Hz, 1 H, H(10)], AB system [δA = 2.82 (dd, ^2J = −15.8, ^3J = 6.9 Hz, 2 H, 9-,11-H*anti*), δB = 2.55 (dd, ^2J = −15.8, ^3J = 3.6 Hz, 2 H, 9-,11-H*syn*)], 2.12 (m, 4 H), 1.7−1.2 (m, 8 H).

***endo*-10,12,12-Trichlorotricyclo[6.3.1.0]dodecane (7b):** A solution of NaOH (1.6 g, 40 mmol) in H_2O (1.6 mL) was added over 15 min, with vigorous stirring, to a mixture of **9** (0.90 g, 4.9 mmol), $CHCl_3$ (4.8 g, 40 mmol), hexadecyltrimethylammonium bromide (0.33 mmol), and a drop of ethanol. The stirring was continued for 18 h at room temperature and 2 h at 45 °C. After the mixture had cooled to room temp., water (30 mL) and CH_2Cl_2 (4 mL) were added, the layers were separated, and the aqueous layer was extracted twice with CH_2Cl_2. The combined organic layers were washed with water, HCl (1 M), and brine, dried with $MgSO_4$, and concentrated under reduced pressure. The crude residual oil was purified by column chromatography (silica gel/pentane) to yield **7b** as a colorless oil (0.78 g, 2.9 mmol, 60%). − ^{1}H NMR (200 MHz): δ = 4.22 (tt, ^3J = 8.1, ^3J = 4.2 Hz, 1 H, 10-H), AB system [δA = 2.55 (dd, ^2J = −16.0, ^3J = 8.1 Hz, 2 H, 9-,11-H*exo*), δB = 2.49 (dd, ^2J = −16.0, ^3J = 4.2 Hz, 2 H, 9-,11-H*endo*)], 1.9−1.1 (m, 12 H). − MS: *m/z*

(%) = 266 (7) [M^+], 231 (33), 196 (100), 159 (22). − HR-MS: calcd. for $C_{12}H_{17}{}^{35}Cl_3$ 266.0396; found 266.0396.

10,10,12,12-Tetrachlorotricyclo[6.3.1.0]dodecane (7c): The reaction described above for **7b** was performed on 10,10-dichlorobicyclo[6.3.0]undec-1(8)-ene[12] (18.5 mmol, 4.06 g). The crude yield was 4.9 g of a brown solid; purification by column chromatography (silica gel/pentane) yielded 3.79 g of colorless crystals (68%), which were recrystallized from ethanol to yield 2.93 g of colorless crystals of **7c** (9.70 mmol, 53%). M.p. 104 °C. − ^{1}H NMR (200 MHz): AB system [δA = 3.28 (d, ^2J = −15.9 Hz, 2 H, 9-,11-H), δB = 3.18 (d, ^2J = −15.9 Hz, 2 H, 9-,11-H)], 1.9−1.2 (m, 12 H). − ^{13}C NMR (50.3 MHz): 24.8 [t, *J*(CH) = 129 Hz], 25.1 [t, *J*(CH) = 128 Hz], 26.4 [t, *J*(CH) = 128 Hz], 42.8 [s, C(1,7)], 57.2 [t, *J*(CH) = 134 Hz, C(9,11)], 76.9 (s, C12), 91.1 (s, C10). − MS: *m*/*z* (%) = 300 (2) [M^+], 265 (21) [M − Cl], 230 (100), 193 (61). − HR-MS:[12] calcd. for $C_{12}H_{16}{}^{35}Cl_4$ 300.0007; found 300.0011.

10-*endo*,12-*endo*-Dichloro-12-*exo*-fluorotricyclo[6.3.1.0]dodecane (7d) and Its 12-Stereoisomer (7d′): Dolbier's method was used.[22] $TiCl_4$ (3.04 g, 16.0 mmol) was added to dry THF (25 mL, cooled to −20 °C) through a septum at such a rate that the temperature did not exceed 5 °C. $LiAlH_4$ (0.62 g, 16.5 mmol) was then added (with the aid of a solid addition tube) to the bright yellow suspension at such a rate that the temperature did not exceed 10 °C. The mixture first turned green and brownish, and then deep black, and it was stirred for 0.5 h at room temp. The black suspension was then transferred under nitrogen to a dropping funnel and slowly added, with stirring, to a cooled mixture of $CFCl_3$ (2.22 g, 16.2 mmol) and **9** (0.80 g, 4.7 mmol) in dry THF (25 mL) at such a rate that the temperature did not exceed 0 °C. After stirring for half an hour at 0 °C, the mixture was allowed to warm to room temp. and stirred for another 3 h. It was then poured into a solution of concentrated HCl (10 mL) in ice/water (100 mL). The mixture was extracted three times with CH_2Cl_2. The combined, black organic layers were washed with a solution of $NaHCO_3$ (7.5% in H_2O, 20 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure to yield 1.00 g of the adduct mixture of **7d** and **7d′** (4 mmol, 93%), which was not fully characterized but was used without further purification. − ^{1}H NMR and GCMS showed that no alkene was left. − GC-MS: *m*/*z* (%) = 250 (4) [M^+], 215 (45) [M − Cl], 180 (100), 109 (29).

Synthesis of 2. − General Procedure: Solid *t*BuOK was slowly added to a solution of **7** in DMSO, from a solid addition tube. The dark mixture was stirred for several hours at room temperature and then poured, with stirring, into a cold water/pentane mixture. The layers were separated and the water layer was extracted three to five times with pentane. The combined organic layers were washed with water (three to five times), dried with $MgSO_4$, filtered, and concentrated under reduced pressure.

[6]Metacyclophane (2a): The synthesis of **2a** from **7a** by the new procedure has recently been described.[6]

12-Chloro[6]metacyclophane (2b): The treatment with *t*BuOK (7.3 mmol, 0.82 g) was performed as described above, but starting from **7b** (2.9 mmol, 0.78 g) in DMSO (35 mL); reaction time 18 h at room temp. Crude yield 0.28 g, after column chromatography 0.25 g (1.3 mmol, 45%) of pure **2b** as a colorless oil. For NMR-spectroscopic data see Tables 1−3. − MS: *m*/*z* (%) = 194 (38) [M^+], 159 (100) [M − Cl], 138 (30), 115 (26), 103 (20). − HR-MS: calcd. for $C_{12}H_{15}Cl$ 194.0862, found 194.0866.

9,12-Dichloro[6]metacyclophane (2c): The treatment with *t*BuOK (7.3 mmol, 0.82 g) was performed as described above, but starting from **7c** (1.00 g, 3.31 mmol) in DMSO (40 mL); reaction time 2 h at room temp. Yield after column chromatography: 0.63 g of pure **2c**[12] as a colorless oil (2.75 mmol, 83%). For NMR-spectroscopic data see Tables 1−3. − MS: *m*/*z* (%) = 228 (35) [M^+], 193 (100) [M − Cl], 172 (72), 115 (71). − HR-MS: calcd. for $C_{12}H_{14}Cl_2$ 228.0473; found 228.0470.

12-Fluoro[6]metacyclophane (2d): The treatment with *t*BuOK (0.78 g, 6.9 mmol) in DMSO (20 mL) was performed as described above, but starting from the mixture of **7d** and **7d′** (vide supra; 0.61 g, 2.4 mmol); reaction time 3 h at room temp. Yield after column chromatography (Al_2O_3/pentane) 0.26 g (1.2 mmol, 50%) of pure **2d** as a colorless oil. − ^{1}H NMR (400 MHz, 213 K): δ = 6.93 (t, ^3J = 7.2 Hz, 1 H, 9-H), 6.85 (dd, ^3J = 7.2 Hz, J_{HF} = 7.0 Hz, 1 H), 6.84 (dd, ^3J = 7.2 Hz, J_{HF} = 7 Hz, 1 H), 3.18 (m, 1 H), 3.02 (m, 1 H), 2.42 (m, 1 H), 2.22 (m, 1 H), 1.92−1.67 (m, 4 H), 1.34 (m, 1 H), 1.11 (m, 1 H), 0.58 (m, 1 H, 2-H*endo*), −1.53 (m, 1 H, 4-H*endo*). − MS: *m*/*z* (%) = 178 (54) [M^+], 163 (24), 149 (27), 135 (31), 122 (100), 109 (24).

12,12,13,13-Tetracyanotricyclo[8.3.1.0^{3,11}]tetradeca-2,10(14)-diene (8): The reaction was performed in an NMR tube. TCNE (30 mg) was added to a solution of **2a** (10 mg) in $CDCl_3$. The solution turned intensely red; this color disappeared after 2 h at room temperature. The product **8** was formed quantitatively. − ^{1}H NMR (200 MHz): δ = 6.30 (ddd, ^3J = 6.0, ^4J = 1.9 Hz, ^4J = 1.7 Hz, 2 H, 8-,10-H), 4.46 (t, ^4J = 1.7 Hz, 1 H, 12-H), 4.45 (t, ^3J = 6.0 Hz, 1 H, 9-H), AB-system [δA = 2.60 (m, 2 H, 1-,6-H*exo*), δB = 2.44 (m, 2 H, 1-,6-H*endo*)], 2.2−0.9 (m, 8 H). − ^{13}C NMR (50.32 MHz): δ = 21.1 (t), 24.2 (t), 32.7 (t, C-1,-6), 43.4 (s), 44.9 (s), 45.9 (d), 49.9 (d), 111.3 (s, CN), 111.8 (s, CN), 126.5 (d, C-8,-10), 152.4 (s, C-7,-11). − MS: *m*/*z* (%) = 288 (2) [M^+], 160 (81, retro DA), 145 (49), 131 (50), 128 (97, TCNE), 117 (43), 104 (100). − HR-MS: calcd. for $C_{18}H_{16}N_4$ 288.1375; found 288.1383.

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[1] F. Vögtle, *Cyclophane Chemistry*, Wiley, Chichester, **1993**.
[2] F. Diederich, *Cyclophanes*, Royal Society of Chemistry, Cambridge, **1993**.
[3] [3a] F. Bickelhaupt, W. H. de Wolf, *Recl. Trav. Chim. Pays-Bas* **1988**, *107*, 459. − [3b] F. Bickelhaupt, W. H. de Wolf, in: *Advances in Strain in Organic Chemistry* (Ed.: B. Halton), JAI Press Ltd., London, **1993**, vol. 3, p. 185. − [3c] F. Bickelhaupt, W. H. de Wolf, *J. Phys. Org. Chem.* **1998**, *11*, 362.
[4] [4a] K. J. Shea, L. D. Burke, R. J. Doedens, *J. Am. Chem. Soc.* **1985**, *107*, 5305 − [4b] L. W. Jenneskens, J. C. Klamer, H. J. R. de Boer, W. H. de Wolf, F. Bickelhaupt, C. H. Stam, *Angew. Chem.* **1984**, *96*, 236; *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 238.
[5] P. C. M. van Zijl, L. W. Jenneskens, E. W. Bastiaan, C. MacLean, W. H. de Wolf, F. Bickelhaupt, *J. Am. Chem. Soc.* **1986**, *108*, 1415.
[6] M. J. van Eis, G. W. Wijsman, W. H. de Wolf, F. Bickelhaupt, D. W. Rogers, H. Kooijman, A. L. Spek, *Chem. Eur. J.* **2000**, *6*, 1537.
[7] M. J. van Eis, W. H. de Wolf, F. Bickelhaupt, R. Boese, *J. Chem. Soc., Perkin Trans. 2* **2000**, 793.
[8] H. D. Beckhaus, R. Faust, A. J. Matzger, D. L. Mohler, D. W. Rogers, C. Rüchardt, A. K. Sawhney, S. P. Verevkin, K. P. C. Vollhardt, S. Wolff, *J. Am. Chem. Soc.* **2000**, *122*, 7819.

[9] M. J. van Eis, C. M. D. Komen, F. J. J. de Kanter, W. H. de Wolf, K. Lammertsma, F. Bickelhaupt, M. Lutz, A. L. Spek, *Angew. Chem.* **1998**, *110*, 1656; *Angew. Chem. Int. Ed.* **1998**, *37*, 1547.
[10] M. J. van Eis, B. S. E. van der Linde, F. J. J. de Kanter, W. H. de Wolf, F. Bickelhaupt, *J. Org. Chem.* **2000**, *65*, 4348.
[11] S. Hirano, H. Hara, S. Hiyama, S. Fujita, H. Nozaki, *Tetrahedron* **1975**, *31*, 2219.
[12] L. W. Jenneskens, Thesis, Vrije Universiteit, Amsterdam, **1986**, chapter 13.
[13] K. L. Noble, H. Hopf, M. Jones, Jr., S. L. Kammula, *Angew. Chem.* **1978**, *90*, 629; *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 602.
[14] Y. Tobe, A. Takemura, M. Jimbo, T. Takahashi, K. Kobiro, K. Kakiuchi, *J. Am. Chem. Soc.* **1992**, *114*, 3479.
[15] P. Grice, C. B. Reese, *J. Chem. Soc., Chem. Commun.* **1980**, 424.
[16] L. A. M. Turkenburg, W. H. de Wolf, F. Bickelhaupt, *Tetrahedron Lett.* **1983**, *24*, 1817.
[17] L. W. Jenneskens, F. J. J. De Kanter, L. A. M. Turkenburg, H. J. R. De Boer, W. H. de Wolf, F. Bickelhaupt, *Tetrahedron* **1984**, *40*, 4401.
[18] G. W. Wijsman, W. H. de Wolf, F. Bickelhaupt, *Recl. Trav. Chim. Pays-Bas* **1994**, *113*, 53.
[19] L. W. Jenneskens, F. J. J. de Kanter, W. H. de Wolf, F. Bickelhaupt, *Magn. Res. Chem.* **1986**, *24*, 308. In that paper, the assignment of C1 and C2 had been erroneously reversed; the new assignments presented here are derived from (C,H)-correlated NMR spectroscopy.
[20] P. A. Kraakman, J. M. Valk, H. A. G. Niederländer, D. B. E. Brouwer, F. M. Bickelhaupt, W. H. de Wolf, F. Bickelhaupt, C. H. Stam, *J. Am. Chem. Soc.* **1990**, *112*, 6638.
[21] [21a] L. R. Melby, in: *The Chemistry of the Cyano Group* (Ed.: Z. Rappoport), Wiley, London, **1970**, p. 639. – [21b] A. Renault, C. Cohen-Addad, J. Lajzerowicz, E. Canadell, O. Eisenstein, *J. Mol. Liq. Cryst.* **1988**, *164*, 179.
[22] [22a] W. R. Dolbier, Jr., C. R. Burkholder, *Tetrahedron Lett.* **1988**, *29*, 6749. – [22b] W. R. Dolbier, Jr., C. R. Burkholder, *J. Org. Chem.* **1990**, *55*, 589.
[23] M. J. S. Dewar, W. Thiel, *J. Am. Chem. Soc.* **1977**, *99*, 4899.

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