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Paracyclophanes: Extending the Bridges. Reactions[‡]

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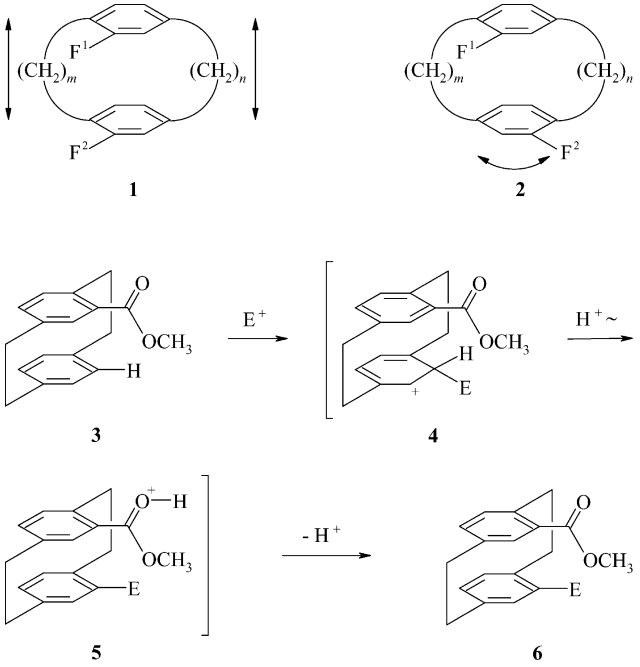
[*m.n*]Paracyclophanes with bridges of equal and unequal length ($m,n \leq 4$) undergo electrophilic aromatic substitution (Friedel–Crafts acylation, bromination) under very mild conditions as long as the bridge contains less than four atoms. Whenever there is a choice, the aromatic ring is attacked at the position closest to the shorter alkano bridge, which indicates that the transannular benzene moiety acts as a neighboring group. By brominating the acetyl derivatives obtained, and the acids and esters derived therefrom, a second substituent is introduced into the pseudo-geminal position, that is, directly opposite the directing group. However, this effect is observed only for those [*m.n*]phanes in which the length of the neighboring bridge does not exceed three atoms. For the butano-bridged derivatives, the regioselectivity is lost completely. Very similar results were observed for [*m.n*]paracyclophanes carrying two ester substituents on one benzene ring, the limiting case being the [4.3]paracyclophane derivative. We propose that the stereocontrolling effect of a substituent can only occur when the intra-annular distance is below 4 Å.

Introduction

In several earlier publications we have suggested using [*m.n*]cyclophanes as "molecular workbenches"[2,3] or "molecular sliding calipers". Taking the paracyclophanes depicted in structure **1** as an example, it is clear that the distance between the two functional groups F^1 and F^2 can be adjusted by changing the lengths of the two alkano bridges (Scheme 1). Depending on the lengths of these tethers the two aromatic subsystems remain parallel ($m = n$) or become tilted with respect to each other ($m \neq n$). Of course, the two functional groups need not be anchored in the same position on the two rings; rather than being positioned directly on top of each other (pseudo-geminal, as in **1**), they could also be bonded in a pseudo-*ortho* orientation (structure **2**), which would lead to a different spatial relationship between them. Depending on the distance and relative orientation, the question then might be asked as to whether and how these functional groups react with each other. By extending this approach to larger values of *m* and *n* one could eventually determine the limit at which functional groups would stop interacting. By replacing the benzene "platforms" in **1** and **2** by other aromatic systems a huge number of spatially different orientations between F^1 and F^2 can be generated.



Scheme 1. [*m.n*]Paracyclophanes as molecular workbenches.

In a related problem, the question can be asked as to how a functional group already present in one of the aromatic moieties influences the regioselectivity of attack of an enter-

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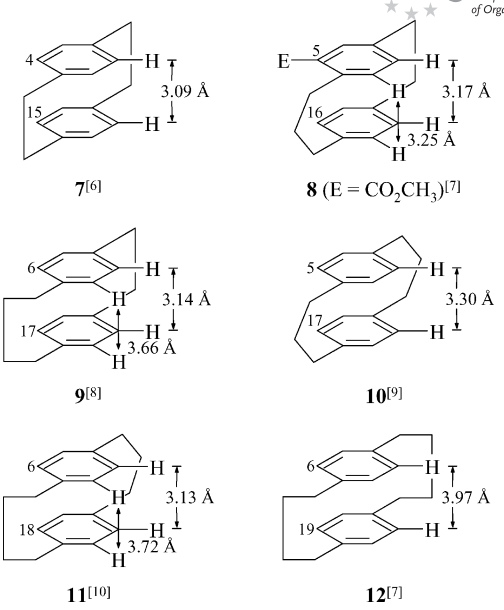
ing reagent such as an electrophile. This question was addressed 40 years ago by Reich and Cram[4] in a now classical paper in which the effect of, for example, an ester group (see **3**) on the site of the second substitution was investigated. It was shown that the electrophile E^+ attacks the more reactive (unfunctionalized) benzene deck from its less sterically hindered side to form the σ complex **4** initially. The charged ring then rearomatizes by transfer of a proton to the most basic atom of the neighboring group to generate the protonated ester **5**. This, in the last step of the sequence, loses a proton and generates the pseudo-geminal reaction product **6**.

To exploit the workbench concept further we needed the exact structures of the [*m.n*]paracyclophanes, all the way up to $m = n = 4$. To go beyond this point is not reasonable as cyclophanes with longer bridges become so flexible that they begin to lose their stereocontrolling properties.[5] Fortunately all these model hydrocarbons are known (see the preceding paper)[1] and for most of them experimentally determined geometric parameters exist for the solid-state structures; a selection of these is included together with the corresponding references and the six structures **7**–**12** in Scheme 2.

In the case of the [3.2]paracyclophane (**8**; E = H) we were unable to obtain single crystals for an X-ray investigation, so we prepared[1] the monoester **8** ($E = CO_2CH_3$) which was suitable for X-ray analysis.[7] For [4.3]paracyclophane (**11**), the intra-annular distances were obtained by a gas-phase geometry optimization performed by DFT calculations;[10] neither the parent hydrocarbon nor any of the derivatives available to us could be crystallized.

To address the above questions we first carried out two typical electrophilic substitution reactions with the above [*m.n*]paracyclophanes, Friedel–Crafts acylation and bromination, and then employed the methyl ketones obtained in the first process to study the intra-annular directing effects of functional groups. Some of the derivatives obtained were also employed in further transformations to the novel cyclophane derivatives needed for future investigations.



7[6] **8** ($E = CO_2CH_3$)[7] **9**[8] **10**[9] **11**[10] **12**[7]

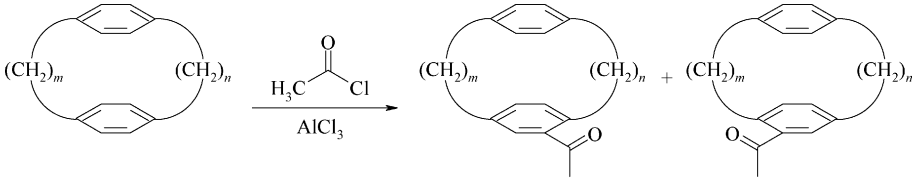
Scheme 2. Intramolecular distances in [*m.n*]paracyclophanes.

Results and Discussion

Electrophilic Aromatic Substitution of [*m.n*]Paracyclophanes

In a first series of experiments the cyclophanes **7**–**12** (for **8**, E = H) were treated with acetyl chloride in the presence of aluminum trichloride under the reaction conditions given in Scheme 3.

As can bee seen from the scheme, in all cases the Friedel–Crafts acylations took place in acceptable-to-good yields. However, there are significant differences concerning the regioselectivity. Of course in the cases of equal-length bridges ($m = n = 2$, 3, and 4) only one ketone can be obtained: **13** (71%),[11] **18** (85%),[12] and **21** (53%, this work).[13] The structure determination of these compounds is straightforward and follows from the spectroscopic data given in the



m	*n*	cyclophane	reaction conditions	yield (%)	
2	2	**7**	10 min, -20 °C	**13** (71)[11]	
3	2	**8** (= H)	30 min, r. t.	**14** (71)	**15** (0)
4	2	**9**	30 min, r. t.	**16** (89)	**17** (0)
3	3	**10**	20 min, r. t.	**18** (85)[12]	
4	3	**11**	45 min, r. t.	**19** (50)[a)]	**20** (7)[a)]
4	4	**12**	3 h, r. t.	**21** (53)[13]	

a) Calculated yield from the ^1H NMR spectra.

Scheme 3. Friedel–Crafts acylation of [*m.n*]paracyclophanes.

Exp. Section. Note that the reactivity of the [*m.n*]paracyclophanes, as judged by the reaction time, decreases with increasing bridge length.

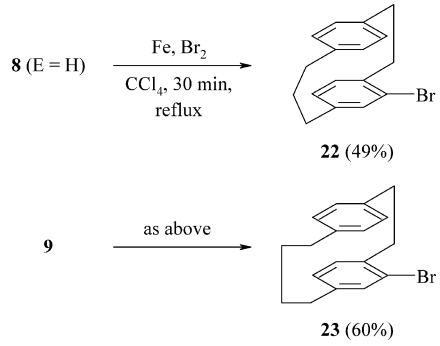
In the less symmetrical cases, **8** (E = H), **9**, and **11**, the incoming functional group may bind closer (*ortho*) to either the shorter or the longer bridge. The first two hydrocarbons both possess an ethano bridge and the aromatic substitution exclusively takes place next to it, providing the two ketones **14** and **16**, respectively, in good yields (71 and 89%, respectively). In these cases the structure elucidation of the products is more difficult, but could nevertheless be performed unambiguously by careful analysis of the NMR spectra of **14** and **16** (see the Section "Structure Elucidation by NMR Spectroscopy", below).

Furthermore, for the [3.2]paracyclophane the alternative substitution pattern, that expected for **15**, was available in the form of the ester **8** (E = CO_2CH_3) for which we also performed an X-ray structural analysis (see above). Comparison of the respective data clearly shows that **15** is not produced in the Friedel–Crafts acylation of **8** (E = H).

In the case of [4.3]paracyclophane (**11**) we indeed observed the formation of two ketones, namely **19** and **20**, which were produced in approximately a 7:1 ratio according to the ^{1}H NMR analysis. These compounds can be distinguished by the bridge methylene proton that points towards the keto group.[14] For the isomer with the acetyl group close to the propano bridge, ketone **19**, this proton absorbs as a multiplet at δ = 3.58 ppm, the assignment resulting from comparison with the corresponding, easily recognizable proton in the [3.3]paracyclophane ketone **18** (δ = 3.55 ppm).[15] Likewise, this proton in **20** absorbs at δ = 3.25 ppm (multiplet), compared with δ = 3.33 ppm for the analogous position in 6-acetyl[4.4]paracyclophane (**21**, see the Exp. Section).

These experiments thus convincingly demonstrated that a) the rate of the substitution process depends on the strain in the starting [*m.n*]paracyclophane and b) in a substrate with two unequal bridges, the new substituent is always introduced into the position displaying the shortest distance to the opposing benzene moiety. This limiting distance is around 3.2 Å. We assume that at this distance the facing benzene ring can provide a "helping hand" to remove the (internal) proton from the initially generated σ complex thus rearomatizing it, similar to the transannular effect of an ester substituent shown in Scheme 1 and the examples that will be addressed below.

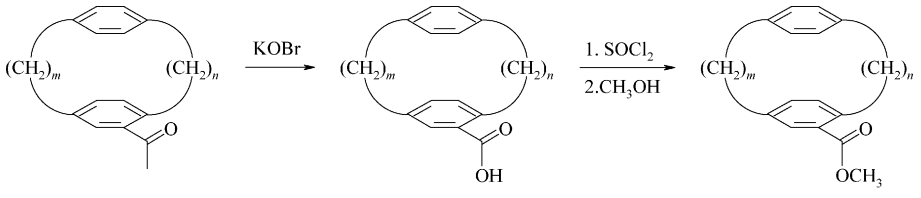
The Fe-catalyzed bromination of the cyclophanes **7**, **10**, and **12**, has been studied extensively.[12,16,17] As expected, the result, especially the problem of monobromination versus polybromination, depends strongly on the reaction conditions. Misumi and co-workers investigated all three hydrocarbons under the same conditions (Fe powder, bromine, carbon tetrachloride, room temperature, 4 h)[17] and showed that the expected monobromides were produced in good and roughly the same yields: 73, 73, and 81% yields from **7**, **10**, and **12**, respectively. Application of these bromination conditions to **8** (E = H) and **9** furnished the two monobromides **22** and **23** (Scheme 4).



Scheme 4. Bromination of selected [*m.n*]paracyclophanes.

Again, as determined largely from a careful analysis of the NMR spectroscopic data of **23** (see below) the incoming substituent prefers the side of the substrate close to the shorter bridge, and we assume that similar reasons are responsible for this, as discussed for the Friedel–Crafts acylation reaction above.

Having functionalized the parent [*m.n*]paracyclophanes by the introduction of preparatively important substituents, these can now be employed in further transformations. Because in the present context we needed the corresponding monoacids as well as their esters we subjected the above methyl ketones to a haloform oxidation (preparation of **24**–**27**) followed by esterification (**28**–**31**). The results are summarized in Scheme 5.



m	*n*	
3	2	**14**
4	2	**16**
3	3	**18**
4	4	**21**

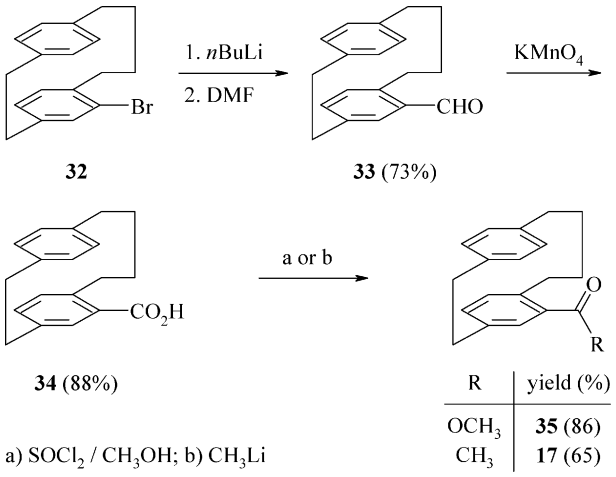
m	*n*	yield (%)
3	2	**24** (97)
4	2	**25** (82)
3	3	**26** (94)
4	4	**27** (88)

m	*n*	yield (%)
3	2	**28** (91)
4	2	**29** (76)
3	3	**30** (89)
4	4	**31** (87)

Scheme 5. Oxidation/esterification of acyl[*m.n*]paracyclophanes.

The structures of the intermediates and products again follow from the usual spectroscopic data (see the Exp. Section) and require no further comment.

Another simple transformation sequence leading to the isomers of **16**, **25**, and **29** in which the functional group is on the side of the longer bridge, derivatives **34**, **35**, and **17**, (Scheme 6) starts with 6-bromo[4.2]paracyclophane (**32**), prepared as described in the preceding paper.[1]



R	yield (%)
OCH_3	**35** (86)
CH_3	**17** (65)

Scheme 6. Use of a bromo[*m.n*]paracyclophane for functionalization reactions.

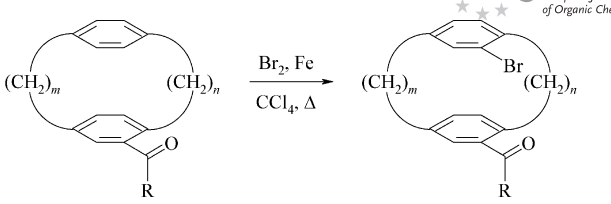
The individual steps require no further comment; the spectroscopic data of the involved intermediates are collected in the Exp. Section.

Transannular Electrophilic Bromination Reactions

The above chemical transformations provided derivatives of the [*m.n*]paracyclophanes in which the functional group can occupy any position in one of the aromatic rings, in other words we have created a situation in which we can investigate how the pseudo-geminal directing effect (see above) depends on the distance between the functional group and the entry point of the second substituent.

The model and reference reaction is the one mentioned in the introduction: The electrophilic bromination of 4-methoxycarbonyl[2.2]paracyclophane (**3**), which furnishes the pseudo-geminal derivative **6** (E = Br) in 89% yield.[4] How do the yield and the directing effect depend on the distance between the directing group and the bonding position of the second substituent in the [*m.n*]paracyclophane? With the acetyl, the carboxy, and the methoxycarbonyl functions we obtained the results shown in Scheme 7.

Beginning with the [3.2]paracyclophane framework as a "molecular workbench", the results (first five experiments, formation of **37a**–**e**) in Scheme 7 demonstrate that it does not matter which carbonyl group is used as the directing substituent and whether it is anchored closer to the ethano or the propano bridge. As shown by the structural data in Scheme 2 there is only a very small difference in the intradeck distance between a [2.2]-, [3.2]-, and [3.3]paracyclophane. Consequently, the [3.3]cyclophanes **18** and **26** also



m	*n*	R	
3	2	CH_3	**14**
2	3	CH_3	**15**
3	2	OH	**24**
2	3	OH	**36**
3	3	CH_3	**18**
3	3	OH	**26**
4	2	CH_3	**16**
4	2	OH	**25**

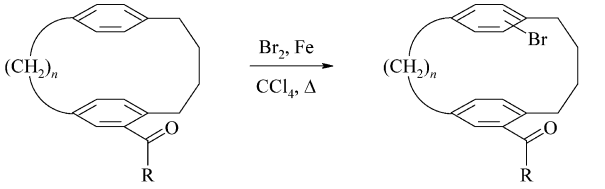
m	*n*	R	**37**, yield (%)
3	2	CH_3	**a** (68)
2	3	CH_3	**b** (59)
3	2	OCH_3[a)]	**c** (53)
2	3	OCH_3[a)]	**d** (56)
3	3	CH_3	**e** (46)
3	3	OCH_3[a)]	**f** (86)
4	2	CH_3	**g** (75)
4	2	OCH_3[a)]	**h** (60)

a) The carboxylic acid obtained was directly esterified by treatment with $SOCl_2$, then CH_3OH.

Scheme 7. Bromination of acyl[*m.n*]paracyclophanes.

give exclusively the pseudo-geminal bromides **37e** and **37f**, respectively. Even if one of the bridges is extended to a tetramethylene unit, as in **16** and **25**, the transannular directing effect (formation of **37g** and **37h**, respectively) does not break down as long as the primary substituent is bonded to the aromatic ring next to the ethano bridge. Again a look at the intra-annular distances summarized in Scheme 2 is instructive and reveals that the distance at the "shorter end" of a [4.2]paracyclophane hardly differs from the analogous distances measured for the lower homologues. Note that in all cases the isolated yields of the bromides **37** are acceptable to good; the structure determination of these doubly substituted [*m.n*]paracyclophanes follows from the spectroscopic data given in the Exp. Section.

However, the regioselectivity completely breaks down when a critical intradeck distance of about 4.0 Å is exceeded. This has been demonstrated by the model reactions of various [4.*n*]paracyclophane derivatives, as summarized in Scheme 8.



n	R	
2	CH_3	**17**
2	OH	**34**
2	OCH_3	**35**
4	CH_3	**21**
4	OH	**27**
4	OCH_3	**31**

n	R	**38**, yield (%)
2	CH_3	**a** (67)
2	OCH_3[a)]	**b** (86)
2	OCH_3	**c** (80)
4	CH_3	**d** (46)
4	OCH_3[a)]	**e** (51)
4	OCH_3	**f** (45)

a) The carboxylic acid obtained was directly esterified by treatment with $SOCl_2$, then CH_3OH.

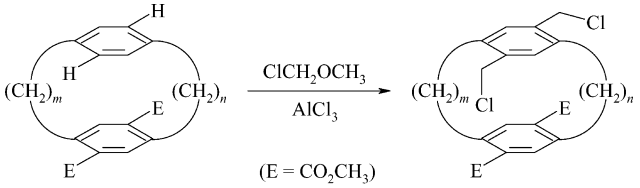
Scheme 8. Bromination of [2.4]paracyclophane derivatives.

In these substrates, the directing group is always next to a tetramethylene bridge and the inter-ring distance is adjusted by the opposing bridge. Regardless of whether this contains two or four methylene groups, in all cases a complex mixture of brominated products **38** is formed without any regiocontrol. That the unsubstituted benzene moiety has been attacked could be inferred primarily from the mass spectra, which showed that no peaks of fragments carrying both a bromine and an acetyl or ester substituent were registered. However, we could not isolate a pure regioisomer of the bromocyclophanes **38** from any of the reaction mixtures by MPLC chromatography or recrystallization. The majority of the ^{1}H NMR spectra of the products **38** clearly display several methyl singlets in the appropriate regions, which indicates the formation of different regioisomers (for details see the Exp. Section). In most cases these were registered as a broad singlet, but for **38e**, for example, four different, yet closely spaced singlets (δ = 3.86–3.90 ppm, see the Exp. Section) were clearly discernible, which shows that in this case all four possible aromatic positions of the unsubstituted benzene ring had been attacked. Likewise, the off-resonance ^{13}C NMR spectra showed different quartets for the methyl groups of the different regioisomers. Note also that the yields of the [4.4]paracyclophane derivatives **38d**,**e** are significantly reduced compared with their lower homologues.

Intra-annular Double Substitution

Besides studying their intra-annular interactions,[2] juxtaposed functional groups in [2.2]paracyclophanes can be used to construct additional bridges in these systems.[18] So far only polybridged cyclophanes with bridges of equal lengths have been prepared, all the way to the corresponding "superphanes" ([n_6]phanes with n = 2[19,20] and 3).[21,22] With the results obtained above it should be possible to construct superphanes in which the lengths of the bridges differ, which leads to a distortion of the aromatic rings different to that known previously for multibridged cyclophanes.[23] The first steps leading towards this goal are described below for the [m.n]paracyclophane diesters prepared in the preceding publication.[1]

As the test reaction we used chloromethylation because by this electrophilic aromatic substitution reaction, a substituent is introduced that has previously been employed successfully for bridge building;[18] the results are summarized in Scheme 9.



m	n	**39**, cyclophane	reaction conditions	**40**, yield (%)
2	2	**a**	1 h, r. t.	**a** (72)[18]
3	2	**b**	1 h, r. t.	**b** (75)
3	3	**c**	1 h, r. t.	**c** (73)
4	2	**d**	1 h, r. t.	**d** (78)
4	3	**e**	1 h, r. t.	**e** (83)
4	4	**f**	2 h, r. t.	**f** (0)

Scheme 9. Chloromethylation of [m.n]paracyclophane diesters.

Beginning with [2.2]paracyclophane diester **39a**, Boekelheide and Gray obtained the bis(chloromethyl) derivative **40a** on treatment with chloromethyl methyl ether in the presence of aluminum trichloride in good yield.[18] Essentially the same results were obtained when the bridges were successively extended from the [3.2]phane **39b** all the way to [4.3]paracyclophane (**39e**), the yield of the isolated dichlorides **40b**–**e** being practically identical. And again, as already seen in the series presented in Scheme 7 and Scheme 8, respectively, the pseudo-geminal directing effect breaks down completely for the [4.4]cyclophane **39f**: Not only had the reaction time to be extended to observe substitution, but the isomer **40f** could not be isolated from the complex product mixture, which was obtained in lower yield (66%) than in most of the previous experiments.

As no structural data were available for **39e** we calculated the distance on the basis of density functional theory. From the results of several theoretical studies,[24] it is well known that in the case of cyclophanes in general the inclusion of electron correlation is inevitable in order to reliably predict unknown geometrical parameters. In particular, the distance between the aromatic rings and therefore also the distance from the pseudo-geminal proton to the carbonyl oxygen atom of the ester group (i.e., the place to which the former has to go on electrophilic aromatic substitution according to the established mechanism, see Scheme 1), is

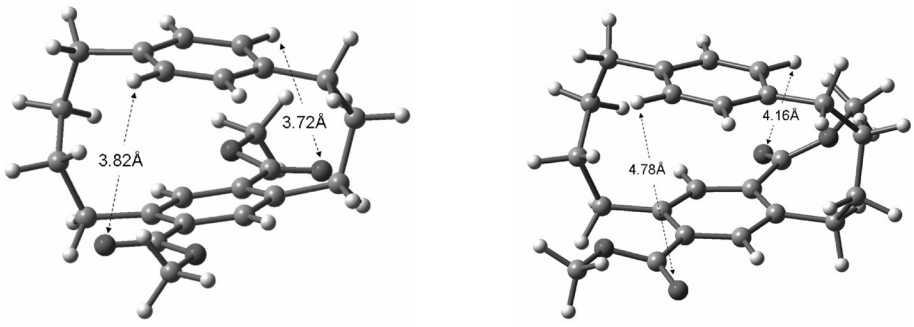


Figure 1. Selected (calculated) intra-annular distances in cyclophane diesters **39e** and **39f**.

very sensitive to the level of theory employed. Comparing the structural data from solid-state experiments with theoretical values, one has to note that, apart from crystal-packing effects (see below), the results of quantum chemical computations of cyclophanes are determined by a subtle equilibrium between attractive and repulsive nonbonded contributions. This is even more important when weak intramolecular C–H···O hydrogen bonds are present, as in the case of our diesters. We therefore applied one of the new hybrid meta functionals (M05-2X), which were developed by Zhao and Truhlar.[25] The result is shown in Figure 1. In the case of [4.3]cyclophane **39e** we still find distances between the pseudo-geminal proton and the carbonyl oxygen atom of the ester group well below 4.0 Å. For **39f**, starting with the single-molecule geometry optimization using our solid-state geometry (ref.[7]), the deviation from planarity of the ester groups relative to the aromatic rings is significantly reduced (from ≈150 to 168°) going from the solid-state to the gas-phase structure. The reason for this can be seen if one includes the next cyclophane neighbors in the analysis: The larger deviation from planarity in the solid state is counterbalanced by several intermolecular C–H···O contacts, which compensate for this distortion. Nevertheless, even in our single-molecule simulation, in which of course all intermolecular interactions are absent, the distance from the pseudo-geminal proton to the carbonyl oxygen atom of the ester group significantly exceeds the 4.0 Å boundary and any stereocontrolling effect is lost.

Structure Eludciation by NMR Spectroscopy

Structures of 14 and 16

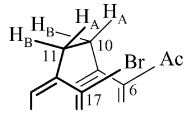
The structure of **16** was derived from its NMR spectra as follows. The four ^{1}H chemical shifts of the ethano bridge were identified from a H,H-COSY spectrum and had values of δ = 3.90, 3.07–3.04 (2 H), and 2.75 ppm. The strong deshielding (δ = 3.90, $\Delta\delta$ = +0.90 ppm) of one of these protons and the moderate shielding of its geminal partner (δ = 2.75, $\Delta\delta$ = –0.25 ppm) relative to the chemical shift of the ethano bridge (δ = 3.00 ppm)[1] in hydrocarbon **9** are typical for ethano protons situated *ortho* with respect to a substituent containing a carbonyl group. Very similar values are observed for **13**,[26] for which δ(2-H$_{syn}$) = 3.96 ($\Delta\delta$ = +0.89) and δ(2-H$_{anti}$) = 2.83 ppm ($\Delta\delta$ = –0.24 ppm), compared with hydrocarbon **7**, for which δ(2-H) = 3.07 ppm. The butano proton chemical shifts in **16** differ little from those of **9**, all chemical shift differences $|\Delta\delta|$ being less than or equal to 0.28 ppm. These observations conclusively prove that the acetyl group in **16** is situated *ortho* to the ethano bridge. The same is true for the acetyl derivative **14** of [3.2]paracyclophane. Its structure was deduced in an analogous manner to that of **16**.

Structure of 23

The structure of **23** was deduced in a similar way to that of **16**, that is, by proving that the most deshielded aliphatic proton, 11-H$_a$ (δ = 3.39 ppm), is part of the four-spin system of the ethano bridge. However, the effect of the bromo substituent upon the chemical shift of the *syn* proton of its *ortho*-CH$_2$ group is distinctly smaller than the effect of the acetyl group in **16**. Hence, additional evidence for the structure of **23** was obtained from an NOE difference (NOEDIF) experiment: Irradiation of the resonance of the isolated aromatic proton, 6-H, effected an enhancement of a proton signal (4-H$_a$) belonging to the eight-spin system of the butano bridge. The latter spin system was identified through a COSY experiment. The NOEDIF experiment also allowed the assignment of 17-H, the proton pseudogeminal to 6-H. In combination with the $^1J_{CH}$ and $^nJ_{CH}$ correlation spectra (HETCOR and COLOC), the ^{1}H and ^{13}C NMR spectra of **23** could then be completely assigned (see the Exp. Section). The positional isomer 6-bromo[4.2]paracyclophane is described in ref.[1]

Structure of 37a

The four-spin system of the ethano protons of **37a** (see Scheme 10) was analyzed iteratively by fitting the calculated transition frequencies to the experimental line positions. The results (Table 1) showed that the two most deshielded of these four protons, that is, the proton *syn* to the acetyl group (10-H$_A$, δ = 4.220 ppm) and the proton *syn* to the bromo substituent (11-H$_A$, δ = 3.401 ppm) share a coupling constant of 10.1 Hz. According to our earlier findings[27] this proves the *cis* orientation of these protons and, hence, the acetyl and the bromo substituent can only be pseudogeminal to one another.



37a

Scheme 10. The ethano bridge at the substituted end of **37a**.

Table 1. ^{1}H NMR parameters of the ethano bridge of **37a**.[a]

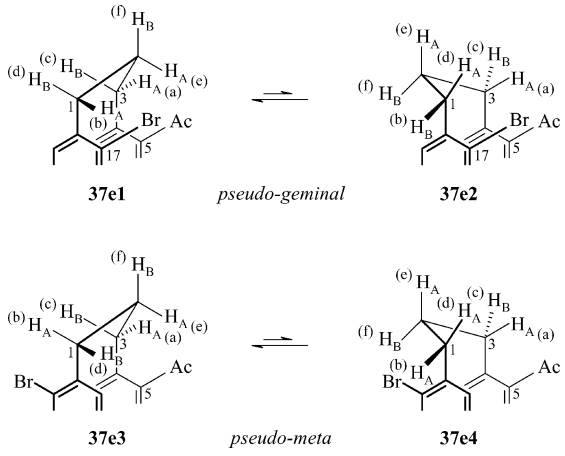
Proton(s)	δ [ppm]
10-H$_A$	4.220
10-H$_B$	2.921
11-H$_A$	3.401
11-H$_B$	2.836
	J [Hz]
10-H$_A$,10-H$_B$	–13.47
10-H$_A$,11-H$_A$	10.10
10-H$_A$,11-H$_B$	4.51
10-H$_B$,11-H$_A$	3.96
10-H$_B$,11-H$_B$	10.53
11-H$_A$,11-H$_B$	–13.52

[a] Obtained by iterative analysis using the LAOCOON procedure; program: Bruker PANIC85, final rms error between calculated and experimental line positions 0.020 Hz. Probable errors in the chemical shifts and coupling constants are <<0.0001 ppm and 0.013–0.016 Hz, respectively.

Structure of 37e

The structure of **37e** was derived as follows. According to an H,H-COSY experiment the two most deshielded ali-

phatic protons both belong to the six-spin system of the propano bridge and each aromatic ring carries one of the two substituents acetyl and bromo. This only leaves the pseudo-geminal and the pseudo-*meta* configuration for **37e**. An attempt to reach a decision between these possibilities on the basis of NOEDIF experiments gave inconclusive results. As proved on numerous previous occasions the most deshielded bridge protons are those that are *syn*-oriented (named H_A) relative to the *ortho* substituent, and the deshielding effect of an acetyl group is distinctly larger than that of a bromo substituent. Similar to the case of **37a** the question of the relative orientation of Ac and Br can be reduced to the question of the *cis* or *trans* orientation of the deshielded protons 1-H_A and 3-H_A at the propano bridge. The *cis* (*trans*) orientation of these protons is synonymous with the pseudo-geminal (pseudo-*meta*) orientation of the Ac and Br substituents. The vicinal H,H coupling constants in the propano bridge and their dependence on torsional angles were used to derive the relative orientation of 1-H_A and 3-H_A. This required us to consider, for both the pseudo-geminal and the pseudo-*meta* isomer, the two conformations that the propano moiety can assume, that is, **37e1** and **37e2** (pseudo-geminal) and **37e3** and **37e4** (pseudo-*meta*; see Scheme 11). The signals of the bridge protons are rather broad at 400 MHz and room temperature, which indicates that a conformational process occurs at an intermediate rate. To facilitate the analysis, the NMR spectrum was therefore recorded at +50 °C at which temperature the signals appeared much sharper. The six-proton spin system of which the two most deshielded protons are a part was analyzed with the aid of decoupling experiments and then refined iteratively. The part of the experimental spectrum of interest and the best-fit computed spectrum are shown in Figure 2; the spectral parameters are given in Table 2.



Scheme 11. Bridge-flipping equilibria in the pseudo-geminal and pseudo-meta isomers of **37e**.

The proton multiplets are labeled a–f in the order of increasing shielding. Multiplets a and b belong to 3-H_A and 1-H_A, respectively, as explained above. Multiplets c and d belong to their geminal partners 3-H_B and 1-H_B, respectively, which follows from the characteristic coupling constants of –14 to –15 Hz. As the substituents Ac and Br at the benzene rings should have little electronic and only a conformational influence on the magnitudes of the bridge proton coupling constants, the following pairs of J_{HH}

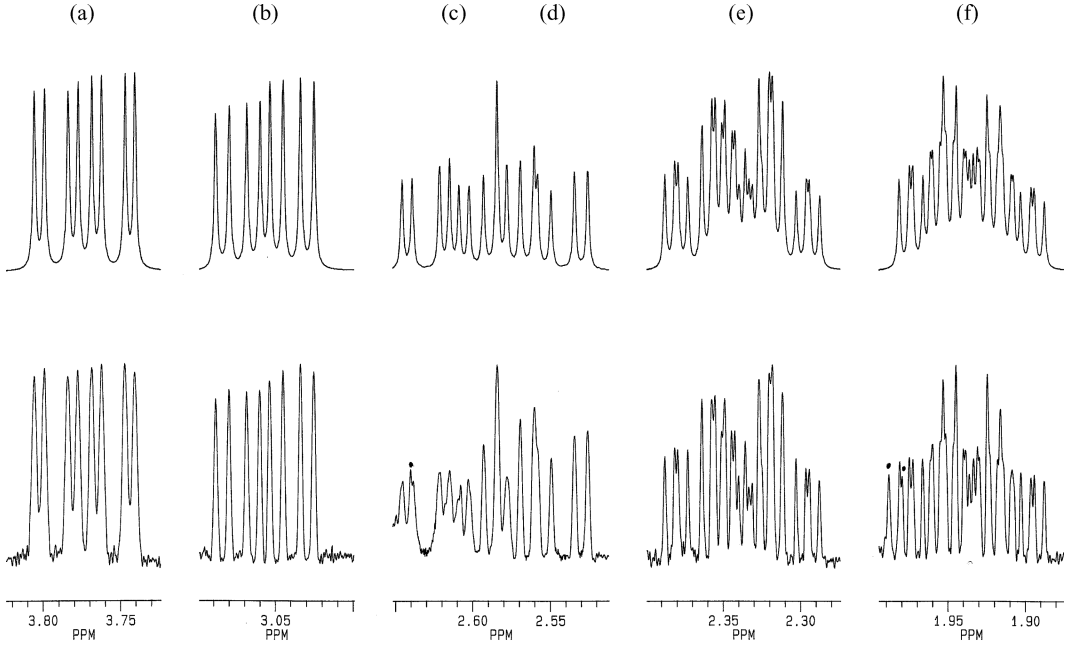


Figure 2. Part of the experimental (bottom) and calculated (top) ^{1}H NMR spectrum of **37e** at 400 MHz and +50 °C in $CDCl_3$. The multiplets of the propano bridge protons *ortho* to the Ac and Br substituents are labelled (a)–(f) in the order of increasing shielding. The rms error between the calculated and experimental line positions is 0.037 Hz. The three lines marked with a dot are not part of the spin system in question.

Table 2. ^{1}H NMR parameters of the propano bridge of **37e**.[a]

Signal(s)	Proton(s)	δ [ppm]
a	3-H_A[b]	3.773
b	1-H_A	3.057
c	3-H_B	2.612
d	1-H_B	2.560
e	2-H_A	2.339
f	2-H_B	1.936
		J [Hz]
a,c	3-H_A,3-H_B	–14.82
a,e	2-H_A,3-H_A	2.61
a,f	2-H_B,3-H_A	8.71
b,d	1-H_A,1-H_B	–14.03
b,e	1-H_A,2-H_A	3.47
b,f	1-H_A,2-H_B	8.00
c,e	2-H_A,3-H_B	9.75
c,f	2-H_B,3-H_B	2.61
d,e	1-H_B,2-H_A	9.60
d,f	1-H_B,2-H_B	3.54
e,f	2-H_A,2-H_B	–14.88

[a] See footnote a of Table 1; coupling constants not listed had calculated magnitudes of <0.03 Hz; final rms error between the calculated and experimental line positions is 0.037 Hz. Probable errors of the chemical shifts and coupling constants are <<0.0001 ppm and <0.04 Hz, respectively. [b] 2-H_A and 3-H_A are *syn* to the acetyl group, 1-H_A is *syn* to the bromo substituent.

should have similar values if **37e** has a pseudo-geminal configuration (the experimental values are given in parentheses): J_{ae} and J_{be} (2.61 and 3.47 Hz), J_{ce} and J_{de} (9.75 and 9.60 Hz), J_{af} and J_{bf} (8.71 and 8.00 Hz), and J_{cf} and J_{df} (2.61 and 3.54 Hz). This is indeed the case, whereas the corresponding similarities that one would expect for the pseudo-*meta* configuration were not observed. The postulated similarities are independent of whether conformation **37e1** or **37e2** is favored. Hence, **37e** is the pseudo-geminal stereoisomer. Force field calculations (MMX87[28], Serena Software) of the conformers and application of the torsional angle dependence of J_{HH} according to Haasnoot et al.[29] gave the best agreement with experimental findings for an equilibrium formed between **37e** and **37e2** in a ratio of 57:43. Knowing this, one can then assign multiplets e and f to 2-H_A and 2-H_B, respectively.

Structure of 37g

This structure was derived in a way similar to those of the preceding compounds with substituents *ortho* to the ethano bridge. The two most deshielded protons, 11-H_A and 12-H_A, are part of a four-spin system and are *cis* to each other on account of their mutual coupling constant of 9.0 Hz; J(11-H_B,12-H_B) is 9.4 Hz (also *cis*). This means that the substituents are pseudo-geminal with respect to one another. For detailed parameters, see the Exp. Section.

Conclusions

By studying the electrophilic aromatic substitution (Friedel–Crafts acylation, bromination, and chloromethylation) of [*m.n*]paracyclophanes it has been shown that a) monosubstitution takes place with ease as long as the lengths of both bridges do not exceed three atoms, b) whenever there is a choice, the entering substituents bind to the aromatic position that is closest to the shortest bridge, c) when an electrophilic substitution is carried out with a [*m.n*]paracyclophane methyl ketone, carboxylic acid, or ester, the second substituent is introduced regioselectively into the pseudo-geminal position as long as the first substituent is next to a bridge not exceeding m = 3 (propano), d) as soon as the directing substituent is positioned next to a butano bridge (m = 4), the directing effect breaks down completely, and e) for double substitution very similar results are observed, with the [4.3]cyclophane constituting the limiting case as far as regioselectivity is concerned. To explain these effects we propose that either the second aromatic ring or the existing substituent(s) function as neighboring groups, picking up the proton to be substituted. For this intra-annular effect to take place the distance between the "decks" of a [*m.n*]paracyclophane must not exceed 3.7–4.0 Å.

Experimental Section

General Remarks: See this section in the preceding paper.[1] The following compounds were prepared as described in the preceding paper: **8** (E = H), **9**, **10**, **11**, **12**, **32**, and **39a**–**f**.[1] The bridge protons labeled with A in the ^{1}H NMR spectra point towards the respective functional group, those with B point away from the substituent. Carbon atom numbering in the second aromatic cyclophane ring follows the same clockwise or anticlockwise sense as the first ring when both are viewed from the same direction.

6-Acetyl[3.2]paracyclophane (14): A mixture of aluminum trichloride (1.10 g, 8.25 mmol) and acetyl chloride (0.6 mL, 8.41 mmol) in dichloromethane (20 mL) was stirred for 30 min under nitrogen. Then [3.2]paracyclophane (**8**, E = H; 1.54 g, 6.93 mmol) in dichloromethane (10 mL) was added dropwise and the mixture stirred for 30 min at room temp. For work-up the reaction suspension was added to crushed ice to which a few mL of concd. hydrochloric acid had been added, the organic phase was separated, and the aqueous phase extracted several times with dichloromethane. The combined organic layers were washed with water, saturated hydrogen carbonate solution, and brine, and dried with sodium sulfate. After solvent removal in vacuo the remainder was purified by thick-layer chromatography on silica gel with dichloromethane. Fraction 1: starting material (140 mg, 9%); fraction 2: **14**, 1.30 g (71%), colorless rhombs (ethanol), m.p. 114 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.08–2.13 (m, 2 H, 2-H), 2.47 (s, 3 H, CH_3), 2.65–2.78 (m, 5 H, 10-H_B, 1-, 3-H), 3.04 (m, 2 H, 11-H), 3.92 (m, 1 H, 10-H_A), 6.31 (dd, J = 7.8, 1.7 Hz, 1 H), 6.43 (m, 2 H), 6.47 (dd, J = 7.8, 1.8 Hz, 1 H), 6.56 (dd, J = 7.8, 1.8 Hz, 1 H, 8-, 13-, 14-, 16-, 17-H), 6.72 (dd, J = 7.7, 1.6 Hz, 1 H, 9-H), 7.05 (d, J = 1.7 Hz, 1 H, 5-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.8 (CH_3), 32.8, 33.4, 34.5, 35.2, 35.4 (CH_2, C-1, -2, -3, -10, -11), 129.7, 130.0, 130.8, 131.7, 132.2, 133.9, 135.9 (CH, C-5, -8, -9, -13, -14, -16, -17), 137.7, 137.8, 138.9, 139.5, 140.0 (C_q, C-4, -6, -7, -12, -15), 200.2 (C_q, C=O) ppm. IR (KBr): $\tilde{\nu}$ = 2920 (s), 2905 (m), 2890 (m), 2850 (m), 1673 (vs), 1555 (m), 1490 (m), 1440 (s), 1350 (s), 1260 (m), 950 (m), 885 (s), 835 (m), 800 (m) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 278 (3.59), 206 (4.56) nm. MS (EI, 70 eV): m/z (%) = 264 (100) $[M]^+$, 149 (6), 146 (42), 117 (6), 91 (3). $C_{19}H_{20}O$ (264.37): calcd. C 86.32, H 7.63; found C 86.21, H. 7.70.

7-Acetyl[4.2]paracyclophane (16): According to the method described for the synthesis of **14**, from [4.2]paracyclophane (**9**; 1.85 g,

7.83 mmol) with aluminum trichloride (1.57 g, 11.7 mmol) and acetyl chloride (0.8 mL, 11.2 mmol) was obtained 1.95 g (89%) of **16**; colorless solid, m.p. 123 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16, 1.70 (both narrow m, 2 H each, 2-, 3-H), 2.12, 2.42 (both m, 2 H each, 1-, 4-H), 2.50 (s, 3 H, CH_3), 2.75 (m, 1 H, 11-H_B), 3.06 (m, 2 H, 12-H), 3.90 (m, 1 H, 11-H_A), 6.32, 6.37, 6.59, 6.66 (dd, J = 8, 2 Hz, 1 H each, 14-, 15-, 17-, 18-H), 6.48 (d, J = 8 Hz, 1 H, 9-H), 6.57 (dd, J = 8, 2 Hz, 1 H, 10-H), 7.06 (d, J = 2 Hz, 1 H, 6-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.8 (CH_3), 28.8, 29.1 (CH_2, C-2, -3), 33.0 (CH_2, C-12), 34.3, 35.20, 35.23 (CH_2, C-1, -4, -11), 127.7 (CH, C-17), 128.1 (CH, C-15), 129.7 (CH, C-18), 130.2 (CH, C-6), 130.5 (CH, C-14), 131.6 (CH, C-10), 134.6 (CH, C-9), 137.4, 138.1, 139.0, 139.6, 140.1 (C_q, C-5, -7, -8, -13, -16), 200.3 (C_q, C=O) ppm. IR (KBr): $\tilde{\nu}$ = 2930 (s), 2860 (m), 1670 (vs), 1560 (m), 1500 (m), 1490 (s), 1530 (s), 1260 (vs), 1220 (m), 950 (s), 880 (s), 810 (s), 770 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 278 (100) $[M]^+$, 147 (11), 146 (51), 145 (80), 131 (27), 116 (27), 115 (26), 105 (26), 104 (26), 91 (16).

7-Acetyl[4.3]paracyclophane (19) and 6-Acetyl[4.3]paracyclophane (20): According to the method described for the synthesis of **14**, from [4.3]paracyclophane (**11**, 0.270 g, 1.08 mmol) with aluminum trichloride (0.230 g, 1.72 mmol) and acetyl chloride (0.2 mL, 2.80 mmol) was obtained after 45 min at room temp. a mixture (0.180 g, 57%) of **19** and **20**. The product ratio (7:1) was determined by ^{1}H NMR analysis, as described in the main section. Other spectroscopic data: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.40–1.75 (m, CH_2), 2.05–2.90 (m, CH_2), 2.51 (s) and 2.52 (s, CH_3), 3.20–3.30 (m, CH_2), 3.54–3.64 (m, CH_2), 6.45–7.15 (m, arom. H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.8, 29.2, 29.47, 29.50, 29.6, 30.1, 32.8, 33.9, 35.5, 35.59, 35.64, 35.9, 36.0 (CH_2), 127.9, 128.23, 128.26, 128.7, 129.0, 129.2, 129.4, 129.6, 130.2, 131.4, 131.7, 132.3, 132.9 (CH), 136.7, 137.1, 138.5, 138.7, 138.8, 138.9, 139.0, 139.1, 139.3 (C_q), 202.1 (C_q, C=O) ppm.

The mixture could not be separated by chromatography (column, thick-layer, MPLC) on silica gel.

6-Bromo[3.2]paracyclophane (22): To a suspension of iron powder (ca. 0.1 g) in dichloromethane (10 mL) was added at room temp. a fraction (5 mL) of a solution of bromine (0.160 g, 1.00 mmol) in carbon tetrachloride (21 mL). After stirring for 15 min, **8** (E = H; 0.200 g, 0.89 mmol) was added to the reaction mixture, the temperature was increased to reflux, and the remainder of the bromine solution was added within 5 min. After heating at reflux for a further 30 min period, the reaction mixture was cooled to room temp. and a solution of sodium thiosulfate was added. The organic phase was separated, washed with brine, and subjected to the usual work-up. The remaining solid was purified by thick-layer chromatography on silica gel with dichloromethane to give 0.133 g (49%) of **22**; colorless needles (ethanol), m.p. 117 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.95–2.12 (m, 2 H, 2-H), 2.55–2.77 (m, 5 H), 2.90–3.10 (m, 2 H, 1-, 3-, 11-H, 10-H_B), 3.39 (m, 1 H, 10-H_A), 6.36 (d, J = 7.6 Hz, 1 H, 8-H), 6.38 (dd, J = 7.8, 1.8 Hz, 1 H), 6.56–6.60 (m, 2 H), 6.64 (dd, J = 7.8, 1.8 Hz, 1 H, 9-, 13-, 14-, 16-H), 6.68 (d, J = 1.5 Hz, 1 H, 5-H), 6.99 (dd, J = 7.8, 1.8 Hz, 1 H, 17-H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 32.1, 32.7, 34.6, 35.0, 35.4 (CH_2, C-1, -2, -3, -10, -11), 129.1, 129.2, 129.9, 132.5, 134.0, 134.6 (CH, C-5, -8, -9, -13, -14, -16, -17), 126.4 (C_q, C-6), 136.8, 136.9, 139.8, 141.9 (C_q, C-4, -7, 12, -15) ppm. IR (KBr): $\tilde{\nu}$ = 2930 (vs), 2920 (s), 2890 (s), 2850 (s), 1600 (m), 1440 (s), 1040 (s), 1020 (m), 880 (s), 825 (s), 790 (m) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 198 (4.56) nm. MS (EI, 70 eV): *m*/*z* (%) = 302 (45) [M, ^{81}Br]$^+$, 300 (45) [M, ^{79}Br]$^+$, 222 (13), 221 (9), 209 (9), 198 (21), 196 (21), 131 (39), 118 (68), 117 (100). $C_{17}H_{17}Br$ (301.23): calcd. C 67.79, H 5.69, Br 26.53; found C 67.51, H 5.64, Br 26.44.

7-Bromo[4.2]paracyclophane (23): According to the procedure described for the synthesis of **22**, prepared from **9** (0.236 g, 1.00 mmol) and bromine (0.200 g, 1.25 mmol), 0.190 g (60%) of **23** was obtained; colorless needles (ethanol), m.p. 101 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15 (narrow m, 1 H, 3-H), 1.16 (narrow m, 1 H, 2-H), 1.69 (narrow m, 1 H, 3-H), 1.71 (narrow m, 1 H, 2-H), 2.06 [br. t, J(av.) = 11.9 Hz, 1 H, 4-H_B], 2.11 [br. t, J(av.) = 12.0 Hz, 1 H, 1-H_A], 2.36 (dd, J = 12.5, 6.3 Hz, 1 H, 4-H_A), 2.43 (dd, J = 12.6, 6.1 Hz, 1 H, 1-H_B), 2.80 (ddd, J = 13.3, 10.0, 7.6 Hz, 1 H, 11-H_B), 3.01 (ddd, J = 13.1, 10.0, 2.2 Hz, 1 H, 12-H_B), 3.17 (ddd, J = 13.1, 9.6, 7.6 Hz, 1 H, 12-H_A), 3.39 (ddd, J = 13.3, 9.6, 2.2 Hz, 1 H, 11-H_A), 6.41 (dd, J = 7.7, 1.7 Hz, 1 H, 10-H), 6.45 (d, J = 7.7 Hz, 1 H, 9-H), 6.49 (dd, J = 7.7, 1.8 Hz, 1 H, 17-H), 6.64 (dd, J = 7.8, 1.8 Hz, 1 H, 15-H), 6.67 (dd, J = 7.8, 1.7 Hz, 1 H, 14-H), 6.79 (d, J = 1.7 Hz, 1 H, 6-H), 6.91 (dd, J = 7.7, 1.7 Hz, 1 H, 18-H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.8 (CH_2, C-2), 29.0 (CH_2, C-3), 31.8 (CH_2, C-12), 34.7 (CH_2, C-11), 35.0 (CH_2, C-4), 35.4 (CH_2, C-1), 125.4 (C_q, C-7), 127.1 (CH, C-10), 128.1 (CH, C-15), 128.3 (CH, C-17), 129.2 (CH, C-18), 130.7 (CH, C-14), 132.1 (CH, C-6), 133.4 (CH, C-9), 137.3 (C_q, C-8), 137.4 (C_q, C-13), 140.1 (C_q, C-16), 142.2 (C_q, C-5) ppm. IR (KBr): $\tilde{\nu}$ = 2930 (vs), 2855 (vs), 1510 (m), 1450 (s), 1440 (m), 1400 (m), 880 (m), 860 (m), 815 (s) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 198 (3.56) nm. MS (EI, 70 eV): *m*/*z* (%) = 316 (100) [M, ^{81}Br]$^+$, 314 (100) [M, ^{79}Br]$^+$, 288 (7), 286 (7), 235 (61), 207 (12), 193 (12), 184 (17), 131 (17), 106 (65), 91 (12). $C_{18}H_{19}Br$ (315.25): calcd. C 68.58, H 6.07; found C 68.47, H 6.07.

General Procedure for the Bromoform Reaction of Methyl Ketones 14, 16, 18, and 21: A solution of potassium hypobromite (100 mmol KOH, 20 mmol bromine, 100 mL of ice water) was added to a solution of the respective acetylcyclophane (1.0 mmol) in dioxane (50 mL) at 5 °C within 30 min. After stirring for 4 h at room temp. sodium sulfite solution (10% in water) was added and the reaction mixture was extracted with chloroform. The aqueous phase was acidified to pH = 1 (concd. HCl), and the precipitated carboxylic acid removed by suction filtration. After washing the precipitate with water several times, the raw product was dissolved in dichloromethane and purified by column chromatography (silica gel) or recrystallization.

[3.2]Paracyclophane-6-carboxylic Acid (24): According to the General Procedure given above the carboxylic acid **24** was prepared (0.383 g, 97%) from methyl ketone **14** (0.390 g, 1.47 mmol); colorless needles (ethyl acetate), m.p. 204 °C. ^{1}H NMR (400 MHz, [D_6]-DMSO): δ = 1.99–2.07 (m, 2 H, 2-H), 2.60–2.74 (m, 5 H), 2.81–2.89 (m, 1 H), 2.98–3.07 (m, 1 H, 1-, 3-, 11-H, 10-H_B), 3.93–4.00 (m, 1 H, 10-H_A), 6.29 (dd, J = 7.7, 1.7 Hz, 1 H), 6.42–6.52 (m, 3 H), 6.58 (dd, J = 7.8, 1.7 Hz, 1 H), 6.77 (dd, J = 7.7, 1.8 Hz, 1 H, 8-, 9-, 13-, 14-, 16-, 17-H), 7.19 (d, J = 1.9 Hz, 1 H, 5-H), 12.44 (br. s, 1 H, COOH) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 32.2, 32.9, 33.9, 34.3, 34.7 (CH_2, C-1, -2, -3, -10, -11), 129.6, 129.8, 130.6, 131.9, 132.3, 133.5, 135.3 (CH, C-5, -8, -9, 13, -14, -16, -17), 130.9 (C_q, C-6), 136.9, 139.2, 139.3, 139.5 (C_q, C-4, -7, -12, -15), 167.9 (C_q, COOH) ppm. IR (KBr): $\tilde{\nu}$ = 3425 (br. m), 3070 (w), 2930 (m), 2910 (m), 2850 (m), 1690 (vs), 1600 (w), 1305 (m), 1275 (m), 870 (w), 800 (w) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 269 (3.41), 202 (4.50) nm. MS (EI, 70 eV): *m*/*z* (%) = 266 (79) $[M]^+$, 248 (12), 161 (32), 148 (14), 118 (27), 117 (26), 106 (35), 105 (100). $C_{18}H_{18}O_2$ (266.34): calcd. C 81.17, H 6.81; found C 60.37, H 6.78.

[4.2]Paracyclophane-7-carboxylic Acid (25): According to the General Procedure (see above) the carboxylic acid **25** was prepared (0.498 g, 82%) from methyl ketone **16** (0.600 g, 2.16 mmol); colorless rhombs (ethyl acetate), m.p. 178 °C. ^{1}H NMR (400 MHz,

$CDCl_3$): δ = 1.05–1.30 (m, 2 H), 1.65–1.85 (m, 2 H), 2.05–2.20 (m, 2 H), 2.38–2.58 (m, 2 H, 1-, 2-, 3-, 4-H), 2.80–2.90 (m, 1 H), 3.10–3.20 (m, 2 H, 11-H_B, 12-H), 4.10–4.18 (m, 11-H_A), 6.47–6.75 (several m, 6 H, 9-, 10-, 14-, 15-, 17-, 18-H), 7.49 (d, J = 1.6 Hz, 1 H, 6-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.9, 29.1, 33.2, 34.9, 35.2, 35.4 (CH_2, C-1, -2, -3, -4, -11, -12), 128.2 (2 C), 130.2, 130.5, 131.9, 133.0, 134.6 (CH, C-6, -9, -10, -14, -15, -17, -18), 128.9 (C_q, C-7), 138.0, 139.9, 140.5, 141.4 (C_q, C-5, -8, -13, -16), 173.3 (C_q, COOH) ppm. IR (KBr): $\tilde{\nu}$ = 2934 (m), 2922 (m), 1678 (vs), 1443 (m), 1417 (m), 1304 (m), 1278 (m), 886 (w) cm^{-1}. UV (acetonitrile): λ_{max} (logε) = 196 (4.74) nm. MS (EI, 70 eV): m/z (%) = 280 (41) $[M]^+$, 256 (4), 189 (5), 188 (9), 175 (10), 149 (23), 131 (20), 105 (100). $C_{19}H_{20}O_2$ (280.37): calcd. C 81.40, H 7.19; found C 81.09, H 7.22.

[3.3]Paracyclophane-5-carboxylic Acid (26): According to the above procedure carboxylic acid **26** was prepared (0.290 g, 94%) from methyl ketone **18** (0.305 g, 1.10 mmol); colorless rhombs (ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.24–2.33 (m, 4 H), 2.54–2.67 (m, 2 H), 2.68–2.96 (m, 5 H, 1-, 2-, 10-, 11-, 12-H, 3-H_B), 3.81–3.90 (m, 1 H, 3-H_A), 6.67–6.83 (m, 6 H, 6-, 8-, 9-, 14-, 15-, 17-, 18-H), 7.55 (d, J = 1.6 Hz, 1 H, 6-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.9, 29.4, 34.6, 35.4, 35.5, 35.9 (CH_2, C-1, -2, -3, -10, -11, -12), 128.9, 129.1, 129.6, 130.5, 132.2, 133.5, 134.7 (CH, C-6, -8, -9, -14, -15, -17, -18), 127.3 (C_q, C-5), 138.2, 138.6, 139.0, 142.0 (C_q, C-4, -7, -13, -16), 173.7 (C_q, COOH) ppm; this compound has been described previously in the literature.[12]

[4.4]Paracyclophane-6-carboxylic Acid (27): According to the General Procedure (see above) the carboxylic acid **27** was prepared (0.700 g, 88%) from methyl ketone **21** (0.790 g, 1.10 mmol); slightly yellow plates (ethyl acetate), m.p. 201 °C. ^{1}H NMR (400 MHz, $[D_6]$DMSO): δ = 1.26–1.72 (m, 8 H), 1.95–2.06 (m, 1 H), 2.06–2.25 (m, 3 H), 2.25–2.43 (m, 3 H, 1-, 2-, 3-, 11-, 12-, 13-, 14-H, 4-H_B), 3.30–3.48 (m, 1 H, 4-H_A), 6.54–6.70 (m, 4 H, 16-, 17-, 19-, 20-H), 6.71 (d, J = 7.7 Hz, 1 H, 10-H), 6.80 (dd, J = 7.7, 1.8 Hz, 1 H, 9-H), 7.27 (d, J = 1.7 Hz, 1 H, 7-H), 12.48 (br. s, 1 H, COOH) ppm. ^{13}C NMR (101 MHz, $[D_6]$DMSO): δ = 27.9, 28.1, 28.2, 28.4, 32.1, 34.2, 34.4, 34.5 (CH_2, C-1, -2, -3, -4, -11, -12, -13, -14), 127.8, 127.9, 128.4, 130.6, 131.1, 131.3 (CH, C-7, -9, -10, -16, -17, -19, -20), 128.9 (C_q, C-6), 138.6, 138.8, 138.9, 140.3 (C_q, C-5, -8, -15, -18), 168.8 (C_q, COOH) ppm. MS (EI, 70 eV): m/z (%) = 308 (100) $[M]^+$, 291 (15), 290 (36), 263 (17), 185 (12), 175 (15), 148 (18), 145 (25), 131 (25), 117 (35), 105 (60), 104 (41), 91 (53); this compound has been described previously in the literature.[13]

General Procedure for the Esterification of the Carboxylic Acids 24–27: The corresponding carboxylic acid (1.0 mmol) was heated under nitrogen with thionyl chloride (2 mL) for 30 min at reflux. The excess thionyl chloride was distilled off under a slight vacuum and to the remaining reaction mixture was added methanol (10 mL, anhydrous). After heating at reflux for 30 min excess alcohol was removed by vacuum distillation. The remaining raw product was purified by chromatographic methods (thick layer, MPLC on silica gel).

Methyl [3.2]Paracyclophane-6-carboxylate (28): According to the procedure for **24**–**27** the methyl ester **28** was prepared (0.210 g, 91%) from carboxylic acid **24** (0.219 g, 0.82 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.04–2.13 (m, 2 H, 2-H), 2.67–2.75 (m, 5 H), 2.92–3.00 (m, 1 H), 3.05–3.12 (m, 1 H, 1-, 3-, 11-H, 10-H_B), 3.89 (s, 3 H, OCH_3), 3.99–4.07 (m, 1 H, 10-H_A), 6.34 (dd, J = 7.8, 1.7 Hz, 1 H), 6.41–6.59 (m, 4 H), 6.74 (dd, J = 7.8, 1.8 Hz, 1 H, 8-, 9-, 13-, 14-, 16-, 17-H), 7.25 (d, J = 1.8 Hz, 1 H, 5-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 32.7, 33.5, 34.7, 35.1, 35.4 (CH_2, C-1, -2, -3, -10, -11), 51.7 (OCH_3), 130.0, 131.1, 132.0, 132.5, 134.0, 135.6 (CH, C-5, -8, -9, -13, -14, -16, -17), 130.3 (C_q, C-6), 137.5, 139.6, 140.0, 140.1 (C_q, C-4, -7, -12, -15), 167.5 (C_q, C=O) ppm. IR (KBr): $\tilde{\nu}$ = 2944 (m), 2931 (m), 2989 (m), 1712 (vs), 1434 (s), 1291 (m), 1269 (s), 1252 (s), 1196 (s), 1077 (s), 785 (m) cm^{-1}. UV (acetonitrile): λ_{max} (logε) = 203 (4.69) nm. MS (EI, 70 eV): m/z (%) = 280 (100) $[M]^+$, 266 (17), 265 (90), 147 (21), 119 (21), 117 (35), 115 (17), 91 (19). $C_{19}H_{20}O_2$ (280.37): calcd. C 81.40, H 7.19; found C 81.11, H 7.20.

Methyl [4.2]Paracyclophane-7-carboxylate (29): According to the procedure for **24**–**27** methyl ester **29** was prepared (0.160 g, 76%) from carboxylic acid **25** (0.200 g, 0.71 mmol); m.p. 73–74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15 (m, 2 H), 1.74 (m, 2 H, 2-, 3-H), 2.05–2.15 (m, 2 H), 2.41–2.51 (m, 2 H, 1-, 4-H), 2.75–2.83 (m, 1 H), 2.97–3.15 (m, 2 H, 12-H, 11-H_B), 3.92 (s, 3 H, OCH_3), 4.00 (ddd, J = 12.8, 9.3, 1.6 Hz, 1 H, 11-H_A), 6.36 (dd, J = 7.7, 1.6 Hz, 1 H), 6.43 (dd, J = 7.7, 1.8 Hz, 1 H), 6.59–6.63 (m, 2 H), 6.68–6.72 (m, 1 H, 10-, 14-, 15-, 17-, 18-H), 6.50 (d, J = 7.7 Hz, 1 H, 9-H), 7.31 (d, J = 1.8 Hz, 1 H, 6-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.9, 29.1 (CH_2, C-2, -3), 33.3, 34.7, 35.2, 35.4 (CH_2, C-1, -4, -11, -12), 51.7 (OCH_3), 128.16, 128.20, 130.1, 130.5, 130.9, 132.0, 134.3 (CH, C-6, -9, -10, -14, -15, -17, -18), 130.0 (C_q, C-7), 138.0, 139.8, 140.3 (2 C) (C_q, C-5, -8, -13, -16), 167.8 (C_q, C=O) ppm. IR (KBr): $\tilde{\nu}$ = 2960 (m), 2945 (s), 2935 (s), 2921 (s), 2855 (m), 1714 (vs), 1296 (m), 1273 (s), 1259 (s), 1201 (s), 1077 (s), 814 (m) cm^{-1}. UV (acetonitrile): λ_{max} (logε) = 196 (4.75) nm. MS (EI, 70 eV): m/z (%) = 294 (100) $[M]^+$, 279 (62), 162 (12), 147 (10), 131 (12), 119 (26), 104 (28). $C_{20}H_{22}O_2$ (294.39): calcd. C 81.60, H 7.53; found C 81.58, H 7.59.

Methyl [3.3]Paracyclophane-5-carboxylate (30): According to the procedure for **24**–**27** methyl ester **30** was prepared (0.140 g, 89%) from carboxylic acid **26** (0.151 g, 0.54 mmol); highly viscous, slowly crystallizing oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.97–2.18 (m, 4 H, 2-, 11-H), 2.48–2.63 (m, 2 H), 2.69 (br. "s", 4 H), 2.80–2.88 (m, 1 H, 1-, 10-, 12-H, 3-H_B), 3.67 (ddd, J = 13.9, 7.6, 3.0 Hz, 1 H, 3-H_A), 3.90 (s, 3 H, OCH_3), 6.62–6.77 (m, 6 H, 8-, 9-, 14-, 15-, 17-, 18-H), 7.34 (d, J = 1.7 Hz, 1 H, 6-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.8, 29.4 (CH_2, C-2, -11), 34.5, 35.4, 35.5, 35.9 (CH_2, C-1, -3, -10, -12), 51.7 (OCH_3), 129.0, 129.5, 130.4, 131.2, 133.1, 133.7 (CH, C-6, -8, -9, -14, -15, -17, -18), 128.6 (C_q, C-5), 138.1, 138.5, 138.8, 140.7 (C_q, C-4, -7, -13, -16), 168.4 (C_q, COO) ppm; this compound has been described previously in the literature.[12]

Methyl [4.4]Paracyclophane-6-carboxylate (31): According to the procedure for **24**–**27** methyl ester **31** was prepared (0.287 g, 87%) from carboxylic acid **27** (0.314 g, 1.02 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30–1.60 (m, 4 H), 1.64–1.84 (m, 4 H), 2.02–2.28 (m, 4 H), 2.35–2.50 (m, 3 H, 1-, 2-, 3-, 11-, 12-, 13-, 14-H, 4-H_B), 3.39–3.46 (m, 1 H, 4-H_A), 3.88 (s, 3 H, OCH_3), 6.61–6.70 (m, 4 H, 16-, 17-, 19-, 20-H), 6.69 (d, J = 7.8 Hz, 1 H, 10-H), 6.79 (dd, J = 7.8, 1.9 Hz, 1 H, 9-H), 7.32 (d, J = 1.9 Hz, 1 H, 7-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.4 (2 C), 28.7, 28.9 (CH_2, C-2, -3, -12, -13), 33.0, 35.0, 35.1, 35.2 (CH_2, C-1, -4, -11, -14), 51.7 (OCH_3), 128.1, 128.2, 128.5, 128.7, 131.0, 131.5, 131.9 (CH, C-7, -9, -10, -16, -17, -19, -20), 128.3 (C_q, C-6), 139.1, 139.5, 139.6, 141.2 (C_q, C-5, -8, -15, -18), 168.4 (C_q, COO) ppm; this compound has been described previously in the literature.[13]

[4.2]Paracyclophane-6-carbaldehyde (33): As described for the formylation of its lower homologue in the preceding publication,[1] 6-bromo[4.2]paracyclophane (**32**; 0.858 g, 2.72 mmol) was converted into **33** (0.526 g, 73%); colorless small needles (ethanol), m.p. 144–145 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10–1.35 (m, 2 H), 1.50–1.80 (m, 2 H), 2.03–2.20 (m, 2 H), 2.30–2.45 (m, 1 H, 1-, 2-, 3-H, 4-H_B), 2.92–3.03 (m, 2 H), 3.08–3.22 (m, 2 H, 11-, 12-H), 3.35–

3.47 (m, 1 H, 4-H_A), 6.38–6.48 (m, 2 H), 6.53–6.73 (m, 4 H, 9-, 10-, 14-, 15-, 17-, 18-H), 7.25 (br. s, 1 H, 7-H), 10.06 (s, 1 H, CHO) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.9, 29.0 (CH_2, C-2, -3), 31.1 (br.), 33.98, 34.02, 35.3 (CH_2, C-1, -4, -11, -12), 127.9, 128.6, 130.6, 130.7, 131.2, 133.4, 136.7 (CH, C-7, -9, -10, -14, -15, -17, -18), 132.7 (C_q, C-6), 137.4, 138.8, 139.8 (C_q, C-8, -13, -16), 143.0 (C_q, C-5), 192.0 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3029 (w), 2955 (m), 2937 (s), 2924 (s), 2856 (s), 1689 (vs), 1561 (m), 1444 (m), 1149 (m), 809 (m) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 200 (4.59), 212 (3.83) nm. MS (EI, 70 eV): *m*/*z* (%) = 264 (86) $[M]^+$, 250 (15), 231 (11), 159 (27), 145 (26), 132 (30), 131 (52), 130 (29), 129 (37), 128 (30), 117 (62), 115 (42), 105 (65), 104 (100), 103 (39), 91 (44), 78 (38). $C_{19}H_{20}O$ (264.37): calcd. C 86.32, H 7.63; found C 86.52, H 7.66.

[4.2]Paracyclophane-6-carboxylic Acid (34): As described for the oxidation of its lower homologue in the preceding publication,[1] [4.2]paracyclophane-6-carbaldehyde (**33**; 0.310 g, 1.17 mmol) was converted into **34** (0.289 g, 88%); colorless needles, m.p. 176–177 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10–1.40 (br. m, 2 H), 1.60–1.80 (br. m, 2 H), 1.96–2.20 (br. m, 2 H), 2.31–2.46 (br. m, 1 H, 1-, 2-, 3-H, 4-H_B), 2.90–3.21 (br. m, 4 H, 11-, 12-H), 3.57–3.67 (m, 1 H, 4-H_A), 6.51–6.59 (m, 3 H), 6.61–6.70 (m, 3 H, 9-, 10-, 14-, 15-, 17-, 18-H), 7.50 (br. s, 1 H, 7-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.7, 29.4 (CH_2, C-2, -3), 33.5 (br.), 34.06, 34.10, 35.4 (CH_2, C-1, -4, -11, -12), 128.0, 128.5, 130.4, 130.9, 131.3, 134.1, 135.7 (CH, C-7, -9, -10, -14, -15, -17, -18), 126.7 (C_q, C-6), 137.4, 138.1, 140.0, 143.0 (C_q, C-5, -8, -13, -16), 173.4 (C_q, COOH) ppm. IR (KBr): $\tilde{\nu}$ = 3040 (m), 2929 (s), 2858 (m), 1684 (vs), 1449 (m), 1409 (m), 1265 (m), 799 (w) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 196 (4.73) nm. MS (EI, 70 eV): *m*/*z* (%) = 280 (90) $[M]^+$, 262 (12), 175 (11), 148 (22), 131 (31), 117 (25), 115 (22), 105 (100), 104 (67), 91 (36). $C_{19}H_{20}O_2$ (280.37): calcd. C 81.40, H 7.19; found C 81.40, H 7.31.

Methyl [4.2]Paracyclophane-6-carboxylate (35): According to the procedure for the esterification of acids **24**–**27**, the methyl ester **35** was prepared (0.103 g, 86%) from carboxylic acid **34** (0.114 g, 0.34 mmol); colorless needles, m.p. 69 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10–1.35 (m, 2 H), 1.52–1.75 (m, 2 H), 1.95–2.19 (m, 2 H), 2.30–2.42 (m, 1 H, 1-, 2-, 3-H, 4-H_B), 2.88–3.02, 3.06–3.18 (both m, 2 H each, 11-, 12-H), 3.38–3.48 (m, 1 H, 4-H_A), 3.86 (s, 3 H, OCH_3), 6.45–6.55 (m, 3 H), 6.58–6.64 (m, 2 H), 6.64–6.68 (m, 6 H, 9-, 10-, 14-, 15-, 17-, 18-H), 7.30 (br. s, 1 H, 7-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.6, 29.3 (CH_2, C-2, -3), 33.4 (br.), 34.08, 34.10, 35.4 (CH_2, C-1, -4, -11, -12), 51.7 (OCH_3), 127.9, 128.4, 130.4, 130.7, 131.3, 133.1, 134.7 (CH, C-7, -9, -10, -14, -15, -17, -18), 137.4, 137.9, 140.0, 141.7 (C_q, C-5, -8, -13, -16), 168.3 (C_q, COO) ppm; signal from C-6 hidden. IR (KBr): $\tilde{\nu}$ = 2956 (m), 2858 (m), 1716 (vs), 1508 (m), 1492 (m), 1268 (s), 1202 (m), 1190 (m), 1077 (s), 796 (m) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 196 (4.74) nm. MS (EI, 70 eV): *m*/*z* (%) = 294 (100) $[M]^+$, 266 (16), 262 (46), 234 (10), 189 (26), 162 (60), 157 (21), 147 (16), 131 (72), 119 (46), 117 (34), 104 (86). $C_{20}H_{22}O_2$ (294.39): calcd. C 81.60, H 7.53; found C 81.60, H 7.55.

6-Acetyl[4.2]paracyclophane (17): Methyllithium (1.4 mL) in hexane (5%) was added to a solution of carboxylic acid **34** (0.160 g, 0.57 mmol) in anhydrous diethyl ether (10 mL) whilst stirring and ice-cooling. After stirring for 1 h at room temp, the reaction mixture was hydrolyzed by the addition of water (10 mL). The organic phase was separated and the aqueous phase extracted carefully with diethyl ether. The combined organic phases were washed with brine, dried (sodium sulfate), and the solvent was removed in vacuo. The raw product was purified by silica gel plate chromatography with dichloromethane: 0.130 g (65%) of **17**, colorless needles, m.p. 80–81 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.13–1.35 (m, 2 H), 1.48–1.72 (m, 2 H, 2-, 3-H), 1.93–2.05 (m, 1 H), 2.09–2.23 (m, 1 H), 2.31–2.39 (m, 1 H, 1-H, 4-H_B), 2.51 (s, 3 H, CH_3), 2.92–3.04 (m, 2 H), 3.07–3.19 (m, 2 H), 3.22–3.32 (m, 1 H, 11-, 12-H, 4-H_A), 6.42–6.71 (several m, 6 H, 9-, 10-, 14-, 15-, 17-, 18-H), 7.05 (br. s, 1 H, 7-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.7, 29.3 (CH_2, C-2, -3), 32.9, 34.1, 34.2, 35.4 (CH_2, C-1, -4, -11, -12), 29.6 (CH_3), 127.7, 128.6, 130.6, 130.9, 131.0, 131.8, 134.3 (CH, C-7, -9, -10, -14, -15, -17, -18), 136.4, 137.3, 137.8, 140.2, 140.3 (C_q, C-5, -6, -8, -13, -16), 201.7 (C_q, C=O) ppm. IR (KBr): $\tilde{\nu}$ = 2931 (m), 2858 (m), 1680 (vs), 1448 (m), 1415 (m), 1265 (m), 818 (w) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 200 (4.58), 260 (3.71) nm. MS (EI, 70 eV): *m*/*z* (%) = 278 (100) $[M]^+$, 263 (44), 260 (14), 235 (16), 173 (10), 159 (12), 146 (39), 145 (39), 131 (78), 105 (24), 104 (25). $C_{20}H_{22}O_2$ (278.39): calcd. C 86.29, H 7.96; found C 86.25, H 7.99.

General Procedure for the Bromination of Acetyl[*m.n*]paracyclophanes: A few mL of the bromine solution (carbon tetrachloride; amounts: see below) were added to a suspension of iron powder (ca. 0.1 g) in dichloromethane (10 mL) at room temp. After 15 min the acetylparacyclophane was added in one portion, the temperature was raised to reflux, and the rest of the bromine solution was added. After 30 min the reaction mixture was cooled to room temp. and an aqueous solution (20 mL, 20%) of sodium thiosulfate was added. The organic phase was separated and the aqueous phase washed three times with dichloromethane. The organic phases were combined, washed with water, and dried (sodium sulfate). The residue obtained after solvent removal in vacuo was dissolved in glacial acetic acid (20 mL) and treated with zinc (ca. 0.5 g), which was added in portions at 90–95 °C. After cooling to room temp., water and diethyl ether were added to the reaction mixture, the organic phase was separated, and the aqueous phase thoroughly extracted with diethyl ether. The combined organic phases were treated with saturated hydrogen carbonate solution and brine, dried (sodium sulfate), and the solvent was removed by rotary evaporation. The remaining solid residue was purified by plate chromatography (silica gel, chloroform).

6-Acetyl-17-bromo[3.2]paracyclophane (37a): By the bromination procedure given above from **14** (0.300 g, 1.14 mmol) and bromine (4.7 mL of a 0.58 M solution in carbon tetrachloride): 0.267 g (68%) of **37a**, colorless small needles (ethanol), m.p. 163 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.96–2.06 (m, 1 H), 2.10–2.20 (m, 1 H, 2-H), 2.56–2.78 (m, 4 H, 1-, 3-H), 2.63 (s, 3 H, CH_3), 2.84 (ddd, *J* = 13.5, 10.5, 4.5 Hz, 1 H, 11-H_B), 2.92 (ddd, *J* = 13.5, 10.5, 4.0 Hz, 1 H, 10-H_B), 3.40 (ddd, *J* = 13.5, 10.1, 4.0 Hz, 1 H, 11-H_A), 4.22 (ddd, *J* = 13.5, 10.1, 4.5 Hz, 1 H, 10-H_A), 6.43 (d, *J* = 7.7 Hz, 1 H, 8-H), 6.48 (d, *J* = 7.7 Hz, 1 H, 13-H), 6.64 (dd, *J* = 7.7, 1.7 Hz, 1 H, 14-H), 6.71 (d, *J* = 1.7 Hz, 1 H, 16-H), 6.74 (dd, *J* = 7.7, 1.8 Hz, 1 H, 9-H), 7.21 (d, *J* = 1.8 Hz, 1 H, 5-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 29.0 (CH_3), 31.2 (CH_2, C-10), 32.7 (CH_2, C-2), 34.0 (CH_2, C-11), 34.95, 34.96 (CH_2, C-1, -3), 126.8 (C_q, C-17), 128.9, 131.3, 133.3, 133.7, 134.4, 136.2 (CH, C-5, -8, -9, -13, -14, -16), 137.0, 137.2, 138.8, 139.5, 141.6 (C_q, C-4, -6, -7, -12, -15), 199.5 (C_q, C=O) ppm. IR (KBr): $\tilde{\nu}$ = 2925 (w), 1672 (vs), 1595 (m), 1480 (m), 1354 (m), 1031 (m), 888 (m), 830 (w) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 204 (4.52) nm. MS (EI, 70 eV): *m*/*z* (%) = 344 (27) [M, ^{81}Br]$^+$, 342 (27) [M, ^{79}Br]$^+$, 264 (4), 263 (16), 146 (100), 145 (33). $C_{19}H_{19}BrO$ (343.26): calcd. C 66.48, H 5.58, Br 23.28; found C 66.58, H 5.54, Br 23.59.

5-Acetyl-16-bromo[3.2]paracyclophane (37b): By the above bromination procedure from **15** (0.070 g, 0.27 mmol) and bromine (0.8 mL of a 1.0 M solution in carbon tetrachloride): 0.054 g (59%)

of **37b**, colorless small needles (ethanol), m.p. 129–130 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.88–2.00 (m, 1 H), 2.35–2.61 (m, 3 H), 2.91–3.15 (m, 5 H, 1-, 2-, 10-, 11-H, 3-H_B), 2.66 (s, CH_3), 3.74–3.85 (m, 1 H, 3-H_A), 6.46–6.72 (several m, 5 H, 8-, 9-, 13-, 14-, 17-H), 7.03 (d, J = 1.7 Hz, 1 H, 6-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.9 (CH_3), 29.2, 33.4, 33.9, 35.6 (CH_2, C-1, -2, -3, -10, -11), 125.6 (C_q, C-16), 131.5, 132.3, 133.9, 135.4, 135.7 (CH, C-6, -8, -9, 13, -14, -17), 133.9, 136.7, 138.7, 139.2, 142.5 (C_q, C-4, -5, -7, -12, -15), 199.7 (C_q, C=O) ppm. IR (KBr): $\tilde{\nu}$ = 2969 (m), 2912 (m), 1671 (vs), 1553 (m), 1480 (m), 1435 (m), 1263 (m), 1201 (m), 860 (w), 608 (m) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 204 (4.57), 280 (3.47) nm. MS (EI, 70 eV): *m*/*z* (%) = 344 (38) [M, ^{81}Br]$^+$, 342 (38) [M, ^{79}Br]$^+$, 184 (15), 182 (15), 160 (55), 159 (100), 117 (41), 115 (62), 103 (27), 91 (22), 77 (26). HRMS: calcd. 342.0619 ($C_{19}H_{19}BrO$), found 342.0619.

5-Acetyl-17-bromo[3.3]paracyclophane (37e): By the above bromination procedure from **18** (0.236 g, 0.85 mmol) and bromine (3.5 mL of a 1.0 M solution in carbon tetrachloride): 0.140 g (46%) of **37e**, colorless small needles (ethanol), m.p. 129 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.94 (m, 1 H, 2-H_B), 2.00–2.20 (m, 2 H, 11-H), 2.34 (m, 1 H, 2-H_A), 2.56 (m, 1 H, 1-H_B), 2.61 (m, 1 H, 3-H_B), 2.69 (s, 3 H, CH_3), 2.62–2.83 (m, 4 H, 10-, 12-H), 3.06 (m, 1 H, 1-H_A), 3.77 (m, 1 H, 3-H_A), 6.70–6.90 (m, 5 H, 8-, 9-, 14-, 15-, 18-H), 7.28 (d, J = 2.0 Hz, 1 H, 6-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 26.2, 29.4 (CH_2, C-2, -11), 29.2 (CH_3), 33.8, 35.4, 35.6, 36.0 (CH_2, C-1, -3, -10, -12), 125.1 (C_q, C-17), 129.2, 131.1, 132.3, 133.3, 133.4 (CH, C-6, -8, -9, -14, -15, -18), 135.9, 137.7, 138.3, 140.5, 140.8 (C_q, C-4, -5, -7, -13, -16), 200.5 (C_q, C=O) ppm. IR (KBr): $\tilde{\nu}$ = 2920 (s), 2850 (m), 1600 (m), 1490 (m), 1440 (s), 1350 (m), 1260 (s), 1170 (m), 890 (m), 820 (s) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 207 (3.46), 236 (2.96), 278 (2.47), 332 (1.93) nm. MS (EI, 70 eV): *m*/*z* (%) = 358 (100) [M, ^{81}Br]$^+$, 356 (100) [M, ^{79}Br]$^+$, 345 (15), 343 (15), 178 (19), 277 (30), 173 (25), 160 (55), 159 (27), 145 (21), 115 (30), 105 (22), 91 (22), 43 (50). $C_{20}H_{21}BrO$ (357.29): calcd. C 67.23, H 5.92, Br 22.36; found C 67.29, H 5.96, Br 22.24.

7-Acetyl-18-bromo[4.2]paracyclophane (37g): By the above bromination procedure from **16** (0.300 g, 1.08 mmol) and bromine (4.0 mL of a 0.58 M solution in carbon tetrachloride): 0.290 g (75%) of **37g**, colorless small needles (ethanol), m.p. 121–123 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26–1.70 (m, 4 H, 2-, 3-H), 2.14–2.22 (m, 1 H), 2.28–2.40 (m, 3 H, 1-, 4-H), 2.63 (s, 3 H, CH_3), 2.90, 2.93, 3.45, 4.24 [all second-order m, J(11-H_A,11-H_B) = –13.4, J(11-H_A,12-H_A) = 9.0, J(11-H_A,12-H_B) = 4.5, J(11-H_B,12-H_A) = 6.0, J(11-H_B,12-H_B) = 9.4, J(12-H_A,12-H_B) = –13.7 Hz, 1 H each, 11-H_B, 12-H_B, 12-H_A, 11-H_A; rms error of iterative analysis = 0.057 Hz], 6.59 (dd, J = 7.7, J = 1.6 Hz, 1 H, 15-H), 6.66–6.76 (m, 4 H, 9-, 10-, 14-, 17-H), 7.15 (br. s, 1 H, 6-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.3, 29.2 (CH_2, C-2, -3), 34.8, 35.2 (CH_2, C-1, -4, -11, -12), 29.2 (CH_3), 127.2, 130.6, 131.5, 132.0, 133.2, 134.8 (CH, C-6, -9, -10, -14, -15, -17), 125.1, 137.5, 139.2, 139.8, 141.6 (C_q, C-5, -7, -8, -13, -16, -18), 200.2 (C_q, C=O) ppm. IR (KBr): $\tilde{\nu}$ = 2940 (vs), 2850 (s), 1670 (vs), 1560 (m), 1490 (s), 1350 (s), 1270 (s), 1250 (s), 1220 (m), 880 (m), 815 (s) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 202 (4.57), 309 (3.04) nm. MS (EI, 70 eV): *m*/*z* (%) = 358 (54) [M, ^{81}Br]$^+$, 356 (54) [M, ^{79}Br]$^+$, 278 (33), 277 (100), 249 (27), 207 (28), 146 (46), 145 (89). $C_{20}H_{21}BrO$ (357.39): calcd. C 67.23, H 5.92, Br 22.36; found C 67.05, H 5.95, Br 22.34.

General Procedure for the Bromination/Esterification of [*m.n*]Paracyclophane-carboxylic Acids: The bromination was carried out as described above for the bromination of acetyl[*m.n*]paracyclophanes. Once obtained, the raw bromo acid was treated with thionyl chloride (2 mL, boiling at reflux for 30 min). Excess thionyl chloride was distilled off under vacuum and the residue treated with anhydrous methanol (10 mL) under ice cooling. The esterification was completed by heating at reflux for 30 min, excess solvent was removed in vacuo, and the raw bromo ester was purified by plate chromatography (silica gel, dichloromethane).

Methyl 17-Bromo[3.2]paracyclophane-6-carboxylate (37c): From **24** (0.190 g, 0.68 mmol) and bromine (2.1 mL of a 0.58 M solution in carbon tetrachloride), 0.130 g (53%) of **37c** was obtained after esterification with methanol; colorless plates (ethanol), m.p. 161 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.98–2.20 (m, 2 H, 2-H), 2.55–2.83 (m, 4 H, 1-, 3-H), 2.83–2.93 (m, 2 H), 3.40–3.52 (m, 1 H, 10-H_B 11-H), 3.87 (s, 3 H, CH_3), 4.27–4.39 (m, 1 H, 10-H_A), 6.43–6.81 (several m, 5 H, 8-, 9-, 13-, 14-, 16-H), 7.46 (d, J = 1.9 Hz, 1 H, 5-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 32.0, 32.6, 33.7, 34.92, 34.94 (CH_2, C-1, -2, -3, -10, -11), 51.6 (OCH_3), 129.1, 132.1, 133.4, 133.9, 134.3, 135.8 (CH, C-5, -8, -9, -13, -14, -16), 126.3, 128.8, 136.8, 139.7, 139.8, 141.7 (C_q, C-4, -6, -7, -12, -15, -17), 167.3 (C_q, C=O) ppm. IR (KBr): $\tilde{\nu}$ = 2942 (s), 2930 (m), 2900 (m), 1712 (vs), 1438 (s), 1292 (m), 1274 (vs), 1264 (vs), 1201 (vs), 1179 (m), 1076 (vs), 900 (m) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 202 (4.71) nm. MS (EI, 70 eV): *m*/*z* (%) = 360 (74) [M, ^{81}Br]$^+$, 358 (74) [M, ^{79}Br]$^+$, 345 (100), 343 (100), 306 (21), 227 (14), 225 (14), 213 (26), 211 (27), 199 (41), 197 (45), 147 (48), 117 (56), 115 (32). $C_{19}H_{19}BrO_2$ (359.26): calcd. C 63.52, H 5.33, Br 22.24; found C 63.52, H 5.37, Br 22.75.

Methyl 16-Bromo[3.2]paracyclophane-5-carboxylate (37d): From **36** (0.096 g, 0.26 mmol) and bromine (0.5 mL of a 1.0 M solution in carbon tetrachloride), 0.073 g (56%) of **37d** was obtained after esterification with methanol; colorless needles (ethanol), m.p. 134–135 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.88–2.00 (m, 1 H), 2.44–2.61 (m, 3 H, 1-H_B, 2-H, 3-H_B), 2.89–3.05 (m, 4 H, 10-, 11-H), 3.05–3.11 (m, 1 H, 1-H_A), 3.79–3.86 (m, 1 H, 3-H_A), 3.87 (s, 3 H, CH_3), 6.42 (dd, J = 7.7, 1.7 Hz, 1 H, 13-H), 6.54 (d, J = 1.7 Hz, 1 H, 17-H), 6.55 (dd, J = 7.8, J = 1.9 Hz, 1 H, 8-H), 6.59 (d, J = 7.7 Hz, 1 H, 14-H), 6.67 (d, J = 7.8 Hz, 1 H, 9-H), 7.23 (d, J = 1.9 Hz, 1 H, 6-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 29.3 (CH_2, C-2), 33.4, 33.7 (CH_2, C-10, -11), 33.6 (CH_2, C-3), 35.4 (CH_2, C-1), 51.5 (OCH_3), 125.1 (C_q, C-16), 127.3 (C_q, C-5), 131.3 (CH, C-13), 132.3 (CH, C-14), 133.4 (CH, C-9), 134.1 (CH, C-6), 135.6 (CH, C-8), 136.0 (CH, C-17), 136.9 (C_q, C-7), 138.5 (C_q, C-15), 139.3 (C_q, C-12), 142.9 (C_q, C-4), 167.5 (C_q, COO) ppm. IR (KBr): $\tilde{\nu}$ = 2925 (m), 1716 (vs), 1433 (m), 1208 (m), 1193 (m), 1040 (w), 815 (w) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 202 (4.69) nm. MS (EI, 70 eV): *m*/*z* (%) = 360 (42) [M, ^{81}Br]$^+$, 358 (42) [M, ^{79}Br]$^+$, 279 (18), 247 (32), 175 (100), 163 (60), 144 (42), 131 (28), 117 (30), 115 (48). $C_{19}H_{19}BrO_2$ (359.26): calcd. C 63.52, H 5.33, Br 22.24; found C 63.36, H 5.31, Br 23.58.

Methyl 17-Bromo[3.3]paracyclophane-5-carboxylate (37f): From **26** (0.251 g, 0.89 mmol) and bromine (2.0 mL of a 1.0 M solution in carbon tetrachloride), 0.289 g (86%) of **37f** was obtained after esterification with methanol; colorless needles (ethanol), m.p. 141 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.87–2.15 (m, 3 H), 2.38–2.85 (m, 7 H, 1-H_B, 2-H, 3-H_B, 10-, 11-, 12-H), 3.06 (m, 1 H, 1-H_A), 3.83 (m, 1 H, 3-H_A), 3.91 (s, 3 H, CH_3), 6.68–6.91 (several m, 5 H, 8-, 9-, 14-, 15-, 18-H), 7.51 (d, J = 1.6 Hz, 1 H, 6-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 26.2, 29.2, 33.8, 35.3, 35.5, 35.8 (CH_2, C-1, -2, -3, -10, -11, -12), 129.1, 131.7, 132.2, 133.0, 133.5 (CH, C-6, -8, -9, -14, -15, -18), 124.7, 127.7, 137.4, 138.4, 140.7 (C_q, C-4, -5, -7, -13, -16, -17), 167.9 (C_q, COO) ppm. IR (KBr): $\tilde{\nu}$ = 2938 (m), 2915 (m), 1717 (vs), 1440 (s), 1285 (m), 1262 (vs), 1230 (m), 1200 (s), 1190 (s), 1077 (vs), 900 (w), 819 (w) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 201 (4.63), 323 (2.84) nm. MS (EI, 70 eV): *m*/*z*

(%) = 374 (100) [M, ^{81}Br]$^+$, 372 (100) [M, ^{79}Br]$^+$, 359 (41), 357 (44), 294 (14), 293 (56), 261 (26), 189 (36), 117 (63), 105 (50). $C_{20}H_{21}BrO_2$ (373.29): calcd. C 64.35, H 5.67, Br 21.41; found C 64.32, H 5.70, Br 21.38.

Methyl 18-Bromo[4.2]paracyclophane-7-carboxylate (37h): From **25** (0.138 g, 0.49 mmol) and bromine (1.9 mL of a 0.58 M solution in carbon tetrachloride), 0.110 g (60%) of **37h** was obtained after esterification with methanol; colorless prisms (ethanol), m.p. 130 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20–1.45 (m, 2 H), 1.47–1.64 (m, 2 H), 2.08–2.45 (m, 4 H, 1-, 2-, 3-, 4-H), 2.85–2.99 (m, 2 H, 11-, 12-H_B), 3.48–3.55 (m, 1 H, 12-H_A), 3.90 (s, 3 H, CH_3), 4.27–4.34 (m, 1 H, 11-H_A), 6.57 (dd, 1 H), 6.64–6.73 (m, 3 H, 9-, 10-, 14-, 15-H), 6.75 (d, J = 1.4 Hz, 1 H, 17-H), 7.41 (br. s, 1 H, 6-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.4, 28.6, 32.5, 33.1, 34.8, 35.1 (CH_2, C-1, -2, -3, -4, -11, -12), 51.7 (OCH_3), 127.2, 131.1, 131.7, 132.3, 133.0, 134.4 (CH, C-6, -9, -10, -14, -15, -17), 124.9 (C_q, C-18), 129.2, 137.2, 140.0, 140.1, 141.7 (C_q, C-5, -7, -8, -13, -16), 167.5 (C_q, COO) ppm. IR (KBr): $\tilde{\nu}$ = 2934 (s), 2939 (s), 2855 (m), 1722 (vs), 1444 (m), 1433 (s), 1290 (s), 1266 (s), 1255 (s), 1216 (m), 1197 (s), 1165 (m), 1079 (s), 886 (w), 814 (m) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 201 (4.63), 300 (3.10) nm. MS (EI, 70 eV): *m*/*z* (%) = 374 (100) [M, ^{81}Br]$^+$, 372 (100) [M, ^{79}Br]$^+$, 359 (93), 357 (94), 294 (35), 293 (60), 279 (11). $C_{20}H_{21}BrO_2$ (373.29): calcd. C 64.35, H 5.67, Br 21.41; found C 64.31, H 5.71, Br 21.45.

Bromination of 6-Acetyl[4.2]paracyclophane (17): According to the general procedure for the bromination of acetyl[*m.n*]paracyclophanes, **17** (0.080 g, 0.30 mmol) was treated with a 1.0 M bromine solution (1.0 mL) in carbon tetrachloride. Separation by MPLC (silica gel, dichloromethane) provided 0.070 g (67%) of a product mixture **38a**. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20–2.30 (several m, CH_2), 2.52 (s, CH_3), 2.57 (s, CH_3), 2.62 (s, CH_3), 2.65 (s, CH_3), 2.70–3.60 (m, CH_2), 6.35–7.45 (m, Ar-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.6, 28.9, 29.1, 29.2, 31.1, 31.4, 31.6, 31.8, 32.3, 33.2, 33.4, 33.7, 34.0, 34.4, 34.8, 35.0, 35.1, 36.7 (CH_2), 29.5, 29.6, 29.6, 29.7 (CH_3), 126.8, 127.6, 130.2, 130.4, 130.7, 131.2, 131.3, 131.9, 132.5, 132.8, 132.9, 133.1, 134.1, 134.2, 134.3, 134.6, 136.4 (CH), 122.0, 123.4, 124.3, 125.3, 132.2, 132.3, 135.3, 135.6, 137.0, 137.2, 139.2, 139.3, 139.6, 141.1, 141.6, 142.0, 142.7 (C_q), 201.0, 201.7 (C_q, C=O) ppm.

Bromination of [4.2]Paracyclophane-6-carboxylic Acid (34): According to the general procedure for the bromination of [*m.n*]paracyclophane-carboxylic acids, **34** (0.070 g, 0.25 mmol) was treated with a 1.0 M bromine solution (0.6 mL) in carbon tetrachloride. Separation by MPLC (silica gel, dichloromethane) provided 0.080 g (86%) of a product mixture **38b**. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10–2.45 (several m, CH_2), 2.75–3.60 (m, CH_2), 3.86 (s, ester CH_3), 6.40–7.00 (m, aryl-H), 7.29 (s, aryl-H), 7.33 (d, aryl-H), 7.36 (d, aryl-H), 7.63 (d, aryl-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.6, 29.2, 33.4, 33.8, 34.1, 34.8, 35.0, 35.4 (CH_2), 51.6, 51.7 (OCH_3), 127.9, 128.4, 130.0, 130.2, 130.4, 130.7, 131.3, 131.4, 132.2, 132.8, 133.1, 133.5, 134.6, 134.7, 135.1 (CH), 123.4, 127.2, 127.5, 134.5, 137.3, 137.9, 139.6, 139.9, 141.7, 142.8 (C_q), 168.3 (C_q, COO) ppm.

Bromination of Methyl [4.2]Paracyclophane-6-carboxylate (35): As described above for the bromination of [*m.n*]paracyclophane-carboxylic acids, a sample of **35** (0.070 g, 0.24 mmol) was treated with a 0.58 M solution of bromine (1.2 mL) in carbon tetrachloride. Separation by MPLC (silica gel, dichloromethane) provided 0.070 g (80%) of a product mixture **38c**, the ^{1}H and ^{13}C NMR spectroscopic data of which were very similar to those described for **38b**.

Bromination of 6-Acetyl[4.4]paracyclophane (21): As described above for the bromination of [*m.n*]paracyclophane-carboxylic acids, a sample of **21** (0.275 g, 0.90 mmol) was treated with a 1.0 M solution of bromine (4.5 mL) in carbon tetrachloride. Separation by MPLC (silica gel, dichloromethane) provided 0.160 g (46%) of a product mixture **38d**. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 24.8, 25.3, 25.7, 25.8, 26.2, 27.7, 28.0, 28.2, 28.3, 28.5, 28.6, 28.9, 29.6, 30.4, 33.0, 33.1, 33.6, 34.9, 35.0, 35.1, 35.2, 35.3 (CH_2), 29.8, 30.0, 30.1 (CH_3), 126.8, 127.3, 128.2, 128.8, 129.0, 129.3, 130.1, 130.5, 130.8, 130.9, 131.3, 131.4, 131.5, 132.0, 132.2, 132.8, 133.0, 134.5, 134.6 (CH), 122.0, 122.4, 125.3, 127.5, 129.6, 132.6, 135.5, 138.0, 139.3, 139.4, 139.5, 139.8, 140.0, 140.1, 140.6, 141.4, 142.1 (C_q), 201.3 (C_q, C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 386 (12) [M, ^{81}Br]$^+$, 364 (12) [M, ^{79}Br]$^+$, 371 (19), 369 (20), 307 (21), 306 (90), 305 (26), 291 (100), 288 (57), 263 (30), 145 (47), 131 (51), 117 (31), 105 (41), 91 (29).

Bromination of [4.4]Paracyclophane-6-carboxylic Acid (27): As described above for the bromination of [*m.n*]paracyclophane-carboxylic acids, a sample of **27** (0.150 g, 0.49 mmol) was treated with a 1.0 M solution of bromine (1.0 mL) in carbon tetrachloride. Separation by MPLC (silica gel, dichloromethane) provided 0.100 g (51%) of a product mixture **38e**. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10–2.90 (m, CH_2), 3.30–3.60 (m, CH_2), 3.86 (s, CH_3), 3.87 (s, CH_3), 3.89 (s, CH_3), 3.90 (s, CH_3), 6.53–7.00 (several m, aryl-H), 7.32 (s, aryl-H), 7.39 (d, aryl-H), 7.48 (d, aryl-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 26.3, 28.1, 28.4, 28.7, 28.9, 33.0, 33.6, 34.7, 34.9, 35.0, 35.2 (CH_2), 51.7 (OCH_3), 127.1, 127.2, 128.1, 128.2, 128.5, 128.7, 130.6, 130.8, 131.0, 131.2, 131.4, 131.9, 133.0 (CH), 139.1, 139.5, 139.6, 141.2 (C_q), 168.3 (C_q, C=O) ppm.

Bromination of Methyl [4.4]Paracyclophane-6-carboxylate (31): By the procedure described for the bromination of acetyl[*m.n*]paracyclophanes from **31** (0.150 g, 0.46 mmol), the isomer mixture **38f** (0.080 g, 45%) was obtained, the spectroscopic data of which were practically indistinguishable from those obtained for **27**.

Dimethyl 13,16-Bis(chloromethyl)[3.2]paracyclophane-5,8-dicarboxylate (40b): Aluminum trichloride (3.66 g, 27.4 mmol) was dissolved in chloromethyl methyl ether (15 mL) under ice cooling. A solution of **39b** (0.144 g, 0.43 mmol) in chloromethyl methyl ether (3 mL) was added to this solution after warming to room temp. within 5 min. After stirring for 1 h the reaction mixture was slowly poured into ice, dichloromethane was added (30 mL), the organic phase was separated, and the aqueous layer washed three times with dichloromethane. The combined organic fractions were dried (sodium sulfate) and the solvent was removed by rotary evaporation. The remaining solid was purified by MPLC (dichloromethane, silica gel): 0.140 g (75%) of **40b**, colorless crystals (ethanol), m.p. 149–150 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.97–2.10 (m, 1 H, 2-H_B), 2.10–2.20 (m, 1 H, 2-H_A), 2.61–2.76 (m, 2 H, 1-, 3-H_B), 2.89–3.04 (m, 3 H, 1-H_A, 10-, 11-H_B), 3.31–3.39 (m, 1 H, 11-H_A), 3.54–3.62 (m, 1 H, 3-H_A), 3.88 (s, 6 H, OCH_3), 4.12–4.59 (m, 5 H, 10-H_A, CH_2Cl), 6.45 (s, 1 H, 17-H), 6.67 (s, 1 H, 14-H), 7.10 (s, 1 H, 6-H), 7.41 (s, 1 H, 9-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 29.4 (CH_2, C-2), 31.4 (CH_2, C-1), 31.9 (CH_2, C-11), 32.3 (CH_2, C-3), 32.4 (CH_2, C-10), 44.0, 44.2 (CH_2Cl), 51.2, 52.0 (OCH_3), 131.57 (C_q, C-8), 131.59 (C_q, C-5), 132.5 (CH, C-14), 134.6 (CH, C-9), 135.0 (CH, C-17), 136.1 (C_q, C-12), 136.3 (C_q, C-16), 136.5 (CH, C-6), 137.3 (C_q, C-13), 138.7 (C_q, C-15), 139.8 (C_q, C-7), 142.0 (C_q, C-4), 166.5, 167.2 (C_q, COO) ppm. IR (KBr): $\tilde{\nu}$ = 2971 (m), 2927 (m), 1712 (vs), 1434 (s), 1286 (s), 1235 (s), 1211 (m), 1183 (m), 1098 (vs), 779 (m) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 210 (4.80), 242 (4.29) nm. MS (EI, 70 eV): *m*/*z* (%) = 436 (66) [M, ^{37}Cl]$^+$, 434 (100) [M, ^{35}Cl]$^+$, 400 (31), 398 (70), 364 (29), 363 (39), 362 (92), 331 (46), 330 (66), 303 (39), 233 (45), 205 (36), 203 (36), 179 (45), 177 (45), 167 (75), 143 (84), 128 (65), 115 (60).

$C_{23}H_{24}Cl_2O_4$ (435.35): calcd. C 63.46, H 5.56, Cl 16.29; found C 63.33, H 5.44, Cl 16.29.

Dimethyl 14,17-Bis(chloromethyl)[3.3]paracyclophane-5,8-dicarboxylate (40c): As described for the synthesis of **40b**, 0.190 g (73%) of **40c** was prepared from **39c** (0.205 g, 0.58 mmol) with aluminum trichloride (5.28 g, 39.6 mmol) and chloromethyl methyl ether; colorless needles, m.p. 139–140 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.06–2.15 (m, 4 H, 2-, 11-H), 2.62–2.78 (m, 4 H, 1-, 3-, 10-, 12-H_B), 2.92–3.02 (m, 2 H, 1-, 12-H_A), 3.56–3.66 (m, 2 H, 3-, 10-H_A), 3.91 (s, 6 H, OCH_3), 4.35, 4.65 (AX, J = 11.7 Hz, 2 H each, CH_2Cl), 6.81 (s, 2 H, 15-, 18-H), 7.44 (s, 2 H, 6-, 9-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.5, 31.6, 32.5 (CH_2, C-1, -2, -3, -10, -11, -12), 44.4 (CH_2Cl), 52.2 (OCH_3), 132.8, 133.8 (CH, C-6, -9, -15, -18), 131.4, 136.0, 137.6, 140.5 (C_q, C-4, -5, -7, -8, -13, -14, -16, -17), 167.5 (C_q, COO) ppm; compound **40c** has previously been described in the chemical literature.[30]

Dimethyl 14,17-Bis(chloromethyl)[4.2]paracyclophane-6,9-dicarboxylate (40d): As described for the synthesis of **40b**, 0.176 g (73%) of **40d** was prepared from **39d** (0.176 g, 0.50 mmol) with aluminum trichloride (4.25 g, 31.9 mmol) and chloromethyl methyl ether; colorless plates, m.p. 152–153 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89–1.10 (m, 2 H), 1.62–1.77 (m, 2 H, 2-, 3-H), 1.98–2.06 (m, 1 H, 1-H_B), 2.33–2.41 (m, 1 H), 2.73–2.81 (m, 1 H, 1-H_A, 4-H_B), 2.91–3.00 (m, 1 H, 11-H_B), 3.03–3.12 (m, 1 H, 12-H_B), 3.15–3.23 (m, 4-H_A), 3.35–3.43 (m, 1 H, 12-H_A), 3.85, 3.90 (s, 3 H each, OCH_3), 4.08–4.16 (m, 1 H, 11-H_A), 4.18 (d, 1 H of 14-CH_2Cl), 4.41 (d, 1 H of 17-CH_2Cl), 4.49–4.54 (m, 1 H each of 14-, 17-CH_2Cl), 6.56 (s, 1 H, 15-H), 6.85 (s, 1 H, 18-H), 7.17 (s, 1 H, 7-H), 7.38 (s, 1 H, 10-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 27.8, 28.7, 29.0, 31.6, 32.5, 33.1 (CH_2, C-1, -2, -3, -4, -11, -12), 43.6, 43.9 (CH_2Cl), 52.1, 52.2 (OCH_3), 131.8, 133.8, 134.2, 135.9 (CH, C-7, -10, -15, -18), 131.3, 131.5, 134.9, 136.1, 136.7, 138.5, 140.0, 141.8 (C_q, C-5, -6, -8, -9, -13, -14, -16, -17), 166.7, 167.6 (C_q, COO) ppm. IR (KBr): $\tilde{\nu}$ = 2947 (s), 2862 (w), 1708 (vs), 1699 (vs), 1450 (m), 1442 (m), 1434 (s), 1392 (s), 1255 (vs), 1222 (s), 1206 (m), 1132 (m), 1125 (s), 1112 (s), 1101 (s), 828 (m) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 206 (4.82), 242 (4.28) nm. MS (EI, 70 eV): *m*/*z* (%) = 450 (9) [M, ^{37}Cl]$^+$, 448 (14) [M, ^{35}Cl]$^+$, 414 (31), 412 (72), 376 (100), 345 (27), 344 (56), 317 (52), 316 (19), 285 (14), 205 (29), 167 (31), 157 (72), 156 (49), 143 (44). $C_{24}H_{26}Cl_2O_4$ (449.37): calcd. C 64.15, H 5.83, Cl 15.78; found C 64.26, H 5.82, Cl 15.89.

Dimethyl 15,18-Bis(chloromethyl)[4.3]paracyclophane-6,9-dicarboxylate (40e): As described for the synthesis of **40b**, 0.194 g (83%) of **40e** was prepared from **39e** (0.182 g, 0.50 mmol) with aluminum trichloride (4.79 g, 35.9 mmol) and chloromethyl methyl ether; colorless needles (ethanol), m.p. 128–129 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34–1.50 (m, 2 H), 1.63–1.76 (m, 2 H, 2-, 3-H), 2.10–2.33 (m, 4 H, 1-H_A, 4-H_B, 12-H), 2.66–2.77 (m, 3 H, 1-, 11-, 13-H_B), 2.96–3.05 (m, 13-H_A), 3.24–3.32 (m, 1 H, 4-H_A), 3.60–3.68 (m, 1 H, 11-H_A), 3.87, 3.91 (s, 3 H each, OCH_3), 4.26, 4.62 (AX, CH_2Cl), 4.31, 4.50 (AX, CH_2Cl), 6.62 (s, 1 H, 16-H), 6.95 (s, 1 H, 19-H), 7.23 (s, 1 H, 10-H), 7.39 (s, 1 H, 7-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.4 (CH_2, C-3), 29.3 (CH_2, C-2), 29.4 (CH_2, C-12), 31.68 (CH_2, C-4), 31.73 (CH_2, C-11), 32.4 (CH_2, C-13), 32.9 (CH_2, C-1), 44.0, 44.1 (CH_2Cl), 52.0, 52.1 (OCH_3), 131.0 (C_q, C-6), 131.9 (C_q, C-9), 132.4 (d, C-16), 132.9 (d, C-19), 133.57 (d, C-10), 133.64 (d, C-7), 135.0 (C_q, C-18), 135.5 (C_q, C-15), 137.9 (C_q, C-14), 138.3 (C_q, C-17), 140.3 (C_q, C-8), 140.7 (C_q, C-5), 167.66, 167.72 (C_q, COO) ppm. IR (KBr): $\tilde{\nu}$ = 2949 (m), 2933 (m), 1721 (s), 1455 (w), 1435 (m), 1270 (vs), 1241 (m), 1099 (vs), 780 (w) cm^{-1}. UV (acetonitrile): λ_{max} (log ε) = 206 (4.88), 238 (4.27) nm. MS (EI, 70 eV): *m*/*z* (%) = 464 (6) [M, ^{37}Cl]$^+$, 462 (9) [M, ^{35}Cl]$^+$, 428 (16), 426 (41), 392 (12), 391 (29), 390 (100), 359 (19), 358 (54), 343 (22), 169 (55), 157 (99), 156 (60). $C_{25}H_{28}Cl_2O_4$ (463.40): calcd. C 64.80, H 6.09, Cl 15.30; found C 64.64, H 6.02, Cl 15.48.

Chloromethylation of Dimethyl [4.4]Paracyclophane-6,9-dicarboxylate (39f): As described for the synthesis of **40b**, **39f** (0.194 g, 0.51 mmol) was treated with aluminum trichloride (2.75 g, 35.9 mmol) in chloromethyl methyl ether, the reaction time being extended to 2 h. A mixture (0.161 g, 66%) of two isomers was obtained from the raw product by MPLC with dichloromethane, which could not be further separated. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10–1.45 (m), 1.70–2.15 (m), 2.35–2.43 (m), 2.76–2.84 (m), 2.88–2.98 (m), 3.21–3.31 (m), 3.44–3.52 (m, CH_2), 3.87 (s), 3.89 (s, CH_3), 4.32–4.54 (several m, CH_2Cl), 6.76–7.31 (several s, aryl-H) ppm.^{13}C NMR (101 MHz, $CDCl_3$): δ = 27.1, 27.3, 27.8, 29.2, 31.4, 31.8, 33.5 (CH_2), 43.2, 43.5 (CH_2Cl), 52.04, 52.07 (OCH_3), 132.7, 132.8, 133.2, 133.9 (CH), 130.9, 132.4, 134.2, 134.6, 138.3, 138.6, 140.8, 141.0 (C_q), 167.1, 167.8 (C_q, COO) ppm. $C_{26}H_{30}Cl_2O_4$ (477.43): calcd. C 65.41, H 6.33, Cl 14.85; found C 65.47, H 6.49, Cl 15.04.

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