Alternative General Synthetic Routes to [2.2]Cyclophanes and [3.2]Cyclophanes from [3.3]Cyclophane-2,11-diones by Photodecarbonylation, and a Structural Study of [3.2]Metacyclophanes[‡]

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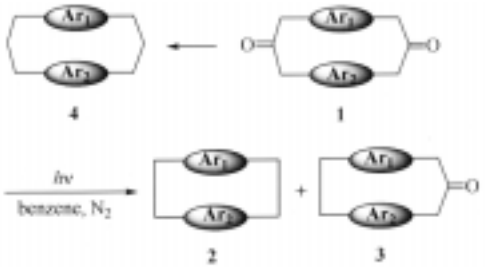
Photodecarbonylation of [3.3]cyclophane-2,11-diones, which are readily prepared by TosMIC coupling, affords [2.2]cyclophanes in high yield. This method also provides a general synthetic method for [3.2]cyclophan-2-ones by taking advantage of the fact that this photochemical reaction proceeds in a stepwise manner through [3.2]cyclophan-2-ones. A series of [2.2]cyclophanes, [3.2]cyclophanes, and [3.3]cyclophanes can thus be made available from the common precursor [3.3]cyclophane-2,11-diones. In sharp contrast to the preferred *syn* geometry of [3.3]metacyclophanes, [3.2]metacyclophanes adopt *anti* geometries and the aryl ring inversion process is observed by variable-temperature ^{1}H NMR spectroscopy. In the crystalline state, the two aryl rings of *anti*-[3.2]metacyclophanes are almost parallel in spite of the unsymmetrical bridge length; they overlap only at the C-9 and C-17 positions, and the transannular distances are shorter than the corresponding distances in [3.3]metacyclophane-2,11-dione.

Introduction

[3.3]Cyclophanes (CPs) undergo two types of photochemical reactions: excitation of the π-π* band of multibridged [3$_n$]CPs (n = 3,[3] 4[4]) results in the formation of polycyclic cage compounds by [2+2] cycloaddition of the facing benzene rings, followed by rearrangement of the carbocation species generated by protonation of a cyclobutane ring of the cycloadduct, while excitation of the n-π* band of [3.3]CP-2,11-diones **1** induces decarbonylation to give [2.2]CPs **2** in high yields, as has been reported in brief.[5]

Quinkert et al. first reported the light-induced decarbonylation of ketones in benzene in 1963[6a] and found that 1,3-diphenyl-2-propanones afford 1,2-diphenylethanes in high yields.[6a–6d] In the course of our studies of multilayered [3.3]metacyclophanes (MCPs), we noticed that the characteristic n-π* bands of the structural units, [3.3]MCP-2,11-diones, appear in the 280–330 nm region.[7] Since our reporting of an alternative synthetic method for [2.2]CPs by decarbonylation of **1**, we have found that this method also provides a general synthetic method for [3.2]CP-2-ones **3**, by taking advantage of the fact that this reaction proceeds in a stepwise manner through [3.2]CP-2-ones **3**. This method thus provides new routes to the synthesis of [2.2]CPs and [3.2]CPs **2** and **3** through adjustment of the irradiation time while using the same starting material, **1**,[8] as used for the synthesis of [3.3]CPs **4** (Scheme 1).



Scheme 1. A new synthetic route to [2.2]cyclophanes and [3.2]cyclophanes **2** and **3** by photodecarbonylation of [3.3]cyclophane-2,11-dione **1**

General synthetic methods for [2.2]CPs have been already established.[9] Most of them employ ring-contraction reactions of 2,11-diheteroatom-substituted [3.3]CPs. Photochemical elimination of sulfur[10] or selenium atoms[11] from [3.3]CP 2,11-disulfide or diselenide and flash vacuum pyrolysis of sulfones[10b,12,13] obtained by the oxidation of the corresponding sulfides are the most general methods. We have reported that 2,11-diaza[3.3]CPs may be converted into the corresponding [2.2]CPs through their nitroso deriv-

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atives by reductive elimination of nitrogen.[14] Photoextrusion reactions of CO_2 from cyclic diesters can also be applied to the synthesis of [2.2]paracyclophanes (PCPs)[15] and [2.2]heterophanes.[16]

Recently, Vögtle et al. reported selective ketone pyrolysis as a new synthetic method for production of monocyclic and polycyclic hydrocarbons. Flash vacuum pyrolysis (10^{-5} Torr, 610−650 °C) of [3.3]CP-2,11-diones **1**, for example, afforded [2.2]CPs **2** in moderate yields.[17] This ketone pyrolysis is widely applicable to the synthesis of triple-bridged cyclophanes and the large cavity cyclophanes starting from $[3_n]$CP-(one)$_n$.

Yamato et al. have reported an orthodox synthesis of 9,17-dimethyl[3.2]MCPs,[18a] while Tsuge et al. have studied the transannular π-electronic interaction of 9,17-dimethyl-[3.2]MCPs, and concluded that the electronic nature is transmitted less effectively to the benzene ring of the other side in the [3.2]MCP than in [2.2]homologue.[18b][18c] Vögtle et al. reported the synthesis of helical and planar-chiral oxa[2.2]pyridinophanes, and studied the dynamic ^{1}H NMR spectra of their synthetic intermediates, thia[3.2]pyridinophanes.[19]

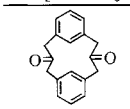
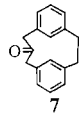
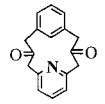
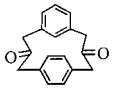
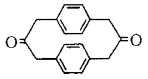
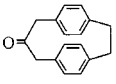
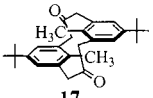
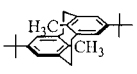
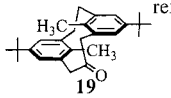
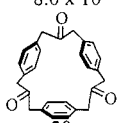
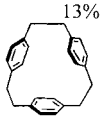
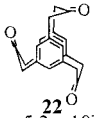
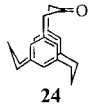
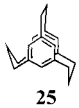
The weaker π-electron-donating ability of [3.2]PCP[20] relative to that of [2.2]PCPs and [3.3]PCPs seems to be the most likely reason why the [3.2]CPs have not attracted much attention, while the lack of general and facile synthetic methods has hindered further studies of them. We describe here an alternative decarbonylation reaction by photochemical processes; this method provides an alternative synthetic route to [2.2]CPs and the simplest approach to the synthesis of [3.2]CPs, which are in general inaccessible directly.

Results and Discussion

Synthesis

Photochemical treatment of [3.3]CP-2,11-dione **1** in benzene gave the corresponding [2.2]CP **2** in satisfactory yields. The isolated yields of products and irradiation times are summarized in Table 1. A benzene solution (4.0×10^{-3} mol/L) of [3.3]MCP-2,11-dione **5** was irradiated with a high-pressure Hg lamp (400 W) as the internal light source at ambient temperatures, while nitrogen was bubbled through the solution. The reaction was rather slow, but [2.2]MCP **6** was obtained in 95% yield after 20 h of irradiation. When irradiation was stopped after 4 h, 9% of **6** and 57% of [3.2]MCP-2-one **7** were isolated. This indicated that the reaction was proceeding in a stepwise manner. This method was also applicable to the synthesis of [2.2]pyridinophane **9** (56%), but longer irradiation times than those required for the treatment of **5** were necessary. Treatment of [3.3]metaparacyclophane(MPCP)-2,11-dione **11** proceeded smoothly to give [2.2]MPCP **12** (94%). [3.3]PCP-2,11-dione **14** was the most reactive of the [3.3]CP-2,11-diones, and afforded [2.2]PCP **15** (97%) after 30 min of irradiation. Benzene may be replaced with other solvents such as ethyl acetate. This reaction was successfully applied to functionalized [2.2]CPs, as exemplified by the synthesis of 7,15-di-*tert*-butyl-4,12-dimethyl[2.2]MCP **18**,[21] and the synthesis of [2^n]CPs with large rings; [3.3.3]PCP-2,11,20-trione **20** gave [2.2.2]PCP **21**[22] (39%) after 20 h of irradiation. However, [3.3.3](1,3,5)CP-2,11,20-trione **22** was inert to the reaction and formation of **23** was not observed, whereas monoketone **24**[23] provided [3.3.2](1,3,5)CP **25** (34%). This suggested the quenching of the photoexcited state of a carbonyl group by neighboring ground-state carbonyl groups in **22**.

Table 1. Yields of [2.2]cyclophanes and [3.2]cyclophane-2-ones prepared by irridiation of diones with a 400-W high-pressure Hg lamp

Dione c [mol L^{-1}]	Irridiation time	Product yields (%)	
 **5** 4.0×10^{-3} 2.3×10^{-3}	 20 h 4 h	 **6** **95%** 9%	 **7** 0% **57%**
 **8** 8.0×10^{-4} 7.5×10^{-3}	 45 h 4 h	 **9** **56%** 0%	 **10** 14% **72%**
 **11** 8.0×10^{-4} 3.1×10^{-3}	 5 h 26 min	 **12** **94%** 14%	 **13** 0% **46%**
 **14** 7.3×10^{-4} 1.1×10^{-3}	 4 h 20 min	 **15** **97%** 10%	 **16** 0% **21%** ref.[21]
 **17** 8.0×10^{-4}	 15 h	 **18** **61%**	 **19** 13%
 **20** 5.3×10^{-4}	 20 h	 **21** 39%	
 **22** 5.3×10^{-4}	 20 h	 **23** 0%	
 ref.[23] **24** 4.0×10^{-4}	 46 h	 **25** 34%	

We can confidently say that the reaction conditions can be adjusted to the preferential formation of [3.2]CP-2-one **3** by control of the time spent irradiating **1**. As described above, [3.2]MCP-2-one **7** was isolated in 57% yield after 4 h of irradiation, together with [2.2]MCP **6** (9%). Similarly

the [3.2]pyridinophan-2-one **10** was obtained in 72% yield after 4 h of irradiation, with 16% recovery of **8**. [3.2]MPCP-2-one **13** (46%) and [3.2]PCP-2-one **16** (21%) were obtained together with their corresponding [2.2]CPs after 40 min and 20 min of irradiation, respectively. In addition, this method is also applicable to the synthesis of [2^n]CPs as host molecules and multilayered [2.2]MCPs.[24]

The intramolecular nature of this reaction was corroborated by the exclusive formation of unsymmetrical [2.2]CPs and [3.2]CPs from unsymmetrical starting ketones, as demonstrated by **8** and **11**. This reaction also proceeds in a stepwise manner. Experimental results show that the preferential formation of [3.2]CP-2-one **3** from the time-controlled reaction of **1** is effective when the reaction is slow, as it is the case of the metacyclophane. Photochemical excitation of the $n\rightarrow\pi^*$ bands of the dione **1** may first generate a benzyl radical after the release of CO, followed by intramolecular recombination of the diradical to give **3**. A similar photochemical cleavage of the remaining $-CH_2COCH_2-$ bridge, involving the formation of the benzyl radical and subsequent intramolecular recombination of the diradical, may afford [2.2]CP **2**.

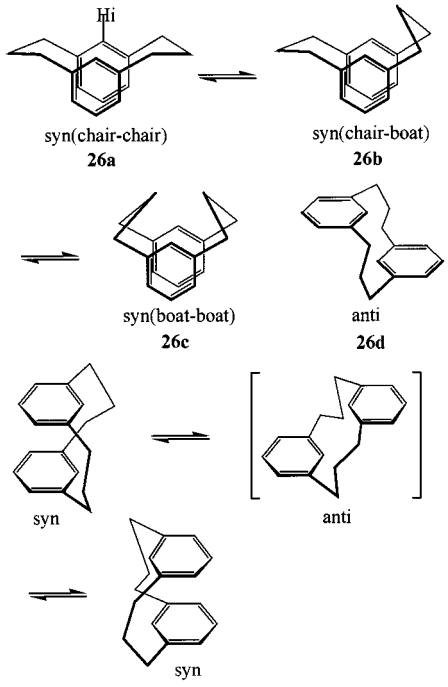
The advantage of our photochemical method over Vögtle's method[17] and other conventional methods[10−16] is the simple and easy experimental procedures (which do not require special apparatus) and the high yields. Thus, [3.3]CP-2,11-diones **1**, which are readily accessible by TosMIC coupling,[8] serve as common precursors not only for the synthesis of [3.3]CPs **4**, but also for [2.2]CPs and [3.2]CPs **2** and **3**. This method provides an alternative synthetic route to [2.2]CPs, and a general synthetic method for [3.2]CPs.

A Conformational Study of [3.2]Metacyclophanes

Ten-membered [2.2]CPs are generally rigid and no dynamic behavior is observed at ambient temperatures in solution,[25,26,9] whereas [3.3]CPs are mobile at ambient temperatures,[25] and chair-boat-type flipping of the trimethylene bridges can be observed by variable-temperature (VT) ^{1}H NMR spectroscopy in [3.3]PCPs[27,28] and [3.3]MCPs,[2,29−32] as well as in multi-bridged [3$_n$]CPs.[33,34] In the [3.3]MCPs, the inversion of the aryl ring is also responsible for the conformational isomerism, but the energy barrier ($\Delta G^{\neq}$) for this process is much lower than that for the bridge flipping (11−12 kcal/mol) and cannot be detected by the VT ^{1}H NMR method.[30b] In contrast, the aryl ring inversion process in the 11-membered [3.2]CPs is amenable to study by the VT ^{1}H NMR method; Griffin et al. reported that the $\Delta G^{\neq}$ values for the aryl ring inversion lie between 16 and 19 kcal/mol, and were dependent upon the steric nature of the 2-substituent in a series of 2-substituted [3.2]MCPs.[35] Sato et al. reported that an increase of $\Delta G^{\neq}$ in 2-thia[3.2]MCP was observed in the sequence going from sulfide to sulfoxide, and then sulfone.[36] Krois and Lehner reported that the $\Delta G^{\neq}$ value of the parent [3.2]MCP **27** was 17.4 kcal/mol (T_c = 90 °C) in perchlorobutadiene[37] in the VT ^{1}H NMR study of a series of [*m.n*]MCPs (*m* = 3, 4; *n* = 2, 3). Here we describe further information on the stable conformations in solution, aryl ring inversion, and some crystal structures of the [3.2]MCPs. Deuterium atoms were introduced into the 2-positions of the trimethylene bridge of [3.2]CPs to simplify the ^{1}H NMR signals.[30b]

[3.2]Metacyclophanes

The most stable conformation of [3.3]MCP, both in the solid state[29,38] and in solution, is *syn*(chair-chair) **26a**.[29,30b] The order of relative thermodynamic stability of the three conformers with the *syn* geometry is: chair-chair **26a**, chair-boat **26b**, and boat-boat **26c**. The *anti* isomers **26d**, however, are predicted to be much less stable than the *syn* conformers, by more than 7 kcal/mol[29,39] on the basis of MM3 and semiempirical MO calculations.[29,39,40] Of the three *syn* conformers, only **26a** is observed by low-temperature ^{1}H NMR spectroscopy.[29,30b] The observed temperature dependence in the VT ^{1}H NMR spectrum of **26** ($\Delta G^{\neq}$ = 11.6 kcal/mol, CD_2Cl_2) is attributable to the bridge-flipping process,[30b,39] the $\Delta G^{\neq}$ value of which is much higher than that of the aryl ring inversion process[30b] (Scheme 2).



Scheme 2. Possible conformers of [3.3]metacyclophane **26**, and its conformational isomerism by chair-boat-type flipping of the trimethylene bridges and aryl ring inversion

In contrast, the preferred conformation of [3.3]MCP-2,11-dione **5** is *anti*, as gauged by the strongly shielded inner aromatic protons (H_i: δ = 5.78 in $CDCl_3$), while the signals of the corresponding protons (H_i) of **26** appear at δ = 6.80 in $CDCl_3$. The dione **5** showed no ^{1}H NMR spectroscopic temperature dependence down to −90 °C in CD_2Cl_2, suggesting energy barriers for the flipping of bridges and inversion of aryl rings much lower than those in **26**. The X-ray structural analysis shows that **5** adopts *anti* geometry and two carbonyl groups take antiparallel arrangement. The *syn*

and *anti* geometries **5** are of comparable thermodynamic stability, and the antiparallel arrangement of the two carbonyl groups stabilizes the molecule because of the cancellation of dipole moments. Of the conformers with the *anti* geometry, **5c** would be expected to be the most stable, with the isomers with twist-boat-like and boat-boat-like conformations **5a** and **5b** less stable than **5c** by 3.3 and 1.0 kcal/mol, respectively, on the basis of AM1 calculations (Figure 1). The twist-boat-like conformation **5a**, however, was observed in the crystal structure of *anti*-[3.3]MCP quinhydrone dimethyl ether.[30c]

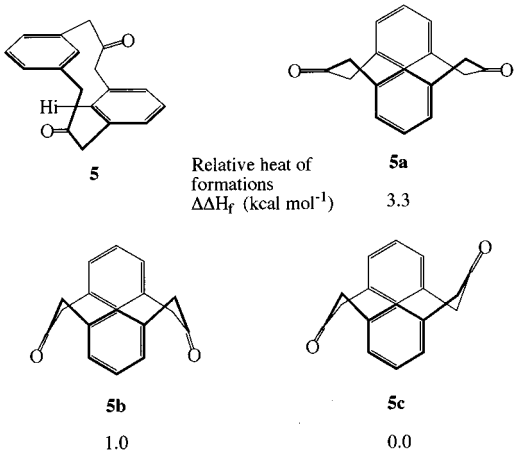


Figure 1. Stable *anti* conformers of [3.3]metacyclophane-2,11-dione **5** and their relative heats of formation [$\Delta\Delta H_f$ (kcal mol^{-1}), AM1], based on **5c**

Figure 2 shows the molecular structure of **5** in the crystalline state at −180 °C. The ORTEP drawings A (top view) and B (side view) show that the two benzene rings assume an *anti* geometry, with the two carbonyl groups of the bridges in an *anti*-parallel arrangement. The crystal data are listed in Table 2. Carbon−carbon and carbon−oxygen bond lengths and angles agree well with normal values. The two benzene rings are parallel, and only the C(9) and C(9*) atoms are overlapped. This suggests that the two benzene rings can interact only through π-orbitals at the C(9) and C(9*) atoms. The transannular distances between C(9) and C(9*) and between C(8) and C(4*) are 2.99 and 3.31 Å, respectively. The benzene ring is slightly distorted towards the boat form; the dihedral angles between the C4−C5−C7−C8 and C4−C9−C8 planes and the C4−C5−C7−C8 and C5−C6−C7 planes are 3.47 and 1.34°, respectively. Crystal-packing diagrams show that the structure contains two separate molecules per unit cell. It should be noted that the intermolecular distances (2.55 Å) between the carbonyl oxygen atom O(1) and the proton H(3) at the benzylic positions of a neighboring molecule are shorter than the sum of van der Waals radii[41] of a hydrogen atom (1.20 Å) and an oxygen atom (1.40 Å) and therefore an attractive interaction through intermolecular hydrogen bonding is to be expected (Figure 3).

2,2-Dideuterio[3.2]MCP **27-D$_2$** shows the following aromatic ^{1}H NMR signals (270 MHz, $CDCl_3$, 20 °C): δ = 5.19 (s, 2 H, H-9), 6.8−6.9 (2 d, 4 H, H-5 and H-7), and 7.12 (t, J = 7.59 Hz, 2 H, H-6). The strongly shielded internal aromatic protons (H-9) show the preferred geometry to be *anti*, and this is in sharp contrast to that of [3.3]MCP **26**. Conformational isomerism between *anti*-**27** and *anti*-**27′** through *syn*-**27** is therefore to be expected (Scheme 3).[35,37] MM3 and PM3 calculations predicted that *anti*-**27** should be more stable than *syn*-**27** by 2.8 and 1.1 kcal/mol, respectively.

The ^{1}H NMR signals due to both bridge protons displayed strong temperature-dependence phenomena, while the aromatic proton signals were almost intact. At 24 °C in

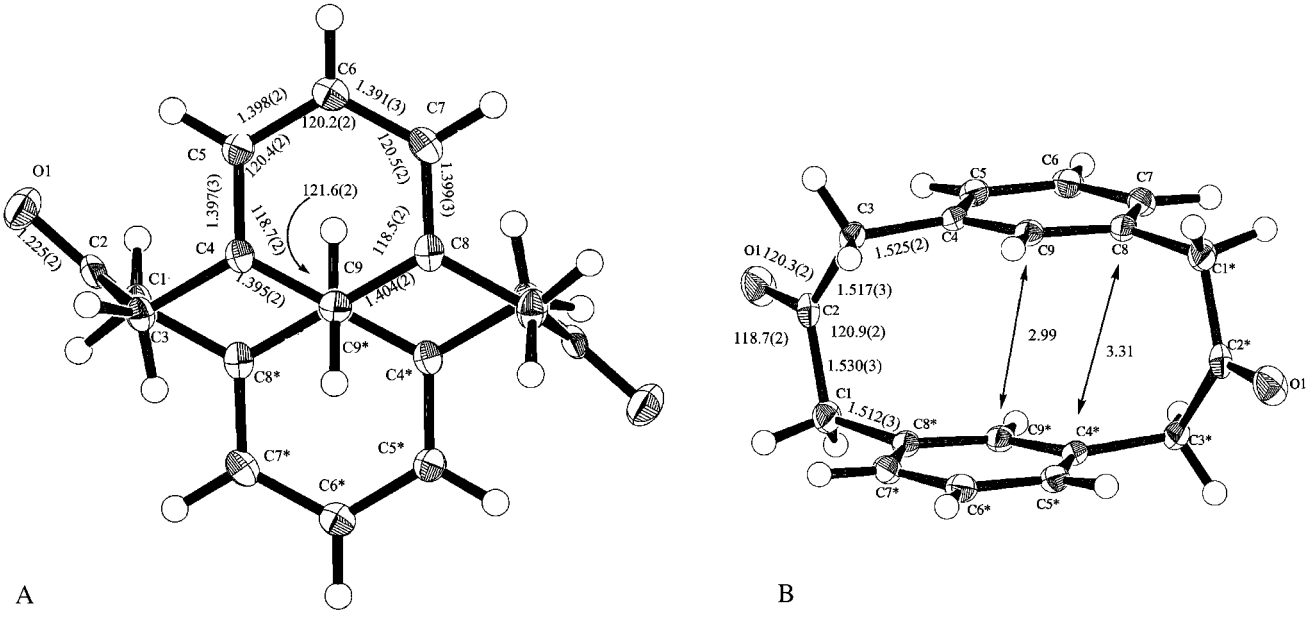


Figure 2. ORTEP drawings A (top view) and B (side view) of [3.3]metacyclophane-2,11-dione **5**, with bond angles [°] and bond lengths [Å] (−180 °C)

Table 2. Summary of crystallographic data and refinement details

Compound	**5**	**7**	**27**	**10**	**28**	**29**
Empirical formula	$C_{18}H_{16}O_2$	$C_{17}H_{16}O_{1.27}$	$C_{17}H_{20}$	$C_{16}H_{15}NO$	$C_{16}H_{17}N$	$C_{18}H_{22}S_2N$
Molecular mass	264.32	240.63	224.35	237.30	223.32	316.50
Crystal color, habit	colorless, prism	colorless, prism	colorless, prism	colorless, prism	colorless, prism	colorless, platelets
Crystal size [mm]	0.2 × 0.3 × 0.2	0.9 × 0.5 × 0.3	0.3 × 0.8 × 0.8	0.8 × 0.6 × 0.8	0.6 × 0.8 × 0.8	0.50 × 0.02 × 0.50
Crystal system	monoclinic	monoclinic	orthorhombic	orthorhombic	orthorhombic	monoclinic
Space group	$P2_1/n$ (no. 14)	$P2_1/n$ (no. 14)	$P2_12_12_1$ (no. 19)	$P2_12_12_1$ (no. 19)	$P2_12_12_1$ (no. 19)	$P2_1/c$ (no. 14)
Temperature [°C]	−180±1	23±1	23±1	23±1	15±1	−180±1
a [Å]	7.635(6)	7.874(3)	11.644(3)	14.68(4)	11.639(4)	7.0404(2)
b [Å]	5.535(2)	14.448(6)	14.063(4)	22.13(4)	14.144(5)	17.7631(4)
c [Å]	15.583(9)	11.426(4)	7.679(2)	7.89(4)	7.71(1)	12.0506(4)
α [°]						
β [°]	93.933(1)	94.57(4)				91.8264(8)
γ [°]						
V [Å^3]	657.00	1295.7(9)	1257.5(6)	2564(12)	1268.8	1506.27(7)
Z	2	4	4	8	4	4
$D_{calcd.}$ [g cm^3]	1.336	1.233	1.185	1.229	1.169	1.396
F(000)	280	513	488	1008	480	676
μ(Mo-K_α) [cm^{-1}]	0.86 (Mo)	0.76 (Mo)	0.66 (Mo)	0.76 (Mo)	0.68 (Mo)	3.46 (Mo)
$2\theta_{max}$ [°]	55 (Mo)	55 (Mo)	55 (Mo)	55 (Mo)	55 (Mo)	55 (Mo)
No. of reflections:						
measured	1348	3115	1686	3356	1181	13840
independent	1348	2973	1686	3351	1181	3447
R_{int}	–	0.033	–	0.033	–	0.029
No. of observations [$I > 3.00\sigma(I)$]	1219	1217	630	1805	764	2850
No. of parameters	124	172	172	355	154	267
Reflection/parameter ratio	9.83	7.08	3.66	5.08	4.96	10.67
R	0.044	0.089	0.048	0.055	0.068	0.031
Rw	0.045	0.070	0.035	0.048	0.064	0.052
GoF	1.09	4.38	2.69	2.94	5.18	1.25
Max. Δ/σ	0.00	0.05	0.98	0.98	0.43	0.002
Max. Δρ [e/nm^{-3}]	0.21	0.24	0.09	0.20	0.17	0.26

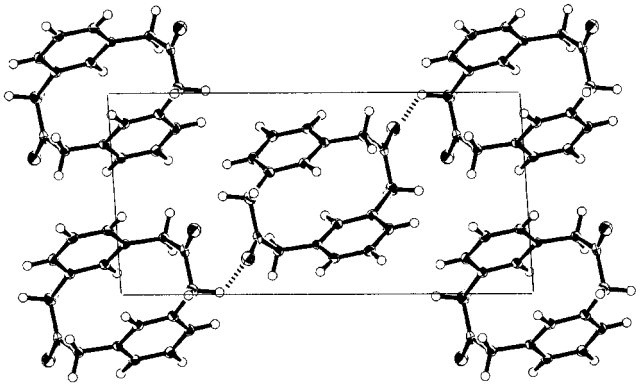
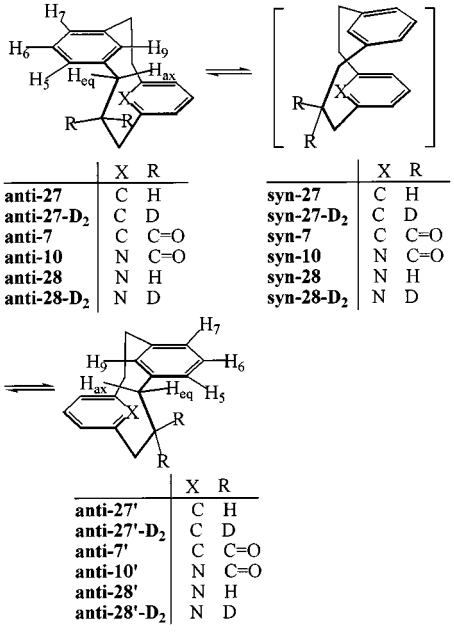


Figure 3. The crystal-packing diagram of [3.3]metacyclophane-2,11-dione **5**



	X	R
anti-27	C	H
anti-27-D$_2$	C	D
anti-7	C	C=O
anti-10	N	C=O
anti-28	N	H
anti-28-D$_2$	N	D

	X	R
syn-27	C	H
syn-27-D$_2$	C	D
syn-7	C	C=O
syn-10	N	C=O
syn-28	N	H
syn-28-D$_2$	N	D

	X	R
anti-27'	C	H
anti-27'-D$_2$	C	D
anti-7'	C	C=O
anti-10'	N	C=O
anti-28'	N	H
anti-28'-D$_2$	N	D

Scheme 3. Conformational isomerism of [3.2]metacyclophanes by an aryl ring inversion process

[D_5]bromobenzene, the benzylic proton signals of the $-CH_2CD_2CH_2-$ bridge appeared as an AB system [δ = 2.24 (d, *J* = 13.5 Hz, 2 H, H_{ax}) and 2.62 (d, *J* = 14.2 Hz, 2 H, H_{eq})], whereas the ethano bridge protons showed an A_2X_2 system [δ = 2.08 (d, *J* = 7.59 Hz, 2 H), 2.88 (d, *J* = 7.26 Hz, 2 H) analyzed as an AB approximation (Figure 4)]. This indicated that the molecule was frozen in an *anti* conformation at this temperature. The AB system gradually broadened with increasing temperature, coalesced at 62 °C, and finally became a sharp singlet above 100 °C. Corresponding to this spectral change, the A_2X_2 signal also coalesced at ca. 80 °C and became a sharp singlet above 140 °C. The energy barrier ($\Delta G^{\neq}$) for the ring-inversion process

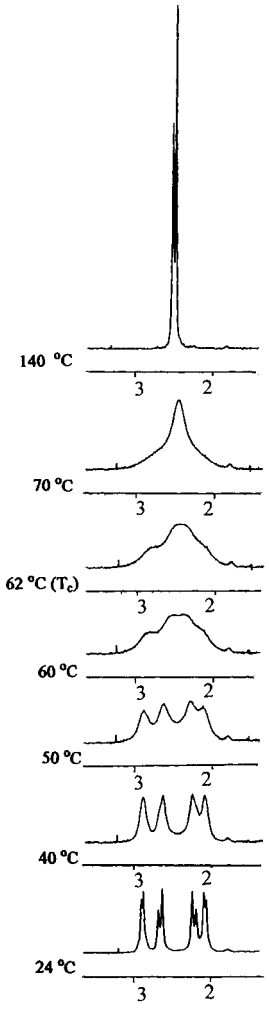


Figure 4. VT ^{1}H NMR spectra of the bridge proton signals of 2,2-dideuterio[3.2]metacyclophane **27-D$_2$** in [D$_5$]bromobenzene (270 MHz)

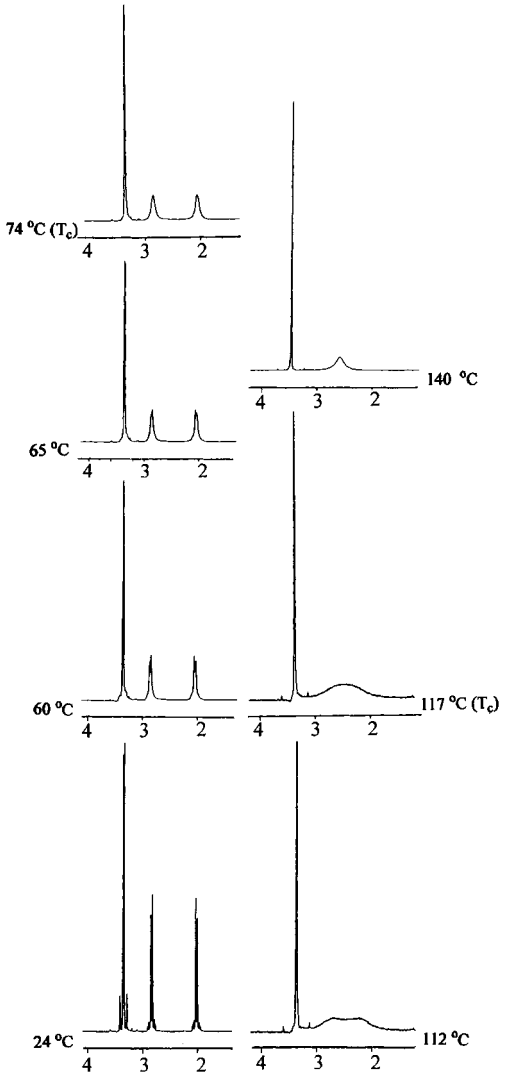


Figure 5. VT ^{1}H NMR spectra of the bridge proton signals of [3.2]metacyclophane-2-one **7** in [D$_5$]bromobenzene (270 MHz)

was estimated to be 15.5 kcal/mol (T_c = 62 °C), based on the AB system.[42]

In the VT ^{1}H NMR spectrum of [3.2]MCP-2-one **7**, AB and A_2X_2 signals were observable separately. At 23 °C in [D$_5$]bromobenzene, the aromatic proton signals appeared at δ = 5.06 (s, H-9), 6.9−7.0 (2 d, 4 H, H-5 and H-7), and 7.13 (t, J = 7.59 Hz, H-6), and the bridge proton signals appeared as an AB [δ = 3.33 (d, J = 14.5 Hz, H_{ax}), 3.38 (d, J = 14.5 Hz, H_{eq})] and an A_2X_2 system [δ = 2.02 (d, J = 7.92 Hz, 2 H,), 2.84 (d, J = 7.92 Hz, 2 H) analyzed as an AB approximation]. These data also indicated that the molecule was fixed in an *anti* conformation at this temperature, and so a similar interconversion between ***anti*-7** and ***anti*-7′** through ***syn*-7** was to be expected (Scheme 3). The benzylic proton signals of both bridges exhibited significant temperature-dependence phenomena (Figure 5). The AB system (H_{ax} and H_{eq}) coalesced at 74 °C, while the A_2X_2 signal coalesced at 117 °C and became a broad singlet at 140 °C. The exchange of both benzylic proton signals clearly indicated the presence of the benzene ring inversion process, the ring-inversion $\Delta G^{\neq}$ value of which was estimated to be 16.9 kcal/mol (T_c = 74 °C), based on the AB system, a value slightly larger than that of the parent [3.2]MCP **27**.[43] The corresponding $\Delta G^{\neq}$ value in [D$_6$]DMSO was 16.6 kcal/mol (T_c = 70 °C) and so no solvent effect was observed.[44]

The crystal structure of **27** shows that the two benzene rings are almost parallel irrespective of the different lengths of the bridges (Figure 6), and they overlap at only one position: at C(9) and C(17). However, the structure could not be considered in detail because of disorder problems, even at −160 °C. Rather similarly to those in the crystal structure of **27**, the two benzene rings of **7** are almost parallel [C(4)−C(16) 3.29 Å, C(8)−C(12) 3.08 Å] and overlap at only one position, at C(9) and C(17) (Figure 7); the situation is also similar in [3.3]MCP-2,11-dione **5**, although the transannular distance between C(9) and C(17) (2.82 Å) is shorter than that in **5** (2.99 Å). Thus, **7** adopts an almost

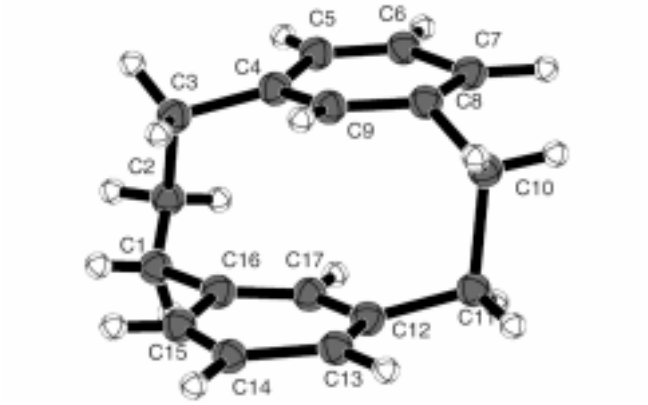


Figure 6. ORTEP drawing of [3.2]metacyclophane **27**

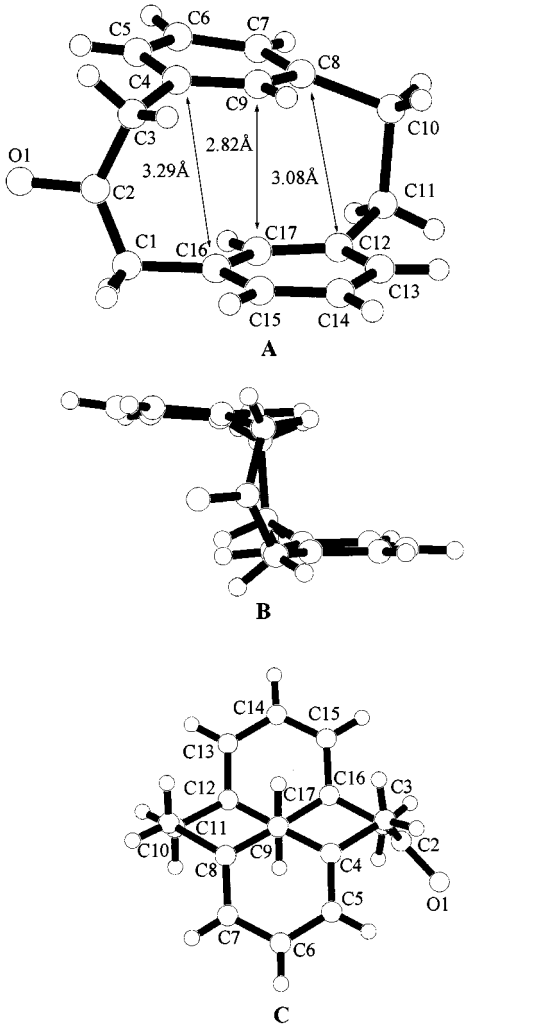


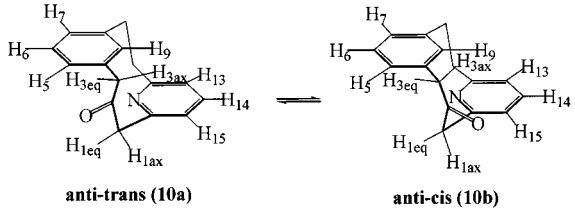
Figure 7. X-ray structure of [3.2]metacyclophane-2-one **7**: A and B (side views) and C (top view)

parallel arrangement of the benzene rings and their transannular distances are slightly shorter than those in **5**.

[3]Metacyclo[2](2,6)pyridinophanes

A similar conformational isomerism to that of [3.2]MCP **27** is to be expected for [3]metacyclo[2](2,6)pyridinophanes, but the $\Delta G^{\neq}$ value for the aryl ring inversion process should be smaller than that in **27** (Scheme 3) because of the smaller steric bulkiness of the lone pair electrons of a nitrogen atom in comparison with a hydrogen atom.

In [3]metacyclo[2](2,6)pyridinophane-2-one **10**, two different conformers, ***anti-trans*** and ***anti-cis***, are to be expected, depending on the orientation of the carbonyl group (Scheme 4). The term "*anti*" refers to an *anti* geometry of the aromatic rings, while the term "*cis*" denotes that the carbonyl group is directed toward the pyridine ring, the other isomer being termed as *trans*. In this compound, two types of conformational isomerism are conceivable: inversion of the aryl ring (Scheme 3) and flipping of the three-carbon bridge (Scheme 4).



Scheme 4. The three-carbon bridge flipping between *anti-trans* (**10a**) and *anti-cis* (**10b**)

At 24 °C in [D_5]bromobenzene, the chemical shifts of the internal aromatic proton signal H-9 (δ = 5.18, s) and the external aromatic proton signals H-6 (δ = 7.18, t, J = 7.59 Hz) and H-14 (δ = 7.23, t, J = 7.59 Hz) suggested that the preferred conformation was *anti*, as in the case of [3.2]MCP-2-one **7**. The benzylic proton signals of the three-carbon bridge appeared as a pair of broad singlets at 24 °C, and this suggested that the bridge was mobile even at this temperature. In contrast, the ethano bridge protons showed a pair of broad signals at 24 °C, with the signals gradually sharpening as the temperature increased and coalescing at 34 °C (T_c) (Figure 8). Using the ethano bridge protons as a basis,[45] the $\Delta G^{\neq}$ value for the aryl ring inversion was estimated to be ca. 14 kcal/mol, which was lower than that in [3.2]MCP-2-one **7** (16.9 kcal/mol). Each singlet signal (20 °C, CD_2Cl_2) arising from the benzylic protons of the three-carbon bridge split into an AB quadruplet below ca. −30 °C, indicating that the bridge flipping (Scheme 4) was frozen below ca. −30 °C (Figure 8).

Interestingly, two conformers, ***anti-cis*** and ***anti-trans***, were observed in the crystal structure of **10** (Figure 9). This indicated that even flipping of the three-carbon bridge was frozen in the solid state. The top views of the two conformers are similar, but the inclination of the pyridine ring in the two conformers is different (Figure 10). The transannular distance between N-2 and C-25 in the ***anti-trans*** conformer (2.64 Å) is shorter than the corresponding distance (N-1−C-9) in the ***anti-cis*** conformer (2.78 Å). Another interesting feature is that the pyridine ring is slightly inclined when the facing benzene ring is situated in the plane, as is to be expected from the unsymmetrical bridge lengths. This is in sharp contrast to the crystal structures of [3.2]MCPs **7** and **27** and [3]metacyclo[2](2,6)pyridinophanes **28** and **29**, in which the two aromatic rings are almost parallel irre-

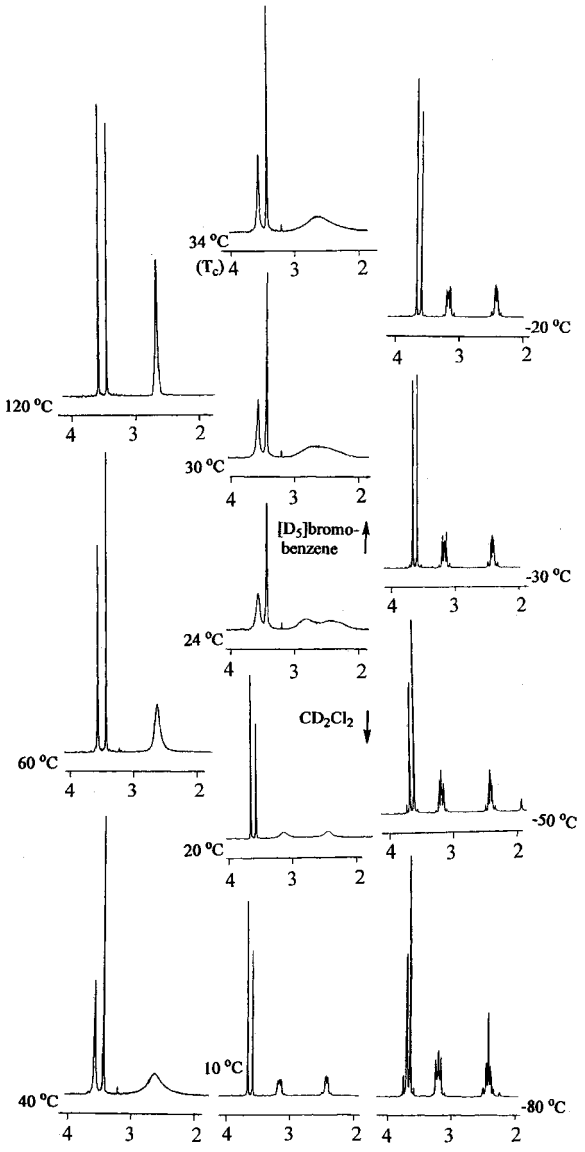


Figure 8. VT ^{1}H NMR spectra of the bridge proton signals of [3]metacyclo[2](2,6)pyridinophane-2-one **10** in [D_5]bromobenzene (24 to 120 °C) and CD_2Cl_2 (20 to −80 °C) (270 MHz)

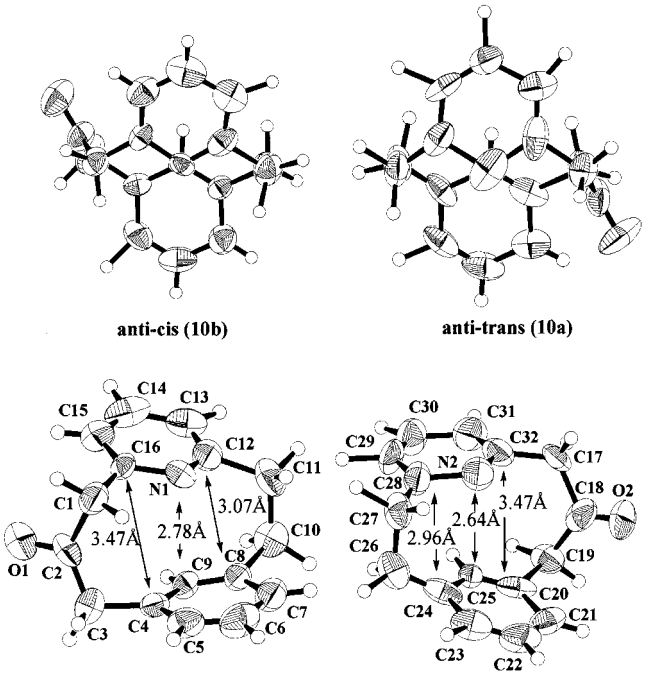


Figure 9. ORTEP drawings of [3]metacyclo[2](2,6)pyridinophane-2-one **10**; two independent molecules [***anti-cis*** (**10b**) and ***anti-trans*** (**10a**)] are observed; top views (top) and side views (bottom)

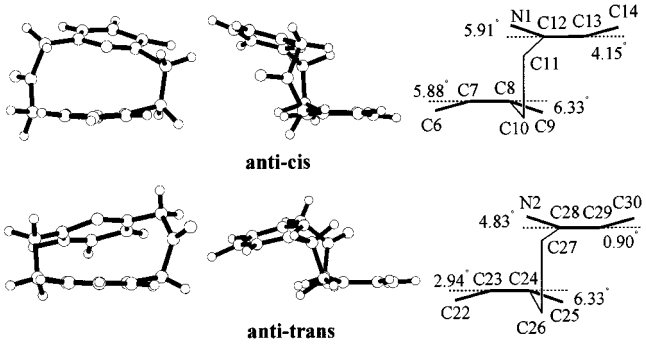


Figure 10. X-ray structures and distortion angles of the aromatic rings of ***anti-cis*** (**10b**) and ***anti-trans*** (**10a**) of [3]metacyclo[2](2,6)-pyridinophane-2-one **10**

spective of the different lengths of the bridges. The benzene rings are more deformed than the pyridine rings (Figure 10). Figure 11 shows the crystal-packing diagram of **10**.

In the VT ^{1}H NMR spectrum of 2,2-dideuterio[3]metacyclo[2](2,6)pyridinophane **28-D$_2$** in CD_2Cl_2, the benzylic proton signals of both bridges displayed significant temperature-dependence phenomena (Figure 12). The two sets of AB and AA′XX′ signals were clearly observed at −50 °C, and each signal gradually broadened as the temperature was increased, finally becoming a broad signal at ca. 20 °C. Although the accurate $\Delta G^{\neq}$ value for the pyridine ring inversion was difficult to determine, it was expected to be much smaller than that of [3.2]MCP **27**.[46]

As in the structures of [3.2]MCPs **27** and **7**, the two aromatic rings are almost parallel in the crystalline state. The two aryl rings overlap only at the N-1 and C-9 positions, with the transannular distances being 2.72 [N(1)−C(9)], 3.19 [C(8)−C(12)], and 3.24 Å [C(4)−C(16)]. The distances are shorter than the corresponding distances in **7** by ca. 0.1 Å (Figure 13). The ORTEP drawing of 2-dithiabutanediyl-[3]metacyclo[2](2,6)pyridinophane **29** is shown in Figure 14. The two aryl rings are almost parallel and overlap only at N(1) and C(9) positions, with the transannular distance being 2.717 Å. The three-carbon bridge adopts a twist-boat-like conformation.

The $\Delta G^{\neq}$ values for the aryl ring inversion of the [3.2]MCPs are in the range of 14 to 17 kcal/mol, and the value for the pyridine ring inversion is slightly smaller than that of the benzene ring.

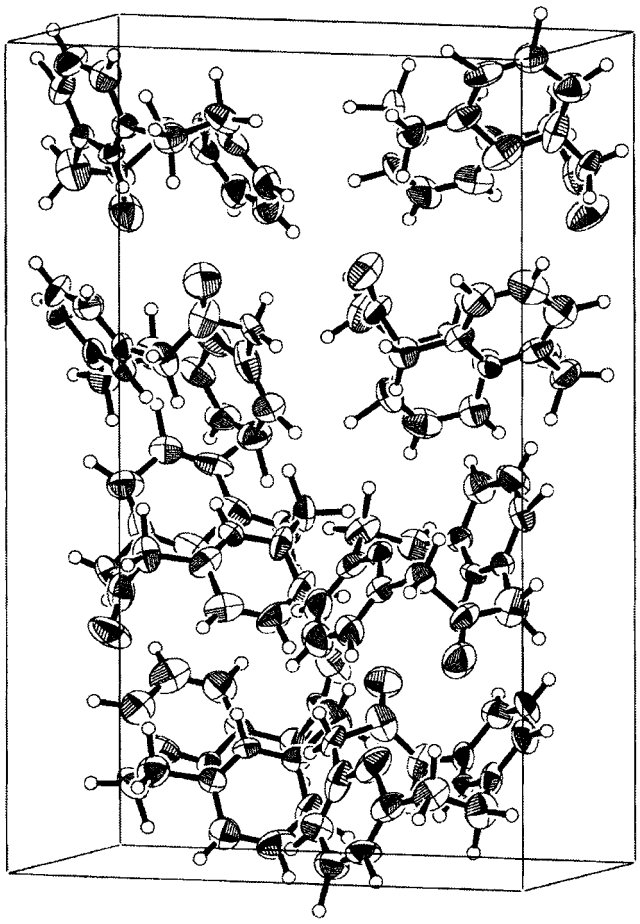


Figure 11. Crystal packing diagram of [3]metacyclo[2](2,6)-pyridinophane-2-one **10**

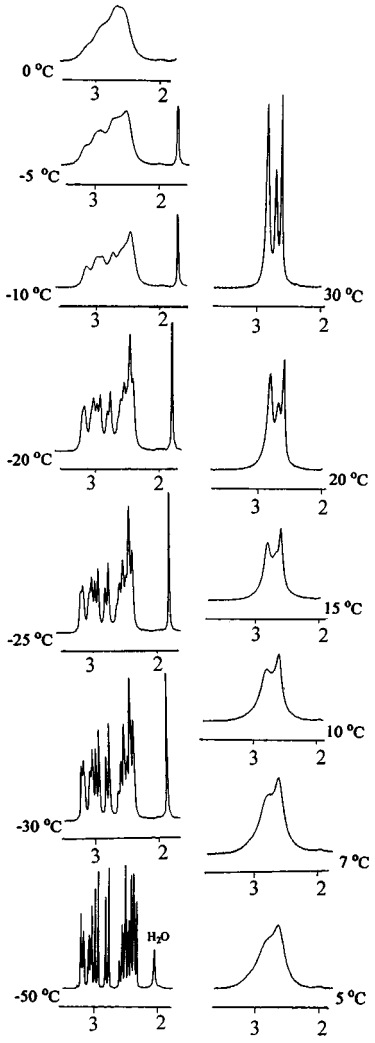


Figure 12. VT ^{1}H NMR spectra of the bridge proton signals of 2,2-dideuterio[3]metacyclo[2](2,6)pyridinophane **28-D$_2$** in CD_2Cl_2 (270 MHz)

Conclusion

The significance of the photodecarbonylation reaction lies in the fact that a series of [3.3]CPs, [3.2]CPs, and [2.2]CPs can be prepared from the same starting compound **1**. The method may therefore be most conveniently used when a series of [3.3]CPs, [3.2]CPs, and [2.2]CPs is required. In sharp contrast to [3.3]MCP **26** and its dione **5**, the aryl ring inversion processes in [3.2]MCPs **27**, **7**, **28**, and **10** were amenable to study by the VT ^{1}H NMR method, and the energy barriers were estimated to be 14−17 kcal/mol. The barriers in [3]metacyclo[2](2,6)pyridinophanes **28** and **10** were slightly lower than those in [3.2]MCPs **27** and **7**, due to the lower steric bulkiness of the pyridine ring nitrogen atom lone pair in comparison with that of a hydrogen atom.

Quite interestingly, the two aryl rings of [3.2]MCPs **27** and **7** and [3]metacyclo[2](2,6)pyridinophanes **28** and **29** are almost parallel in spite of the unsymmetrical bridge lengths, whereas the pyridine ring of [3]metacyclo[2](2,6)pyridinophane-2-one **10** is slightly inclined. In all [3.2]MCPs, two aryl rings overlap only at one position, and the transannular distances are shorter than those of [3.3]MCP-2,11-dione **5**. In the crystal structure of **10**, two conformers (***anti-trans*** and ***anti-cis***) are observed.

Several new [3.2]CPs, such as [3]metacyclo[2](2,6)pyridinophanes **10**, **28**, **29** and [3.2]MPCP-2-one **13**, were obtained as racemic mixtures and interesting chiroptical properties are to be expected for their individual enantiomers.[47] Resolutions of the racemic mixtures are in progress and the results will be reported elsewhere.

Experimental Section

General: Melting points: Yanaco micro melting point apparatus MP-S3. − High-pressure Hg lamp: Shigemi Standard Shoji AHH400S (400 W). − NMR: JEOL JNM-EX 270 or JEOL JNM-AL300. $CDCl_3$ as solvent unless otherwise noted, TMS as internal standard. − FAB-MS: JEOL JMS-HX 110A (*m*-nitrobenzyl alcohol). − UV/Vis: Hitachi U-3500. − IR: Hitachi Nicolet I-5040 FT-IR. − Elemental analysis: Service Center for the Elementary Analysis of Organic Compounds affiliated with the Faculty of Science, Kyushu University. − Analytical thin layer chromatography (TLC) and column chromatography were performed on 60 F_{254} silica gel

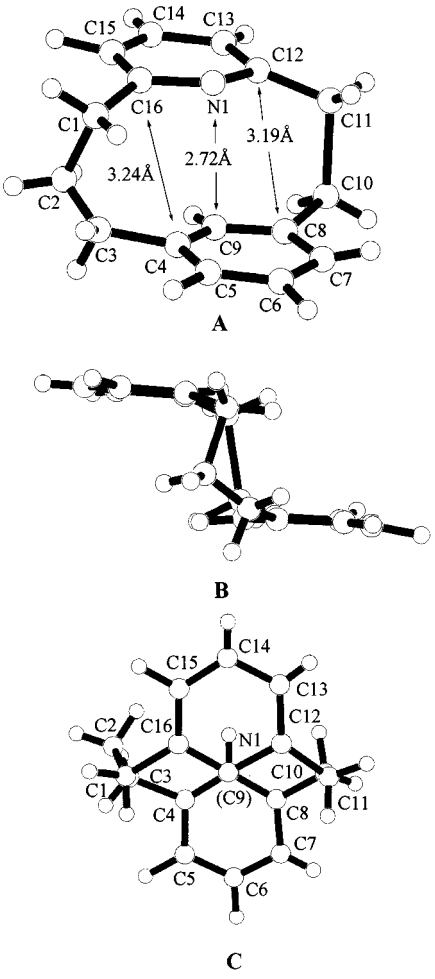


Figure 13. X-ray structure of [3]metacyclo[2](2.6)pyridinophane **28**

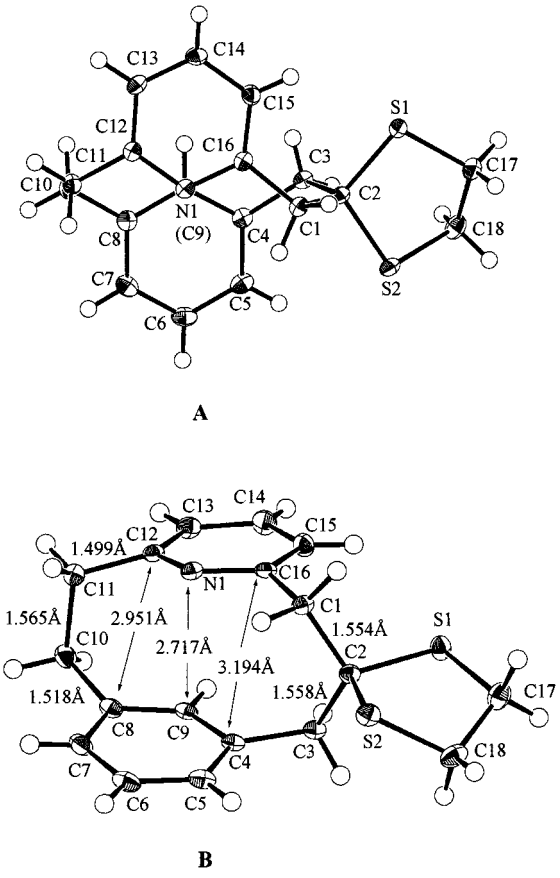


Figure 14. ORTEP drawings of 2-dithiabutanediyl[3]metacyclo[2]-(2,6)pyridinophane **29** (−180 °C): (A) top view and (B) side view

(Merck) and 60 silica gel (Merck, 40−63 μm), respectively. − Benzene was used without further purification. Xylene was distilled from CaH_2. [3.3]MCP-2,11-dione **5**,[48a] [3.3]MPCP-2,11-dione **11**,[8a] [3]metacyclo[3](2,6)pyridinophane-2,11-dione **8**,[8b] [3.3]PCP-2,11-dione **14**,[48b] [3.3.3]PCP-2,11,20-trione **20**,[8a] and [3.3.3](1,3,5)CP-2,11,20-trione **22**,[33a] and [3.3.2](1,3,5)CP-2-one **24**,[23] were prepared according to literature procedures. nBu$_3$SnD was prepared by $LiAlD_4$ reduction of nBu$_3$SnCl in Et_2O.[49]

X-ray Crystallographic Study: All measurements were made with a Rigaku RAXIS-IV imaging plate area detector with graphite-monochromated Mo-K_α radiation and a rotating anode generator. The crystal structure was solved by direct methods [SIR88[50] (**5**), SHELXS86[51] (**7**), SIR92[52] (**10**, **27**, **28**, **29**)] and expanded using Fourier techniques [DIRDIF94[53]]. The non-hydrogen atoms were refined anisotropically, and hydrogen atoms were refined isotopically. All the computations were performed using the teXsan program.[54] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications no. CCDC-116788 (**10**), -116789 (**5**), -116790 (**28**), and -116791 (**27**), -116792 (**7**), and -149324 (**29**). Copies of the data can be obtained free of charge upon request to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

[2.2]Metacyclophane (6): A benzene solution (500 mL) of [3.3]MCP-2,11-dione **5** (106 mg, 0.40 mmol), flushed for 30 min with N_2, was irradiated with a high-pressure Hg lamp as the internal light source at ambient temperatures while N_2 was bubbled through the solution. Progress of the reaction was monitored by TLC (silica gel, CH_2Cl_2). After 9.5 h of irradiation, the solvent was removed in vacuo, and the residue was purified using a short column of silica gel with CH_2Cl_2 to give **6** (83 mg, 98%, R_f = 0.83) as a white solid. When the reaction was carried out on a larger scale (**5**, 1.06 g, 4.0 mmol), 95% yield of **6** (792 mg) was obtained after 20 h of irradiation. − ^{1}H NMR: δ = 2.10 (AA′, 4 H, $-CH_2CH_2-$), 3.10 (XX′, 4 H, $-CH_2CH-$), 4.27 (s, 2 H, ArH), 7.05 (dd, J = 7.3, 1.7 Hz, 4 H, ArH), 7.28 (t, J = 7.6 Hz, 2 H, ArH) [ref.[55] (CCl_4): δ = 2.03 (AA′, 4 H, $-CH_2CH-$), 3.09 (XX′, 4 H, $-CH_2CH_2-$), 4.25 (s, 2 H, ArH), 7.03 (m, 4 H, ArH), 7.25 (t, J = 7.8 Hz, 2 H, ArH)].

[3.2]Metacyclophane-2-one (7): A benzene solution (500 mL) of **5** (600 mg, 2.27 mmol) was irradiated for 4 h as described for **6**. The reaction mixture was concentrated to dryness, and the residue was separated by column chromatography (SiO_2, toluene) to give **7** (307 mg, 57%, R_f = 0.39), along with **6** (87 mg, 9%) and recovered **5** (389 mg). − **7:** Colorless crystals (hexane), m.p. 111−112 °C. − ^{1}H NMR: δ = 2.21 (AA′, 2 H, $-CH_2CH_2-$), 3.09 (XX′, 2 H, $-CH_2CH_2-$), 3.47 (d, J = 14.9 Hz, 2 H, $-CH_2COCH_2-$), 3.55 (d, J = 14.9 Hz, 2 H, $-CH_2COCH_2-$), 5.21 (s, 2 H, ArH, H-9), 7.12−7.15 (m, 4 H, ArH, H-6 + H-7), 7.31 (d, J = 7.26 Hz, 2 H, ArH, H-5). − IR (KBr): $\tilde{\nu}$ = 1698 (−CO) cm^{-1}. − FABMS: m/z = 236 [M$^+$]. − $C_{17}H_{16}O$ (236.3): calcd. C 86.40, H 6.82; found C 86.35, H 6.90.

[3.2]Metacyclophane (27): A mixture of the ketone **7** (132 mg, 0.56 mmol), hydrazine hydrate (100%, 2 mL), KOH (500 mg), and

diethylene glycol (30 mL) was heated at ca. 130 °C for 3 h and then at ca. 200 °C for 3 h. After cooling, the mixture was poured into dilute aqueous HCl solution and extracted with Et_2O. The combined extracts were washed with brine, dried with $MgSO_4$, and filtered, and the filtrate was concentrated to dryness. The residue was purified by column chromatography (SiO_2, hexane) to give [3.2]MCP **27** as colorless crystals (113 mg, 91%, R_f = 0.35), m.p. 55−56 °C (ref.[56] 59−61 °C). − ^{1}H NMR: δ = 2.17 (AA′, 2 H, $-CH_2CH_2-$), 3.04 (XX′, 2 H, $-CH_2CH_2-$), 1.94 (m, 2 H, $-CH_2CH_2CH_2-$), 2.35 (m, 2 H, $-CH_2CH_2CH_2-$), 2.77 (m, 2 H, $-CH_2CH_2CH_2-$), 5.09 (s, 2 H, ArH, H-9), 6.9−7.1 (m, 4 H, H-5 and H-7), 7.23 (t, J = 7.3 Hz, 2 H, H-6) [ref.[55]: δ = 2.16 (AA′, 4 H, $-CH_2CH_2-$), 3.03 (XX′, 2 H, $-CH_2CH_2-$), 1.93 and 2.32 ($A_2B_2C_2$, 6 H, $-CH_2CH_2CH_2-$), 5.09 (s, 2 H, ArH), 7.00−7.22 (m, 6 H, ArH)].

2,2-Dideuterio[3.2]metacyclophane (27-D_2): Compound **7** (211 mg, 0.89 mmol) was dissolved in AcOH (10 mL) and 1,2-ethanedithiol (1 mL, 12 mmol) and 10 drops of $BF_3{\cdot}OEt_2$ were added in succession. The mixture was stirred for 38 h at room temperature. The reaction was quenched by the addition of water and the mixture was extracted with CH_2Cl_2. The combined organic extracts were washed with saturated aqueous $NaHCO_3$ solution, dried with $MgSO_4$, and filtered. The filtrate was concentrated to dryness in vacuo to give 2-dithiabutanediyl[3.2]MCP as colorless crystals [264 mg, 94%, R_f = 0.86 (SiO_2, toluene)]. A sample was crystallized from CH_2Cl_2/hexane, m.p. 172−174 °C (decomp.). − ^{1}H NMR: δ = 2.23 (AA′, 2 H, $-CH_2CH_2-$), 3.03 (XX′, 2 H, $-CH_2CH_2-$), 2.72 (d, J = 14.9 Hz, 2 H, $-CH_2CCH_2-$), 3.52 (d, J = 14.5 Hz, 2 H, $-CH_2CCH_2$-), 3.2−3.4 (m, 2 H, $-SCH_2CH_2S-$), 3.4−3.6 (m, 2 H, $-SCH_2CH_2S-$), 4.89 (s, 2 H, ArH), 7.09 (d, J = 7.3 Hz, 2 H, ArH), 7.26 (t, J = 7.6 Hz, 2 H, ArH), 7.62 (d, J = 7.6 Hz, 2 H, ArH). − FABMS: m/z = 312 [M^+]. − $C_{19}H_{20}S_2$ (312.5): calcd. C 73.03, H 6.45; found C 72.88, H 6.52. − A mixture of the thioacetal (105 mg, 0.34 mmol), nBu$_3$SnD (2 mL, 7.4 mmol), AIBN (50 mg), and xylene (20 mL) was refluxed for 24 h under N_2. The solvent was removed in vacuo and the residue was separated by preparative TLC (SiO_2, hexane, R_f = 0.46) to give **27-D_2** (49 mg, 64%). A sample was recrystallized from MeOH at low temperatures to give colorless crystals, m.p. 59−60 °C. − ^{1}H NMR: δ = 2.17 (AA′, J = 7.9 Hz, 2 H, $-CH_2CH_2-$), 3.04 (XX′, J = 7.9 Hz, 2 H, $-CH_2CH_2-$), 2.31 (d, J = 14.2 Hz, 2 H, $-CH_2CD_2CH_2-$), 2.78 (d, J = 14.2 Hz, 2 H, $-CH_2CD_2CH_2-$), 5.09 (s, 2 H, H-9), 7.00−7.03 (m, 4 H, H-5 and H-7), 7.23 (t, J = 7.59 Hz, 2 H, H-6). − EIMS: m/z = 224 [M^+]. − $C_{17}H_{16}D_2$ (224.3): calcd. C 91.02, H 8.09; found C 90.87, H 8.09.

[2]Metacyclo[2](2,6)pyridinophane (9): A benzene solution (1 L) of [3]metacyclo[3](2,6)pyridinophane-2,11-dione **8** (212 mg, 0.8 mmol) was irradiated as described for **6**. Progress of the reaction was monitored by TLC [SiO_2, CH_2Cl_2/AcOEt (5:1), R_f values of **9** and **10** were 0.51 and 0.49]. After 45 h, the solvent was removed in vacuo and the residue was separated by preparative TLC [Al_2O_3, hexane/ether (5:1)] to give **9** (93 mg, 56%) and [3]metacyclo[2](2,6)-pyridinophane-2-one **10** (26 mg, 14%). − **9:** ^{1}H NMR: δ = 2.25−2.42 (m, 4 H, $-CH_2CH_2-$), 3.13−3.23 (m, 4 H, $-CH_2CH_2-$), 4.39 (s, 1 H, ArH), 7.07−7.12 (m, 4 H, ArH), 7.31 (t, J = 7.4 Hz, 1 H, ArH), 7.60 (t, J = 7.6 Hz, 1 H, ArH). [ref.[57]4.40 (s, 1 H, ArH), 7.05 (d, J = 8 Hz, 2 H, PyH), 7.57 (t, J = 8 Hz, 1 H, PyH).

[3]Metacyclo[2](2,6)pyridinophane-2-one (10): A benzene solution (500 mL) of **8** (800 mg, 2.84 mmol) was irradiated for 4 h as described for **6**. The solvent was removed in vacuo and the residue was purified by column chromatography [SiO_2, CH_2Cl_2/AcOEt (10:1)] to give **10** (485 mg, 72%, R_f = 0.51) as colorless crystals. − **10:** Colorless plates (CH_2Cl_2/hexane), m.p. 121−122 °C. − ^{1}H NMR: δ = 2.5 (br s, 2 H, $-CH_2CH_2-$), 3.2 (br s, 2 H, $-CH_2CH_2-$), 3.61 (s, 2 H, $-CH_2COCH_2-$), 3.71 (s, 2 H, $-CH_2COCH_2-$), 5.32 (s, 1 H, ArH), 7.10−7.22 (m, 4 H, ArH, PyH), 7.36 (t, J = 7.6 Hz, 1 H, ArH), 7.60 (t, J = 7.6 Hz, 1 H, PyH). − IR (KBr): $\tilde{\nu}$ = 1698 (CO) cm^{-1}. − FABMS: m/z = 237 [M^+]. − $C_{16}H_{15}NO$ (237.3): calcd. C 80.98, H 6.37, N 5.90; found C 80.81, H 6.46, N 5.94.

[3]Metacyclo[2](2,6)pyridinophane (28): A mixture of **8** (220 mg, 0.93 mmol), hydrazine hydrate (100%, 4 mL), KOH (1.0 g), and diethylene glycol (25 mL) was heated at ca. 130 °C for 2 h and then at ca. 200 °C for 2 h. After cooling, the reaction mixture was diluted with water and the mixture was extracted with Et_2O. The combined extracts were washed with brine, dried with $MgSO_4$, and filtered, and the filtrate was concentrated to dryness. The residue was passed through a short silica gel column with CH_2Cl_2/AcOEt [R_f = 0.79, CH_2Cl_2/AcOEt (5:1)], and the eluate was concentrated to dryness to give **28** as colorless crystals (200 mg, 97%). − **28:** Colorless plates (CH_2Cl_2/hexane), m.p. 85−86 °C (decomp.). − ^{1}H NMR: δ = 2.01 (m, 2 H, $-CH_2CH_2CH_2-$), 2.5−3.2 (m, 8 H, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$), 5.70 (s, 1 H, H-9), 6.90−6.93 (m, 4 H, H-5, H-7, H-13, H-15), 7.10 (t, J = 7.59, 7.26 Hz, 1 H, H-6), 7.44 (t, J = 7.59 Hz, 1 H, H-14). − EIMS: m/z = 223 [M^+]. − $C_{16}H_{17}N$ (223.3): calcd. C 86.05, H 7.67, N 6.27; found C 85.95, H 7.63, N 6.25.

2,2-Dideuterio[3]metacyclo[2](2,6)pyridinophane (28-D_2): Compound **10** (146 mg, 0.615 mmol) was dissolved in AcOH (10 mL), 1,2-ethanedithiol (1 mL, 12 mmol) and $BF_3{\cdot}OEt_2$ (0.2 mL) were added in succession, and the mixture was stirred for 20 h at room temperature. An additional quantity of $BF_3{\cdot}OEt_2$ (0.2 mL) was added and the mixture was stirred for an additional 24 h. The reaction mixture was neutralized by addition of saturated aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were dried with $MgSO_4$, and filtered. The filtrate was concentrated in vacuo and the concentrate was separated by preparative silica gel TLC with CH_2Cl_2 (R_f = 0.25) to give 2-dithiabutanediyl[3]metacyclo[2](2,6)pyridinophane **29** (136 mg, 71%). A sample was recrystallized from AcOEt/CH_2Cl_2 to give colorless crystals, m.p. 166.5−167.5 °C. − ^{1}H NMR: δ = 2.51 (AA′, 2 H, $-CH_2CH_2-$), 3.51 (XX′, 2 H, $-CH_2CH_2-$), 2.78 (d, J = 14.5 Hz, 1 H, $-CH_2CCH_2-$), 3.54 (d, J = 14.5 Hz, 1 H, $-CH_2CCH_2-$), 2.98 (d, J = 14.5 Hz, 1 H, $-CH_2CCH_2-$), 3.63 (d, J = 14.2 Hz, 1 H, $-CH_2CCH_2-$), 2.9−3.6 (m, 4 H, $-SCH_2CH_2S-$), 4.83 (s, 1 H, H-9), 7.13 (d, J = 7.3 Hz, 2 H, H-5, H-7), 7.26 (t, J = 7.3 Hz, 1 H, H-6), 7.5−7.7 (m, 3 H, PyH). − FABMS: m/z = 314 [M + H]$^+$. − $C_{18}H_{19}NS_2{\cdot}0.05\ CH_2Cl_2$ (after drying at 100 °C in vacuo for 1 d) (317.7): calcd. C 68.23, H 6.06, N 4.41; found C 67.94, H 6.16, N 4.36. − A mixture of **29** (68 mg, 0.217 mmol), nBu$_3$SnD (1.5 g, 5.1 mmol), AIBN (50 mg), and xylene (15 mL) was refluxed for 36 h under N_2. The solvent was removed in vacuo and the residue was first separated by preparative silica gel TLC with CH_2Cl_2. Two bands were observed, and the lower band was further purified by silica gel column chromatography [CH_2Cl_2/AcOEt (10:1), R_f = 0.27] to give colorless crystals (25 mg, 52%). − **28-D_2:** Colorless granules (CH_2Cl_2/AcOEt), m.p. 74−75 °C. − ^{1}H NMR: δ = 2.5−3.1 (m, 8 H, $-CH_2CH_2-$, $-CH_2CD_2CH_2-$), 5.70 (s, 1 H, H-9), 6.9 (m, 4 H, H-5, H-7, H-13, and H-15), 7.10 (t, J = 7.58 Hz, 1 H, H-6), 7.44 (t, J = 7.59 Hz, 1 H, H-14). − EIMS: m/z = 225 [M^+]. − $C_{16}H_{15}D_2N$ (225.4): calcd. C 85.29, H 7.61, N 6.22; found C 85.15, H 7.58, N 6.15.

[2.2]Metaparacyclophane (12): A benzene solution (1 L) of [3.3]MPCP-2,11-dione **11** (211 mg, 0.8 mmol) was irradiated as described for **6**. Progress of the reaction was monitored by TLC (SiO_2, CH_2Cl_2). After 5 h of irradiation, the solvent was removed in vacuo, and the residue was purified using a short column of silica gel with CH_2Cl_2 to give **12** (158 mg, 94%, R_f = 0.83) as a colorless solid. When the reaction was discontinued after irradiation times of 30 min and 1 h, **12** (43%), [3.2]MPCP-2-one **13** (47%), and the starting material **11** (10%), and **12** (85%) and **13** (14%), respectively, were isolated. Separation was carried out by silica gel preparative TLC (CH_2Cl_2) (R_f values of **12**, **13**, and **11** were 0.83, 0.50, and 0.25). − **12:** ^{1}H NMR: δ = 2.10−2.22 (m, 2 H, $-CH_2CH_2-$), 2.47−2.58 (m, 2 H, $-CH_2CH_2-$), 2.72−2.80 (m, 2 H, $-CH_2CH_2-$), 3.11−3.18 (m, 2 H, $-CH_2CH_2-$), 5.41 (s, 1 H, ArH), 5.85 (d, J = 2.3 Hz, 2 H, ArH), 6.76 (m, 2 H, ArH), 6.95 (t, J = 7.4 Hz, 1 H, ArH), 7.19 (d, J = 2.0 Hz, 2 H, ArH) [ref.[20]: δ = 1.87−3.12 (m, 8 H, $-CH_2CH_2-$), 5.24 (s, 1 H, ArH), 5.70 (d, J = 1.9 Hz, 2 H, ArH), 6.63 (m, 3 H, ArH), 6.97 (d, J = 1.9 Hz, 2 H, ArH)].

[3.2]Metaparacyclophane-2-one (13): A benzene solution (500 mL) of **11** (405 mg, 1.53 mmol) was irradiated for 26 min as described for **6**. The solvent was removed in vacuo and the residue was purified by preparative silica gel TLC with CH_2Cl_2 to give **13** (167 mg, 46%, R_f = 0.54) as a colorless solid, along with **12** (46 mg, 14%, R_f = 0.93) and recovered starting material **11** (89 mg, 22%, R_f = 0.33). − **13:** Colorless crystals (hexane), m.p. 121.0−122.5 °C. − ^{1}H NMR: δ = 2.7 (br s, 2 H, $-CH_2CH_2-$), 2.9 (br s, 2 H, $-CH_2CH_2-$), 3.28 (s, 2 H, $-CH_2COCH_2-$), 3.62 (s, 2 H, $-CH_2COCH_2-$), 5.38 (s, 1 H, ArH), 6.2−6.8 (m, 4 H, ArH), 6.79 (d, J = 7.3 Hz, 1 H, ArH), 6.90 (d, J = 7.9 Hz, 1 H, ArH), 7.01 (t, J = 7.6 Hz, 1 H, ArH). − IR (KBr): $\tilde{\nu}$ = 1698 (CO) cm^{-1}. − FABMS: m/z = 237 [M + H]$^+$. − $C_{17}H_{16}O$ (236.3): calcd. C 86.40, H 6.82; found C 86.29, H 6.84.

[2.2]Paracyclophane (15): A benzene solution (1 L) of [3.3]PCP-2,11-dione **14** (194 mg, 0.73 mmol) was irradiated as described for **6**. After 4 h of irradiation, the solvent was removed in vacuo and the residue was purified using a short column of silica gel with CH_2Cl_2 to give **15** (149 mg, 97%, R_f = 0.92) as a white solid. − **15:** ^{1}H NMR: δ = 3.08 (s, 8 H, $-CH_2CH_2-$), 6.48 (s, 8 H, ArH) [ref.[58]: δ = 3.04 (s, 8 H, $-CH_2CH_2-$), 6.30 (s, 8 H, ArH)].

[3.2]Paracyclophane-2-one (16): A benzene solution (500 mL) of **14** (142 mg, 0.54 mmol) was irradiated for 20 min as described for **6**. The solvent was removed in vacuo, and the residue was purified by preparative silica gel TLC with CH_2Cl_2 to give **16** (27 mg, 21%, R_f = 0.62) as a white solid, along with **15** (11 mg, 10%) and starting material **14** (29 mg, 20%). − **16:** ^{1}H NMR: δ = 2.98 (s, 4 H, $-CH_2CH_2-$), 3.70 (s, 4 H, $-CH_2CCH_2-$), 6.45 (d, J = 7.9 Hz, 4 H, ArH) [ref.[17b]: δ = 2.96 (s, 4 H, $-CH_2CH_2-$), 3.68 (s, 4 H, $-CH_2CCH_2-$), 6.4−6.7 (AA′BB′, 8 H, ArH)].

[2.2.2]Paracyclophane (21): A benzene solution (500 mL) of [3.3.3]PCP-2,11,20-trione **20** (106 mg, 0.27 mmol) was irradiated for 17 h as described for **6**. The solvent was removed in vacuo, and the residue was separated by preparative silica gel TLC (SiO_2, CH_2Cl_2) to give **21** (33 mg, 39%, R_f = 0.76) as a white solid. − ^{1}H NMR: δ = 2.94 (s, 12 H, $-CH_2CH_2-$), 6.69 (s, 12 H, ArH) [ref.[22]: δ = 2.93 (s, 12 H, $-CH_2CH_2-$), 6.62 (s, 12 H, ArH)].

[3.3.2](1,3,5)Cyclophane (25): A benzene solution (500 mL) of [3.3.3](1,3,5)CP-2-one **24** (580 mg, 2.00 mmol) was irradiated as described for **6**. After 46 h of irradiation, the reaction mixture was concentrated to dryness, and the residue was separated by silica gel column chromatography with toluene to give **25** (178 mg, 34%, R_f = 0.86) and recovered starting material **24** (237 mg, 41%, R_f = 0.57). − **25:** Colorless plates (benzene/EtOH), m.p. 156.5−158.5 °C. − ^{1}H NMR: δ = 1.94−2.14 (m, 4 H, $-CH_2CH_2CH_2-$), 2.51−2.68 (m, 4 H, $-CH_2CH_2CH_2-$), 2.77−2.92 (m, 4 H, $-CH_2CH_2CH_2-$), 3.02 (s, 4 H, $-CH_2CH_2-$), 6.13 (s, 4 H, ArH), 6.72 (s, 2 H, ArH). − EIMS: m/z = 262 [M$^+$]. − $C_{20}H_{22}$ (262.4): calcd. C 91.55, H 8.45; found C 91.49, H 8.41.

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[1] H. Isaji, Ph.D. Dissertation, Kyushu University, **1999**.
[2] Part 5: K. Sako, H. Tatemitsu, S. Onaka, H. Takemura, S. Osada, G. Wen, J. M. Rudzinski, T. Shinmyozu, *Liebigs Ann.* **1996**, 1645−1649.
[3] [3a] Y. Sakamoto, T. Kumagai, K. Matohara, C. Lim, T. Shinmyozu, *Tetrahedron Lett.* **1999**, *40*, 919−922. − [3b] K. Matohara, C. Lim, M. Yasutake, R. Nogita, T. Koga, Y. Sakamoto, T. Shinmyozu, *Tetrahedron Lett.* **2000**, *41*, 6803−6807.
[4] [4a] C. Lim, M. Yasutake, T. Shinmyozu, *Angew. Chem. Int. Ed.* **2000**, *39*, 578−580. − [4b] C. Lim, M. Yasutake, T. Shinmyozu, *Tetrahedron Lett.* **1999**, *40*, 6781−6784.
[5] H. Isaji, K. Sako, H. Takemura, H. Tatemitsu, T. Shinmyozu, *Tetrahedron Lett.* **1998**, *39*, 4303−4304.
[6] [6a] G. Quinkert, K. Opitz, W. W. Weirsdorff, J. Weinlich, *Tetrahedron Lett.* **1963**, 1863−1868. − [6b] P. S. Engel, *J. Am. Chem. Soc.* **1970**, *92*, 6074−6076. − [6c] W. K. Robbins, R. H. Eastman, *J. Am. Chem. Soc.* **1970**, *92*, 6076−6077. − [6d] W. K. Robbins, R. H. Eastman, *J. Am. Chem. Soc.* **1970**, *92*, 6077−6079.
[7] M. Shibahara, T. Shinmyozu, manuscript in preparation.
[8] [8a] K. Kurosawa, M. Suenaga, T. Inazu, T. Yoshino, *Tetrahedron Lett.* **1982**, *23*, 5335−5338. − [8b] T. Shinmyozu, Y. Hirai, T. Inazu, *J. Org. Chem.* **1986**, *51*, 1551−1555. − [8c] H. Sasaki, T. Kitagawa, *Chem. Pharm. Bull.* **1983**, 31, 2868−2878. − [8d] J. Breitenbach, F. Vögtle, *Synthesis* **1992**, 41−42.
[9] For a review see: F. Vögtle, *Cyclophan-Chemie*, B. G. Teubner, Stuttgart, **1990**.
[10] [10a] V. Boekelheide, I. D. Reingold, M. Tuttle, *J. Chem. Soc., Chem. Commun.* **1973**, 406−407. − [10b] W. Rebafka, H. A. Staab, *Angew. Chem. Int. Ed. Engl.* **1973**, *12*, 776−777. − [10c] R. Gray, V. Boekelheide, *Angew. Chem. Int. Ed. Engl.* **1975**, *14*, 107−108.
[11] H. Higuchi, K. Tani, T. Otsubo, Y. Sakata, *Bull. Chem. Soc. Jpn.* **1987**, *60*, 4027−4036.
[12] R. S. Givens, R. J. Olsen, P. L. Wylie, *J. Org. Chem.* **1979**, *44*, 1608−1613.
[13] F. Vögtle, *Angew. Chem.* **1969**, *81*, 258.
[14] H. Takemura, T. Shinmyozu, T. Inazu, *Tetrahedron Lett.* **1988**, *29*, 1031−1032.
[15] [15a] M. L. Kaplan, E. A. Truesdale, *Tetrahedron Lett.* **1976**, 3665−3666. − [15b] M. Hibert, G. Solladia, *J. Org. Chem.* **1980**, *45*, 4496−4498.
[16] S. H. Mashraqui, K. R. Nivalkar, *Tetrahedron Lett.* **1997**, *38*, 4487−4488.
[17] [17a] J. Breitenbach, F. Ott, F. Vögtle, *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 307−308. − [17b] F. Ott, J. Breitenbach, M. Nieger, F. Vögtle, *Chem. Ber.* **1993**, *126*, 97−101.
[18] [18a] T. Yamato, H. Sakamoto, K. Kobayashi, M. Tashiro, *J. Chem. Research (M)* **1986**, 2864−2872. − [18b] A. Tsuge, M. Yasutake, T. Moriguchi, K. Sakata, T. Yamato, S. Mataka, M. Tshiro, *Chem. Lett.* **1997**, 413−414. − [18c] T. Moriguchi, M. Yasutake, K. Sakata, A. Tsuge, *J. Chem. Research (S)* **1999**, 78−79.

[19] [19a] K. J. Przybilla, F. Vögtle, *Chem. Ber.* **1989**, *122*, 347−355. − [19b] S. Billen, F. Vögtle, *Chem. Ber.* **1989**, *122*, 1113−1117.
[20] D. J. Cram, R. C. Helgeson, D. Lock, A. Singer, *J. Am. Chem. Soc.* **1966**, *88*, 1324−1325.
[21] H. Isaji, T. Shinmyozu, *J. Org. Chem.*, submitted for publication.
[22] I. Tabushi, H. Yamada, Z. Yoshida, R. Oda, *Tetrahedron* **1971**, *27*, 4845−4853.
[23] K. Matohara, T. Shinmyozu, unpublished results.
[24] We have confirmed that this reaction was applicable to the synthesis of triple-layered [2.2]metacyclophanes from the corresponding triple-layered [3.3]metacyclophanetetraones. The result will be reported elsewhere.
[25] For a very recent review see: L. Ernst, *Prog. Nucl. Magn. Reson. Spectrosc.* **2000**, *37*, 47−190.
[26] R. H. Mitchell in *Cyclophanes* (Eds.: P. M. Keehn, S. M. Rosenfeld), Academic, New York, **1983**, part 1, p. 239−310.
[27] F. A. L. Anet, M. A. Brown, *J. Am. Chem. Soc.* **1969**, *91*, 2389−2391.
[28] K. Sako, T. Meno, H. Takemura, T. Shinmyozu, T. Inazu, *Chem. Ber.* **1990**, *123*, 639−642.
[29] M. F. Semmelhack, J. J. Harrison, D. C. Young, A. Gutiérrez, S. Rafii, J. Clardy, *J. Am. Chem. Soc.* **1985**, *107*, 7508−7514.
[30] [30a] K. Sako, T. Hirakawa, N. Fujimoto, T. Shinmyozu, T. Inazu, H. Horimoto, *Tetrahedron. Lett.* **1988**, *29*, 6275−6278. − [30b] K. Sako, T. Shinmyozu, H. Takemura, M. Suenaga, T. Inazu, *J. Org. Chem.* **1992**, *57*, 6536−6541. − [30c] T. Shinmyozu, T. Hirakawa, G. Wen, S. Osada, H. Takemura, K. Sako, J. M. Rudzinski, *Liebigs Ann.* **1996**, 205−210. − [30d] H. Takemura, H. Kariyazono, M. Yasutake, N. Kon, K. Tani, K. Sako, T. Shinmyozu, T. Inazu, *J. Org. Chem.* **1999**, *64*, 9077−9079. − [30e] G. Wen, W. Matsuda-Sentou, K. Sameshima, M. Yasutake, D. Noda, C. Lim, T. Satou, H. Takemura, K. Sako, H. Tatemitsu, T. Inazu, T. Shinmyozu, *J. Am. Chem. Soc.*, in press. − [30f] T. Satou, T. Shinmyozu, *J. Chem. Soc., Perkin Trans. 1*, submitted for publication.
[31] [31a] Y. Fukazawa, Y. Yang, T. Hayashibara, S. Usui, *Tetrahedron. Lett.* **1995**, *36*, 3449−3352. − [31b] Y. Fukazawa, T. Hayashibara, Y. Yang, S. Usui, *Tetrahedron. Lett.* **1996**, *52*, 2847−2862.
[32] [32a] H. Sasaki, T. Kitagawa, *Chem. Pharm. Bull.* **1987**, *35*, 4747−4756. − [32b] H. Sasaki, K. Ogawa, Y. Iijima, T. Kitagawa, *Chem. Pharm. Bull.* **1988**, *36*, 1990−1996.
[33] [33a]T. Meno, K. Sako, M. Suenaga, M. Mouri, H. Takemura, T. Shinmyozu, T. Inazu, *Can. J. Chem.* **1990**, *68*, 440−445. − [33b] T. Shinmyozu, S. Kusumoto, S. Nomura, H. Kawase, T. Inazu, *Chem. Ber.* **1993**, *126*, 1815−1818. − [33c] T. Shinmyozu, M. Hirakida, S. Kusumoto, M. Tomonou, T. Inazu, J. M. Rudzinski, *Chem. Lett.* **1994**, 669−672. − [33d] Y. Sakamoto, N. Miyoshi, M. Hirakida, S. Kusumoto, H. Kawase, J. M. Rudzinski, T. Shinmyozu, *J. Am. Chem. Soc.* **1996**, *118*, 12267−12275. − [33e] K. Hori, W. Sentou, T. Shinmyozu, *Tetrahedron Lett.* **1997**, *38*, 8955−8958. − [33f] Y. Sakamoto, T. Shinmyozu, *Recent Res. Dev. Pure Appl. Chem.* **1998**, *2*, 372−399.
[34] H. F. Bettinger, P. v. R. Schleyer, H. F. Schaefer III, *J. Am. Chem. Soc.* **1998**, *120*, 1074−1075.
[35] R. W. Griffin, Jr., R. A. Coburn, *J. Am. Chem. Soc.* **1967**, *89*, 4638−4641.
[36] [36a] T. Sato, M. Wakabayashi, M. Kainosyo, K. Hata, *Tetrahedron Lett.* **1968**, 4185− 4189. − [36b] T. Sato, K. Wakabayashi, K. Hata, M. Kainosho, *Tetrahedron* **1971**, *27*, 2737−2755.
[37] D. Krois, H. Lehner, *Tetrahedron* **1982**, *38*, 3319−3324.
[38] T. Hirakawa, T. Inazu, unpublished results.
[39] T. Shinmyozu, J. M. Rudziński, M. Matsushita, H. Shimauchi, K. Sako, T. Matsunaga, S. Kusumoto, T. Inazu, *The 2nd Symposium on Computational Chemistry, Abstracts of papers*, Tokyo, Japan Chemistry Program Exchange, **1992**, pp. 103−106.
[40] The computations were performed with MM3−92, MOPAC93 programs, graphically facilitated by ANCHOR II™ from Fujitsu Limited and Kureha Chemical Industries.
[41] L. Pauling, *The Nature of the Chemical Bonds*, Cornell University Press, Ithaca, New York, **1960**, pp. 260.
[42] [42a] A. Mannschreck, G. Rissmann, F. Vögtle, D. Wild, *Chem. Ber.* **1967**, *100*, 335−346. − [42b] I. C. Calder, P. J. Garratt, *J. Chem. Soc. B.* **1967**, 660−662. $\Delta G^{\neq}$ [cal/mol] = 2.303 × 1.987 T_c (10.319 − $\log_{10}\kappa_c$ + $\log_{10}T_c$) where $\kappa_c = \pi 2^{1/2}(\nu_A - \nu_B)^2 + 6J_{AB}^2]^{1/2}$. **27-$D_2$** in [$D_5$]bromobenzene: $\nu_A - \nu_B$ = 116, J = 14.2 Hz, T_c = 62 °C (335 K).
[43] Compound **7** in [D_5]bromobenzene: $\nu_A - \nu_B$ = 13.0, J = 14.5 Hz, T_c = 74 °C (347 K).
[44] Compound **7** in [D_6]DMSO: $\nu_A - \nu_B$= 22.1, J = 14.5 Hz, T_c = 70 °C (343 K).
[45] Compound **10** in [D_5]bromobenzene: $\nu_A - \nu_B$ = 206, J = 8.9 Hz, T_c = 34 °C (307 K).
[46] In the VT ^{1}H NMR spectra of **28-D_2** in CD_2Cl_2, T_c of the AB system could not be determined because of the complexity of the signal.
[47] W. Matsuda-Sentou, T. Shinmyozu, *Tetrahedron: Asymmetry*, in press.
[48] [48a] W. Sentou, T. Satou, M. Yasutake, C. Lim, Y. Sakamoto, T. Itoh, T. Shinmyozu, *Eur. J. Org. Chem.* **1999**, 1223−1231. − [48b] W. Matsuda-Sentou, T. Shinmyozu, *Eur. J. Org. Chem.* **2000**, 3195−3203.
[49] [49a] G. J. M. Van der Kerk, J. G. Noltes, J. G. A. Luitjen, *J. Appl. Chem.* **1957**, *7*, 366−369. − [49b] G. M. Whitesides, J. S. Fillippo, Jr., *J. Am. Chem. Soc.* **1970**, *92*, 6611−6624.
[50] M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, G. Polidori, R. Spagna, D. Viterbo, *J. Appl. Crystallogr.* **1989**, *22*, 389−303.
[51] G. M. Sheldrick in *Crystallographic Computing 3* (Eds.: G. M. Sheldrick, C. Kruger, R. Goddard), Oxford University Press, London, **1985**, pp. 175−189.
[52] A. Altomare, M. C. Burla, M. Camalli, M. Cascarano, C. Giacovazzo, A. Guagliardi, G. Polidori, *J. Appl. Crystallogr.* **1994**, *27*, 435.
[53] P. T. Beurskens, G. Admiral, G. Beurskens, W. P. Bosman, R. de Gelder, R. Israel, J. M. M. Smits, *The DIRDIF-94 program system*, Technical Report of the Crystallography Laboratory, Univeresity of Nijmegen, The Netherlands, **1994**.
[54] *Crystal Structure Analysis Package*, Molecular Structure Corporation, The Woodland, Texas, **1985**, **1992**.
[55] D. J. Wilson, V. Boekelheide, R. W. Grifinn, Jr., *J. Am. Chem. Soc.* **1960**, *82*, 6302−6304
[56] D. Krois, H. Lehner, *J. Chem. Soc., Perkin Trans. 1* **1982**, 477−481.
[57] J. R. Fletcher, I. O. Sutherland, *J. Chem. Soc., Chem. Commun.* **1969**, 1504−1505.
[58] F. Vögtle, P. Neumann, *Top. Curr. Chem.* **1974**, *48*, 73.

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