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Synthesis, Structure, and Transannular $\pi-\pi$ Interaction of Multilayered [3.3]Metacyclophanes[1]

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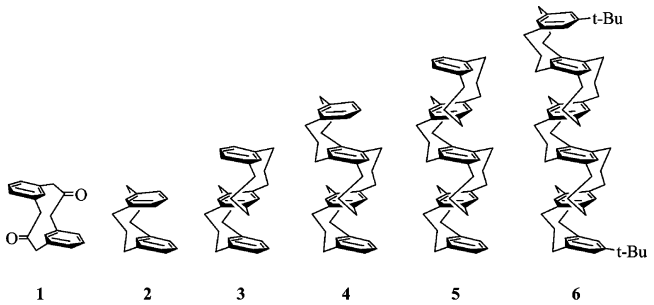

The synthesis of a series of three- to six-layered [3.3]metacyclophanes ([3.3]MCPs) **3**−**6** has been successfully accomplished by the (*p*-tolylsulfonyl)methyl isocyanide (TosMIC) method as a critical coupling reaction. Their important synthetic intermediates are the two- and three-layered bis(bromomethyl) compounds **11**, **17**, **21**, and tetrakis(bromomethyl) compounds **25** and **28**. The structures of the three- to six-layered [3.3]MCPs (**3**−**6**) as well as three- to six-layered [3.3]MCP-di- (**22**−**24**) and tetraones (**26**, **27**, and **29**) as the synthetic intermediates have been elucidated based on the ^{1}H NMR data and X-ray structural analysis. These multilayered cyclophanes are constructed with two different geometries, *syn*-[3.3]MCP and *anti*-[3.3]MCP-2,11-dione. In principle, their geometries are maintained in the multilayered [3.3]MCPs, but deformation of the dihedral angle of the two benzene rings of the *syn*-[3.3]MCP moiety is generally observed. In the four-layered MCP **4**, the central [3.3]MCP moiety takes an anti geometry. These data indicate the structural flexibility of the [3.3]MCP moiety. In the electronic spectra, rather simple and structureless absorption curves are observed, and the most significant spectral change is observed for the two to three layers and becomes less effective even if it is more layered. In the charge-transfer (CT) bands of the multilayered [3.3]MCPs with tetracyanoethylene (TCNE), the λ_{max} gradually shifts to the longer wavelength region, but the extent of the shift is much smaller as the number of layers increases. In the multilayered [3.3]MCP-di- and tetraones, the *anti*-[3.3]MCP-dione moiety works as an insulator. Therefore, the CT interaction of the four- and five-layered [3.3]MCPs with one *anti*-[3.3]MCP-dione moiety (**23** and **24**) shows the almost comparable magnitude of the interaction with the two- and three-layered [3.3]MCPs (**2** and **3**), respectively. The tetraones of the three and four-layered MCPs (**29** and **26**) do not show CT interactions except for the six-layered MCP **27**.

Introduction

Multistory compounds constructed with cyclophane building blocks are called multilayered cyclophanes. We can construct various types of new multistory compounds with various types of structural units by choosing the appropriate cyclophane building blocks. This structural versatility makes multilayered cyclophanes suitable model compounds for the study of their characteristic structural properties and transannular $\pi-\pi$ interactions between not only faced aryl rings but remote aryl rings. These novel properties may lead to applications as new

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(1) Multilayered [3.3]cyclophanes, part 1.

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nanoscale materials. Among the possible multilayered cyclophanes, the synthesis and interesting chemical and physical properties of a series of multilayered [2.2]para- (PCP),[2] metapara- (MPCP),[3] and metacyclophanes (MCP)[4] were extensively studied by Misumi and Otsubo.[5a−c] The synthesis of optically active multilayered [2.2]PCPs (up to six layers) was accomplished by Yamamoto and Nakazaki starting from the (*R*)-(−)-4-methyl[2.2]PCP, and their interesting chiroptical properties were reported.[6] The properties of the multilayered [3.3]CPs have not been as extensively studied as those of the multilayered [2.2]CPs, probably because of their difficulty in synthesis. In a series of all carbon multilayered CPs described previously, only the three-layered [3.3]PCP,[7] [3.3]MCP **3** (Figure 1),[8] and three- and four-layered [3.3]orthocyclophanes (OCPs)[9] have been reported to date. Recently, Vögtle et al. reported the synthesis and structures of a series of multilayered diaza[3.3]MCPs with *N*-tosyl groups and named the series of compounds molecular ribbons.[10] They successfully synthesized up to a nine-layered [3.3]MCP[10f] with zigzag folded all-syn conformations and attained π stacks of nanometer dimensions.

[3.3]CP is the better system for studying transannular π-π interactions than the [2.2]CP system and its higher homologues because of less strain[11] and more flexibility than the [2.2]CP system, as well as a more suitable transannular distance.[12,13] Our recent study on the transannular $\pi-\pi$ interaction of a series of multibridged [3_n]CPs ($n = 2-6$) showed that their electron-donating ability increased with the increase in the number of bridges because of the effective hyperconjugation between the benzylic hydrogens and the benzene rings. [3_6]CP shows the strongest donating ability in the [3_n]CPs (λ_{max} of the CT band with TCNE, 728 nm in $CHCl_3$).[14] In contrast, this type of electronic interaction is hampered in the [2_n]CPs by the significant bending of the methylene groups out of the plane of the attached benzene ring (20°).[15]

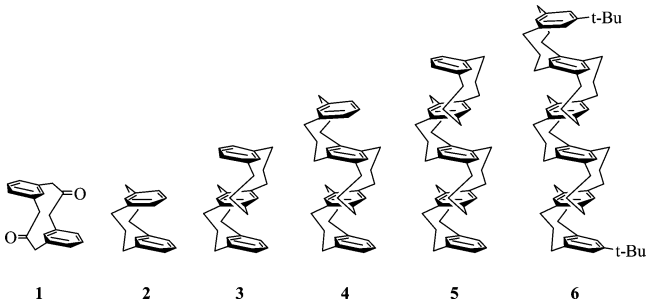

FIGURE 1. Multilayered [3.3]MCPs **2**−**6** and [3.3]MCP-2,11-dione **1**.

Another interesting feature of [3.3]CPs stems from their flexible nature; their conformational behavior in solution has attracted much attention.[16−19] Since our first synthesis of [3.3]-MCP **2**,[20] we have studied the conformational behavior of the [3.3]MCPs[21] and related systems.[22−25] In [3.3]MCP **2**, two geometries with syn and anti configurations are considered

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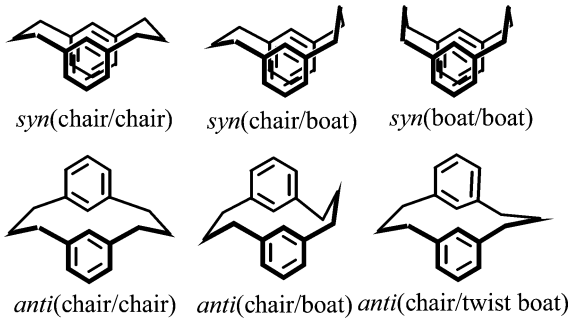
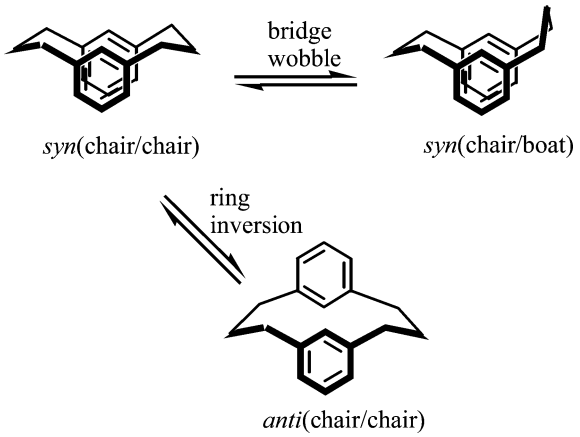


FIGURE 2. Possible conformations of [3.3]MCP **2**.

SCHEME 1. Bridge Wobble and Ring Inversion Processes of [3.3]MCP 2



(Figure 2), and the former is more stable than the latter based on the experimental data and theoretical calculations.[17,21a,b,24] In the three conformations with the *syn* geometry of **2**, the stability order is syn(chair/chair) > syn(chair/boat) > syn(boat/boat).[17,21a,b,24] In the solid state, **2** adopts the syn(chair/chair) with the dihedral angle between two benzene rings being 24°,[17] and the syn(chair/chair) is the most stable conformation in solution.[17,21a,b] In the anti geometry, similar conformations such as anti(chair/chair), anti(chair/boat), and anti(chair/twist boat) are also expected.[26] In the conformational isomerism of **2**, bridge wobbling (BW) and ring inversion (RI) processes are considered (Scheme 1). On the basis of the total line shape simulations of the benzylic methylene region in the temperature-dependent ^{1}H NMR spectra of **2**, we proposed the presence of the RI processes of the syn(chair/chair) and syn(chair/boat) via anti conformations.[19,26]

Our multilayered [3.3]MCPs are constructed with two types of structural units: [3.3]MCP **2** and [3.3]MCP-2,11-dione **1**. In contrast to the stable syn geometry of **2**, the dione **1** takes the anti(chair/boat) in the solid state, and the preferred anti geometry is expected in solution, as gauged by the strongly shielded inner aromatic protons (Hi_1 δ 5.78 in $CDCl_3$).[24] A systematic study of the multilayered [3.3]MCPs containing these unique structural units may provide information on the dependence of the transannular $\pi-\pi$ interaction on the stacking mode of the benzene rings (i.e., syn and anti). The purpose of our present study is (1) to develop general synthetic methods of multilayered [3.3]MCPs, (2) to elucidate their structural properties and examine the relationship between the molecular structure and the electronic $\pi-\pi$ interactions as models of the tilted or partially overlapped π electronic systems, (3) to study the dynamic conformational behavior in solution, (4) to study their inclusion phenomena as host molecules with wide π surfaces for the formation of clathlates with organic molecules, and (5) to find their practical applications as nanometer scale materials. We describe here the synthesis, structure, electronic absorption spectra, and charge-transfer (CT) spectra of the three- to six-layered [3.3]MCPs **3**−**6** and **31** as well as the [3.3]MCP-di- **22**−**24** and tetraones **26**, **27**, **29**, and **30** as their synthetic intermediates.

Results and Discussion

Synthesis. For the synthesis of multilayered [3.3]MCPs, the (*p*-tolylsulfonyl)methyl isocyanide (TosMIC) method[27] has been successfully employed in the critical coupling reactions.[28] The key synthetic intermediates are the two- and three-layered bis(bromomethyl)[3.3]MCPs **11**, **17**, and **21** as well as tetrakis(bromomethyl) compounds **25** and **28**.[10g,29] The two-layered bromides **11** and **17** were synthesized by the coupling reaction between dimethyl 4,6-bis(bromomethyl)benzene-1,3-dicarboxylate **7** and the TosMIC adduct **8** or **14**[28] in the presence of NaOH and *n*-Bu_4NI in a mixture of CH_2Cl_2 and water under phase-transfer conditions, followed by acid treatment to afford the two-layered ketoesters **9** (37%) and **15** (44%) (Scheme 2).

The Wolff−Kishner reduction of the ketoesters **9** or **15** and subsequent reduction of the methyl ester of **10** or **16** with $LiAlH_4$ in THF, followed by bromination of the resultant diol with PBr_3 in C_6H_6, gave the desired dibromides **11** (32% from **9**) and **17** (34% from **15**). The TosMIC adducts **13** and **18** were readily prepared by the reaction of bromide **11** or **17** and TosMIC **12**.

The three-layered bis(bromomethyl) compound **21** was synthesized in a similar way. Bromide **7** and the two-layered TosMIC adduct **13** were coupled to give the three-layered ketoester **19** (42%). Reduction of the carbonyl groups of **19** by the Wolff−Kishner reduction, followed by esterification, afforded the methyl ester **20** (64%). Ester **20** was converted into the three-layered bis(bromomethyl) compound **21** by $LiAlH_4$ reduction in THF and subsequent bromination with PBr_3 in C_6H_6 (51%).

The two-layered bromide **11** was coupled with the TosMIC adduct **8** to provide the three-layered dione **22** (22%) (Scheme 3). The modified Wolff−Kishner reduction of **22** afforded the three-layered CP **3** (82%). A similar coupling reaction of the dibromide **11** with the two-layered TosMIC adduct **13** provided the four-layered dione **23** (20%). Reduction

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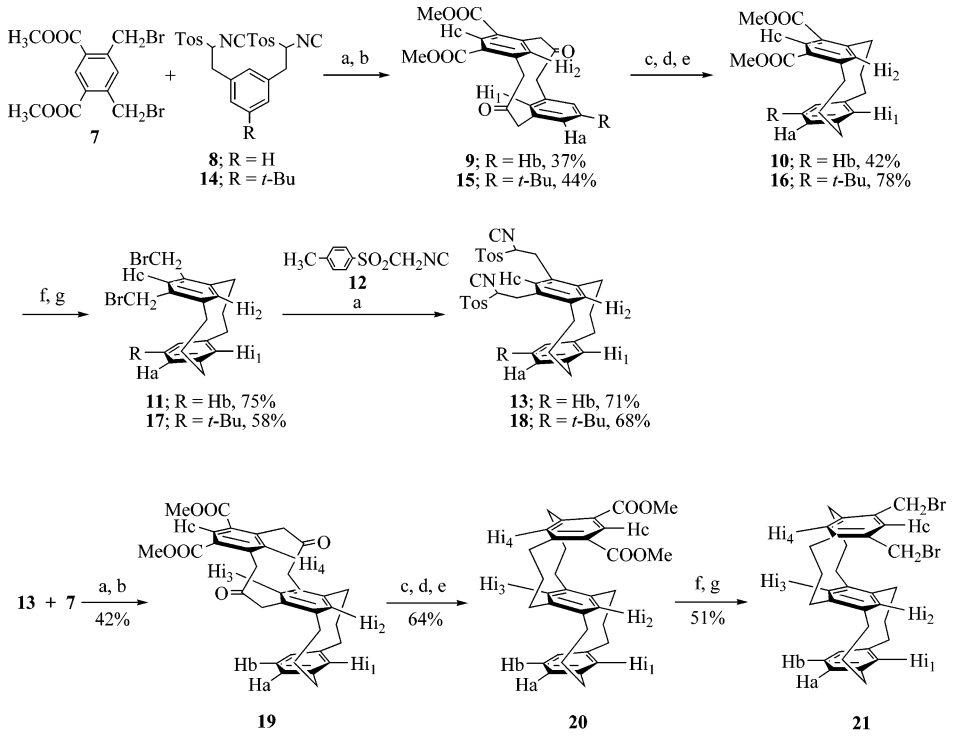
SCHEME 2. Synthetic Route to Two- and Three-Layered Bis(bromomethyl) Compounds 11, 17, and 21



(a) n-Bu_4NI, NaOH, CH_2Cl_2-H_2O. (b) concd HCl. (c) $NH_2NH_2 \cdot H_2O$, KOH, $HOCH_2CH_2OCH_2CH_2OH$. (d) dil HCl. (e) CH_3OH, C_6H_6, concd H_2SO_4. (f) $LiAlH_4$, THF; (g) PBr_3, C_6H_6.

of the carbonyl groups of **23** provided the four-layered CP **4** (77%). The three-layered bromide **21** and two-layered TosMIC adduct **13** were coupled to give the five-layered dione **24** (32%), which was converted to the five-layered CP **5** (58%) by the reduction of the carbonyl groups.

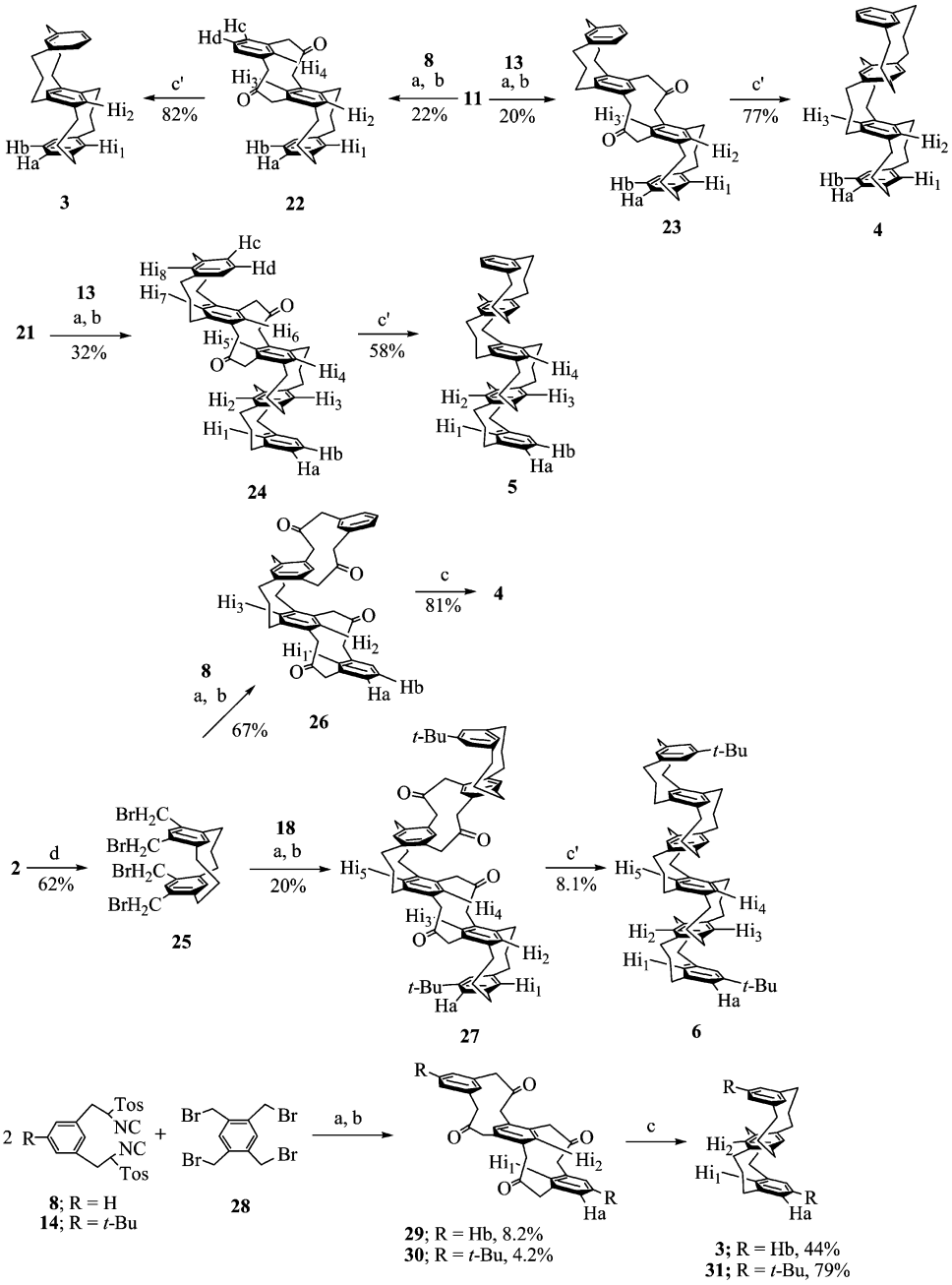
Tetrakis(bromomethyl)[3.3]MCP **25** is a versatile synthetic intermediate, and this is most conveniently prepared by the one-step bromomethylation of [3.3]MCP **2** with paraformaldehyde and 30% HBr in AcOH at 95 °C (62%), which was the modified reaction conditions originally reported by Vögtle et al.[10g] First, we attempted to synthesize the parent six-layered [3.3]MCP and confirmed its formation by HRMS, but we could not characterize it due to its poor solubility in any organic solvents. Therefore, we introduced *tert*-butyl groups to the skeleton of the six-layered [3.3]MCP for improvement of solubility. The *tert*-butyl group substituted six-layered [3.3]MCP **6** was synthesized by the coupling of the tetrakis(bromomethyl) compound **25** with 2 molar equiv of the *tert*-butyl group substituted two-layered TosMIC adduct **18**, followed by acid hydrolysis (20%) and reduction of the carbonyl groups of the resultant **27** (8.1%).

For the synthesis of the three-layered [3.3]MCP-tetraone **29**, the one-step coupling between TosMIC adduct **8** and 1,2,4,5-tetrakis(bromomethyl)benzene **28** in a ratio of 2:1 is the most convenient method (8.2%). A similar coupling between the *tert*-butyl substituted **14** and the tetrabromide **28** gave the tetraone **30** (4.2%). Although the yields were low, the desired three-layered [3.3]MCPs with the anti−anti geometries **29** and **30** were directly and preferentially formed in this reaction. The Wolff−Kishner reduction of their carbonyl groups afforded the three-layered [3.3]MCP **3** (44%) and its *tert*-butyl derivative **31** (79%).

^{1}H NMR Spectral Properties.[16] As described previously, the assignment of an anti geometry to **1** is based on the highly shielded inner aromatic protons [Hi_1 δ 5.78 (br s)] from the outer aryl protons [Ha δ 7.19 (d) and Hb δ 7.32 (t)] due to the ring current effect of the facing benzene ring (Figure 3).[24] Two kinds of inner aromatic protons of the three-layered tetraone **29** [Hi_1 δ 6.09 (br s) and Hi_2 δ 5.54 (sharp s) (Figure S35)] are strongly shielded, while the outer aromatic protons appear in the normal aromatic region [Ha δ 7.22 (dd) and Hb δ 7.37 (t)], suggesting the anti−anti geometry. In contrast, the inner aromatic protons of **2** [Hi_1 δ 6.87 (br s)] with a syn geometry are slightly shielded as compared to the outer aromatic protons of **1** in $CDCl_3$. Two kinds of highly shielded inner aromatic protons [Hi_3 δ 5.55 (s) and Hi_4 δ 5.27 (s) (Figure S29)] as well as the two kinds of slightly shielded aromatic protons [Hi_1 δ 7.00 (br s) and Hi_2 δ 6.75 (s)] indicate the anti−syn geometry for the three-layered dione **22**. The fact that the Hi_4 proton is more shielded than the Hi_3 proton supports the expected molecular structure because the [3.3]MCP moiety shows a stronger diamagnetic ring current effect than the benzene ring. Similarly, the inner aromatic protons [Hi_3 δ 5.06 (s) (Figure S30)] of the four-layered dione **23** show a more significant upfield shift than the Hi_3 proton of **22**, and this indicates the syn−anti−syn geometry. In the four-layered tetraone **26**, only two kinds of inner aromatic protons [Hi_2 δ 5.50 (sharp s) and Hi_1 δ 5.24 (br s) (Figure S33)] are strongly shielded, while other aromatic protons appear in the normal aromatic region. These data suggest an anti−syn−anti geometry.

The one and two inner aromatic protons of **3** [Hi_2 δ 5.92 (s) (Figure S9)] and **4** [Hi_2 δ 6.05 (s) and Hi_3 δ 6.10 (s) (Figure S10)] are moderately shielded, whereas the other aromatic protons appear in the normal aromatic region. These

SCHEME 3. Synthetic Route to Three- to Six-Layered [3.3]MCPs 3−6



(a) n-Bu_4NI, NaOH, CH_2Cl_2-H_2O. (b) concd HCl. (c) $NH_2NH_2{\cdot}H_2O$, KOH, $HOCH_2CH_2OCH_2CH_2OH$. (c') $NH_2NH_2{\cdot}H_2O$, $NH_2NH_2{\cdot}2HCl$, KOH, $HOCH_2CH_2OCH_2CH_2OH$. (d) $(HCHO)_n$, 30%HBr in AcOH.

moderately shielded protons relative to the Hi_1 protons of **2** are attributable to the diamagnetic anisotropy of the stacked benzene rings in a syn fashion, and this is consistent with syn−syn and syn−syn−syn geometries for **3** and **4**, respectively. The assignments of the Hi_2 and Hi_3 proton signals of **4** are made by the NOESY spectrum (Figure S41). In the five-layered dione **24**, the highly shielded inner aromatic protons [Hi_5 δ 5.07 (s) and Hi_6 δ 5.00 (s) (Figure S31)] are explained by the anisotropic ring current effects of the facing two- and three-layered [3.3]-MCP moieties. These data and the moderately shielded inner aromatic protons [Hi_2 δ 5.88 (s) and Hi_3 δ 6.45 (s)] support a syn−anti−syn−syn geometry for **24**. The presence of only two kinds of highly shielded protons [Hi_3 δ 4.96 (s) and Hi_4 δ 4.79 (s) (Figure S34)] as well as the appearance of other aromatic proton signals in the normal region (δ 6.5−7.0) suggest a syn−anti−syn−anti−syn geometry for the six-layered tetraone **27**.

The three kinds of moderately shielded inner aromatic protons for **5** [Hi_2 δ 6.03 (s), Hi_3 δ 6.08 (s), and Hi_4 δ 6.19 (s) (Figure S13)] and **6** [Hi_2 δ 6.10 (s), Hi_3 δ 6.03 (s), Hi_4 δ 6.00 (s), and Hi_5 δ 6.12 (s) (Figure S15)] are attributable to the diamagnetic anisotropy of the syn stacked benzene rings, and these data are consistent with all-syn geometries for **5** and **6**. The assignments of the Hi_2, Hi_3, and Hi_4 protons of **5** are made based on the NOESY spectrum (Figure S42). Similarly, the NOESY spectrum of **6** supports the Hi_2 to Hi_5 proton assignments (Figure S43).

X-ray Structural Analysis. To confirm the crystalline structure of the multilayered [3.3]MCPs, we carried out single-

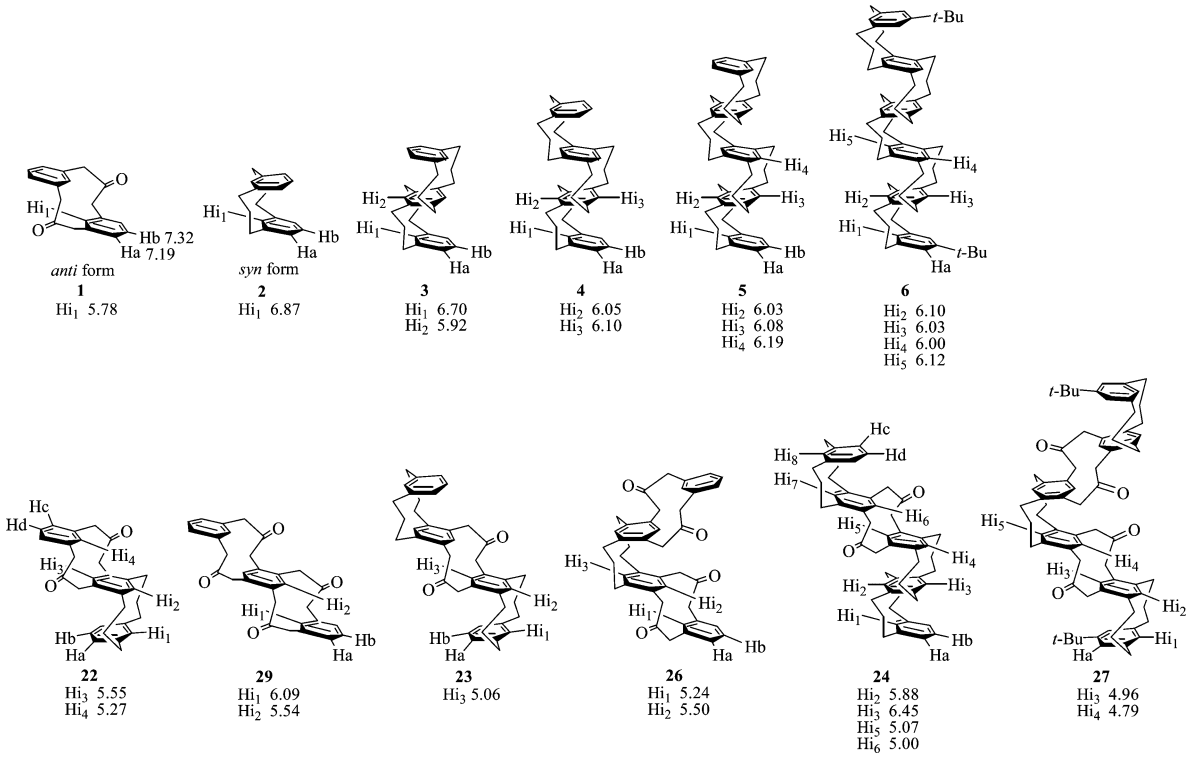


FIGURE 3. Selected ^{1}H NMR data of the aromatic protons of multilayered [3.3]MCPs (δ, $CDCl_3$, 300 MHz).

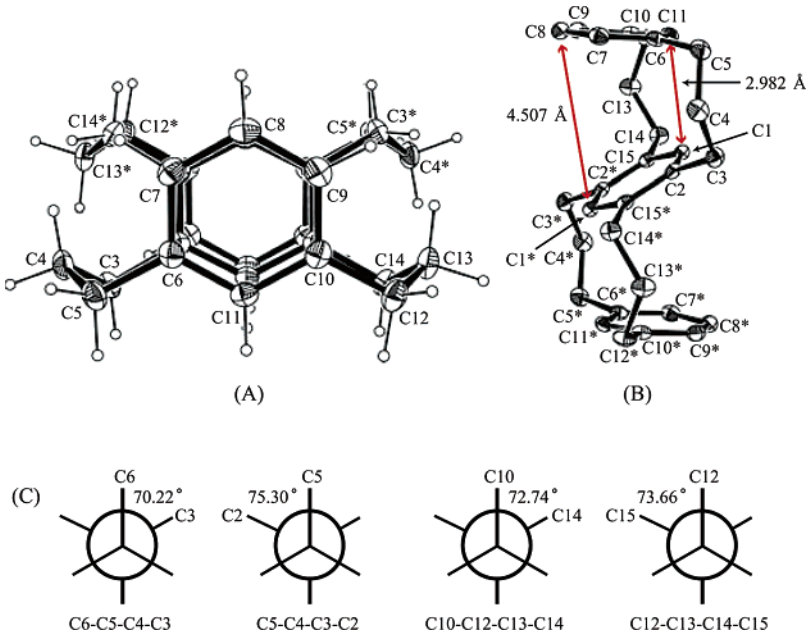


FIGURE 4. Molecular structures of three-layered [3.3]MCP **3** (−150 °C); top view (A), side skeleton view (B), and dihedral angles at trimethylene bridges (C).

crystal X-ray structural analyses of some of them. The crystal data are summarized in Table S1. Figure 4 shows the ORTEP drawing of three-layered [3.3]MCP **3** (−150 °C) as top (A) and side views (B). The [3.3]MCP unit takes the syn(chair/chair) geometry with the tilt of the benzene rings of 34.5°, which is larger than that of the parent **2** (24°)[17] by 10°. Although a twist in the benzene rings of **2** is ca. 15° about the axis through the center of each ring,[17] the twist of the outer and central benzene rings of **3** is only ca. 1.3°, and the benzene rings completely overlap each other (Figure 4A). Corresponding to the increased tilt of the [3.3]MCP unit of **3**, the transannular distance between C1 and C11 (2.982 Å) is slightly shorter than that of **2** (2.995 Å), while the distance of C1* and C8 (4.507 Å) becomes longer than the corresponding distance in **2** (4.171 Å) (Figure 4B).[17] The outer benzene ring is slightly deformed into a boat form, whereas the central benzene ring is deformed into a chair form; the dihedral angles between the C6−C7−C9−C10 and C6−C11−C10 planes, the C6−C7−C9−C10 and C7−C8−C9 planes, as well as the C2−C15−C2*−15* and C2−C1−C15 planes are 4.70, 1.59, and 2.50°, respectively.

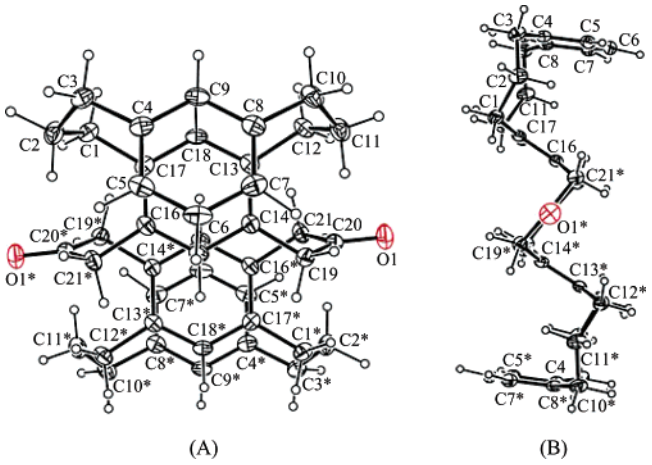


FIGURE 5. Molecular structures of four-layered [3.3]MCP-dione **23** (−160 °C); top view (A) and side view (B).

The average bond lengths of the aromatic C−C (1.393 Å), C_{arom}−C_{benzyl} (1.514 Å), and aliphatic C−C (1.540 Å) are normal. The dihedral angles at the trimethylene bridges are depicted in Figure 4C, and this indicates that the trimethylene bridges are in a nearly gauche conformation and that the deviation from a complete gauche conformation is about 13°. The gauche conformation of the trimethylene bridge may be the most important factor for the syn geometry of the multilayered [3.3]MCPs.

Figure 5 shows the molecular structures of the four-layered MCP-dione **23** (−160 °C). The ORTEP drawing shows that the [3.3]MCP unit takes the syn(chair/chair) conformation with the tilt of the benzene rings of 26.2°, which is comparable to that of the parent **2**. The twist in the benzene rings of the [3.3]MCP moiety is only 1.1°. The central [3.3]MCP-dione unit takes the anti(twist boat/twist boat) conformation, where overlap of the benzene rings is increased as compared to that of the anti(chair/chair) conformation of the parent **1** (Figure 5A).[24] Similar to the case of the three-layered MCP **3**, the outer benzene rings are slightly distorted into the boat form [1.60° for C4−C5−C7−C8 and C5−C6−C7 planes and 4.61° for C4−C5−C7−C8 and C4−C9−C8 planes], whereas the inner benzene rings are distorted to the chair form [1.52° for C13−C14−C16−C17 and C13−C18−C17 planes and 2.56° for C13−C14−C16−C17 and C14−C15−C16 planes, respectively] in **23**.

Figures 6 and 7 show the molecular structures of the four-layered MCP-tetraone **26** (−160 °C) and the short contacts of the selected crystal-packing diagram, respectively. The ORTEP drawing shows that the central [3.3]MCP unit takes the syn(chair/chair) conformation and that the outer [3.3]MCP-dione units assume the anti(chair/chair) conformation. Tilting of the central [3.3]MCP unit is 32.5°, which is slightly greater than that of **2**. Different from the previous examples, the two benzene rings of the [3.3]MCP-dione unit are not parallel but are significantly tilted by 28.2° for the C4−C5−C7−C8 and C13−C14−C16−C17 planes as well as 18.2° for the C22−C23−C25−C26 and C34−C35−C37−C38 planes. It should be noted that the twist in the benzene rings of the [3.3]MCP-dione moiety is quite large [11.6° (C4−C5−C6−C7−C8−C9 and C13−C14−C15−C16−C17−C18) and 6.6° (C22−C23−C24−C25−C26−C27 and C34−C35−C36−C37−C38−C39)]. The transannular distances between the neighboring benzene rings in **26** [2.935 Å (C9−C18), 2.942 Å (C15−C27), and 2.933 Å (C24−C39)] are much shorter than the corresponding distances

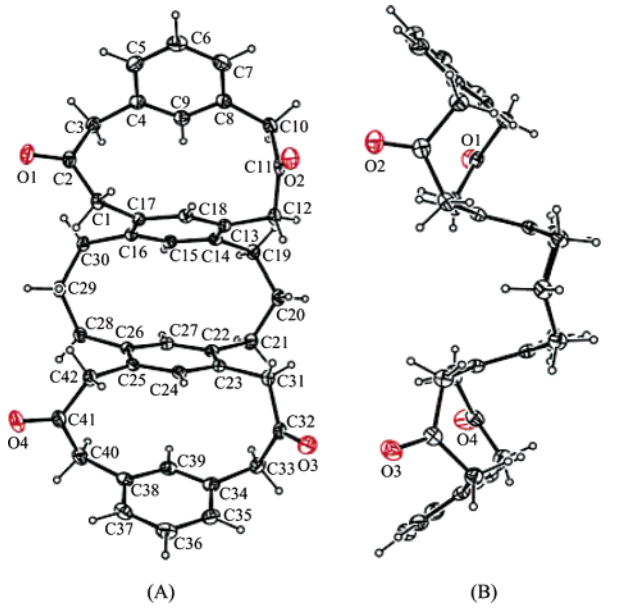


FIGURE 6. Molecular structures of four-layered [3.3]MCP-tetraone **26** (−160 °C); side views (A and B).

of **1** (2.99 Å)[24] and **2** (2.995 Å).[17] Moreover, the transannular distance between C18 and C24 in the [3.3]MCP unit (4.363 Å) is much longer than that of **2** (4.171 Å).[17] The outer benzene rings are slightly distorted to a boat form, whereas the inner benzene rings deform into the chair form. With regard to the angle of the C−CO−C bridge, three of the four moieties are normal values (ca. 120°), but the C10−C11−C12 angle of the remaining bridge is slightly deformed (116.6°). In the crystal-packing diagram of **26** (Figure 7A), hydrogen bonds between the carbonyl oxygen atom and the benzylic proton of the neighboring molecule are observed [(Figure 7B) O4−H16 (2.571 Å) on the *ac*-plane and (Figure 7C) O3−H9 (2.595 Å) overlapped molecules in Figure 7A]. The distance of the former hydrogen bond is shorter than the sum of the van der Waals radii[30] of a hydrogen atom (1.20 Å) and an oxygen atom (1.40 Å).

Figure 8 shows the molecular structure of the four-layered MCP **4** (−150 °C). The ORTEP drawing shows that the two outer [3.3]MCP units are syn(chair/chair) with the tilt of the two facing benzene rings of 34.6° [C4−C6−C7−C9 and C13−C15−C16−C18 planes] and 22.3° [C22−C24−C25−C27 and C34−C36−C37−C39 planes]. The transannular distances of each unit are 3.009 Å (C5−C14), 4.600 Å (C8−C17), 2.997 Å (C26−C35), and 3.969 Å (C23−C38). Contrary to our expectation, the central [3.3]MCP moiety assumes the deformed anti(boat−boat) conformation, and the dihedral angle between the two benzene rings is 42.0° (C13−C15−C16−C18 and C22−C24−C25−C27 planes). The outer [3.3]MCP units are twisted 0.12° (C4−C5−C6−C7−C8−C9 and C13−C14−C15−C16−C17−C18) and 0.78° (C22−C23−C24−C25−C26−C27 and C34−C35−C36−C37−C38−C39), and the inner [3.3]MCP unit is twisted 1.4°. The second benzene rings are distorted into the twist chair form by 7.1° [C13−C15−C16−C18 and C13−C14−C15 planes] and 7.7° [C13−C15−C16−C18 and C16−C17−C18 planes] as well as 1.3° [C22−C24−C25−C27 and C22−C23−C24 planes] and 3.0° [C22−C24−C25−C27 and C25−

(30) Pauling, L. *The Nature of the Chemical Bond*; Cornell University Press: Ithaca, NY, 1960; p 260.

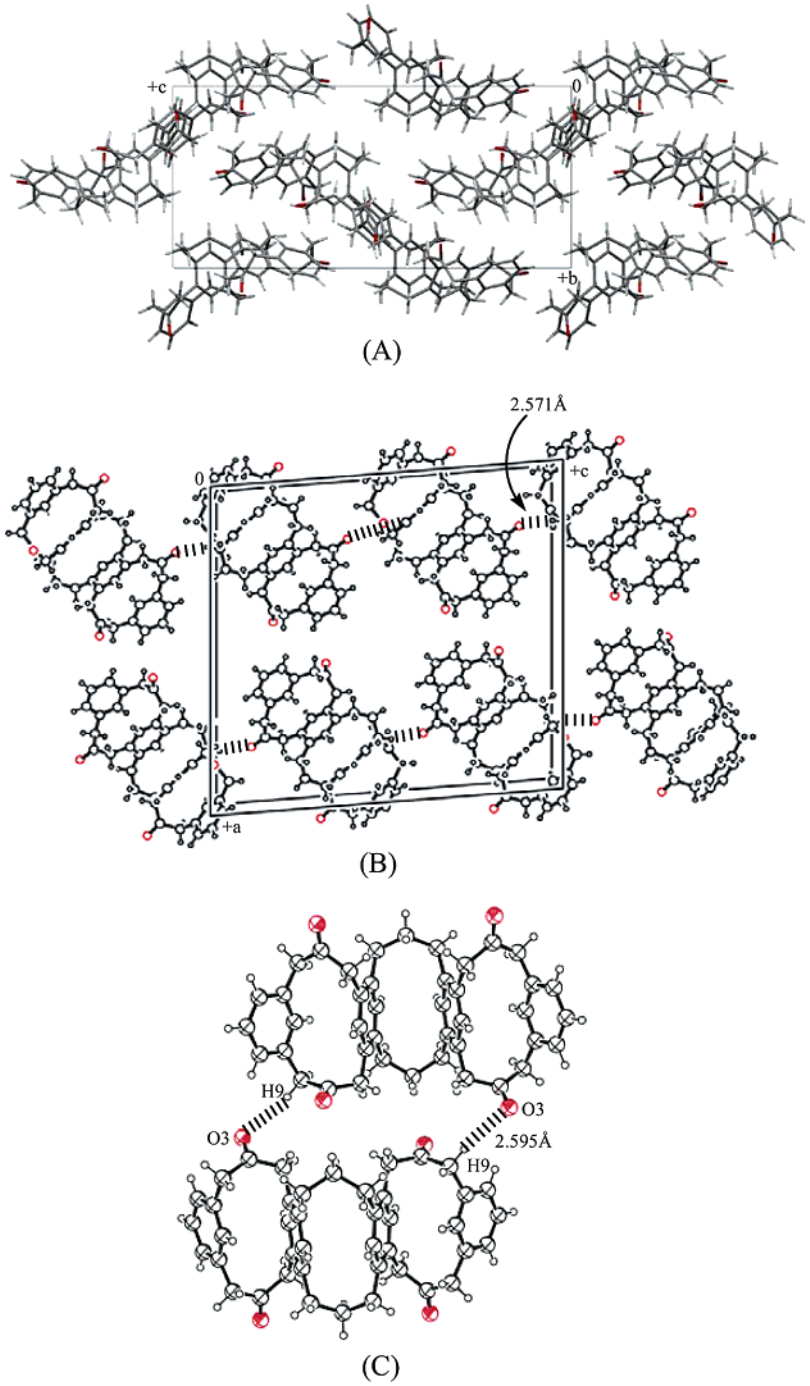


FIGURE 7. Short contacts of four-layered [3.3]MCP-tetraone **26**. (A) Crystal-packing diagram along the *a*-axis. (B) Hydrogen bonds between carbonyl oxygen (O4) and benzylic proton (H16) along the *b*-axis. (C) Hydrogen bonds between carbonyl oxygen (O3) and benzylic proton (H9). Hydrogen bonds are represented as dashed lines.

C26−C27 planes]. The dihedral angles of the trimethylene bridges (C19−C20−C21 and C28−29−C30) of the central *anti*-[3.3]MCP unit are depicted in Figure 8B, and the dihedral anglesare quite different from the corresponding angles of the three-layered [3.3]MCP **3** with a syn geometry. Almost eclipsed interactions are observed in C19−C20 and C29−C30 (0.0−3.9°), and this indicates the presence of a repulsive interaction in the bridges. Thus, the gauche interaction in the trimethylene bridge is observed in the *syn*-[3.3]MCP unit, whereas the eclipsed interaction is present in the *anti*-[3.3]MCP unit.

The PM3[31] calculations predicted that the most stable geometry of **4** should be all-syn(chair/chair), while the syn−anti−syn geometry found in the solid state should be less stable than the all-syn(chair/chair) by 2.1 kcal/mol.[32] Formation of the syn−anti−syn geometry in the solid state may be ascribed to crystal-packing forces. These results suggest that the structure of [3.3]MCP and its dione moieties are flexible and can be

(31) Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209−220.
(32) The computations were done with MOPAC2002 programs, graphically facilitated by CAChe from Fujitsu Limited.

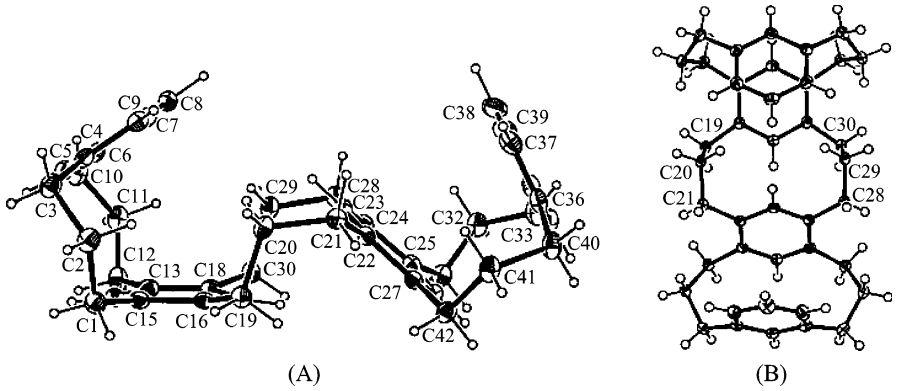


FIGURE 8. Molecular structures of four-layered [3.3]MCP **4**; side views (A and B).

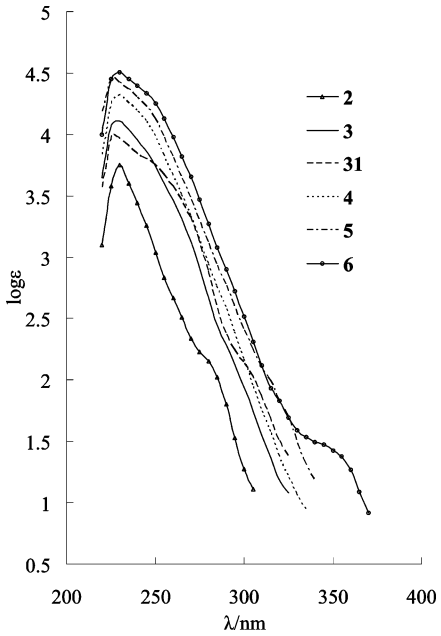


FIGURE 9. Electronic spectra of multilayered [3.3]MCPs **2**−**6** and **31** in CH_2Cl_2.

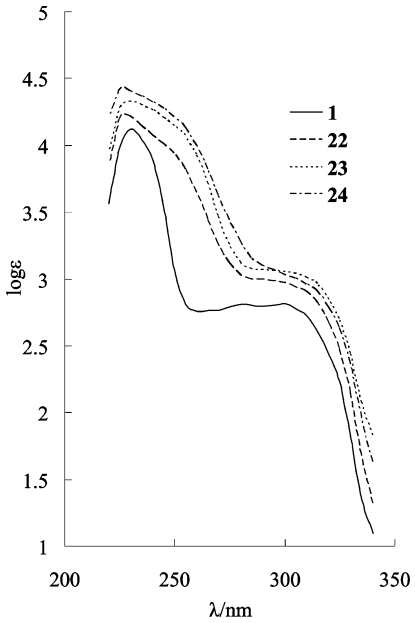


FIGURE 10. Electronic spectra of multilayered [3.3]MCP-diones **1** and **22**−**24** in CH_2Cl_2.

changed to some extent in responding to the external environment even in the solid state. However, the stable structure of **4** is expected to be syn−syn−syn in solution based on the ^{1}H NMR data as described previously. Flexibility of multilayered [3.3]MCPs is in sharp contrast to the rigid structures of multilayered [2.2]MCPs.[7] We have not succeeded in the preparation of single crystals of **5** and **6** for the X-ray structural analysis yet, and the result will be reported elsewhere.

Electronic Spectra. Figure 9 denotes the electronic absorption spectra of the multilayered [3.3]MCPs **2**−**6** and **31** in CH_2Cl_2. [3.3]MCP **2** with a syn geometry displays two absorption bands at 230 (ϵ 5680) and 276 (sh, ϵ 164) in CH_2Cl_2. Strong bathochromic shifts and hyperchromic effects are observed as the layer is varied from two to three, whereas the magnitude decreases with an increase in the number of layers. The absorption curve becomes almost a straight line as the number of layers increases. It is noteworthy that *tert*-butyl substituted MCPs **31** and **6** show new bands at 301 and 341 nm as shoulders, respectively, probably due to the electron-donating ability of the *tert*-butyl groups. The [3.3]MCP-2,11-dione **1** with an anti geometry shows $\pi-\pi^*$ bands and abnormally intense $n-\pi^*$ bands [230 (ϵ 13200), 282 (ϵ 646), 301 (ϵ 654), 309 (sh, ϵ 540), and 321 nm (sh, ϵ 249) in CH_2Cl_2] (Figure 10). The unusual strength of the $n-\pi^*$ transitions has been reported[33] and is attributed to the homoconjugation between carbonyl groups and benzene rings. A similar weak bathochromic shift and hyperchromic effect of the absorptions are also observed as an increase of the number of layers in the multilayered [3.3]-MCP-diones. The spectral change from two to three is more significant than that from three to four. In the electronic spectra of a series of multilayered [3.3]MCP-tetraones (Figure 11), almost no spectral change is observed except the appearance of the new bands above 350 nm for the *tert*-butyl substituted MCPs **27** and **30**.

Charge-Transfer Bands. The electron-donating ability of a cyclophane is most conveniently evaluated in a qualitative manner by the λ_{max} of the CT band with TCNE as an acceptor in solution.[12,34] Previously, we reported that the CT bands of the multibridged [3_n]CPs ($n = 2-6$) with TCNE show signifi-

(33) (a) Cookson, R. C.; Wariyar, N. S. *J. Chem. Soc.* **1956**, 2302−2311. (b) Mislow, K.; Glass, M. A.; O'Brien, R. E. W; Rutkin, P.; Steinberg, D. H.; Weiss, J.; Djerassi, C. *J. Am. Chem. Soc.* **1962**, *84*, 1455−1478. (c) Labhart, H.; Wagniere, G. *Helv. Chim. Acta.* **1959**, *42*, 2219−2227.

(34) Merrifield, R. E.; Phillips, W. D. *J. Am. Chem. Soc.* **1958**, *80*, 2778−2782.

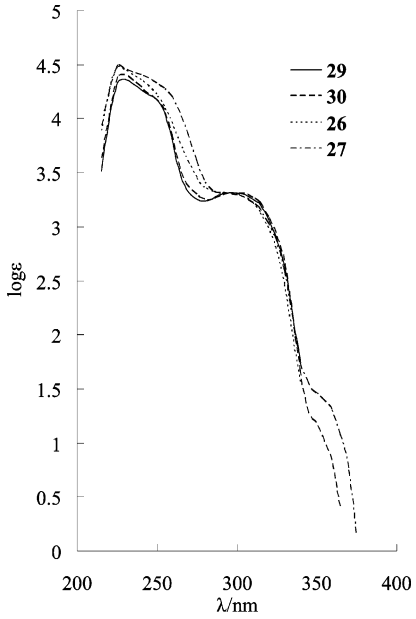
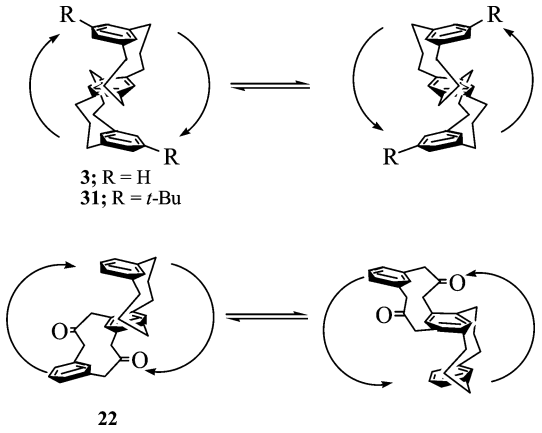


FIGURE 11. Electronic spectra of multilayered [3.3]MCP-tetraones **26**, **27**, **29**, and **30** in CH_2Cl_2.

cant bathochromic shifts with an increase of the number of bridges, and [3$_6$](1,2,3,4,5,6)CP shows the strongest CT interaction (λ_{max} 728 nm, $CHCl_3$) among the [*m.n*]CPs and multibridged CPs.[14b] The very strong donating ability of [3$_6$]CP was further supported by the first half-wave oxidation potential ($E_{1/2}$ +0.39 V vs Fc/Fc^+ in $ClCH_2CH_2Cl$).[35] In a similar manner, we evaluated the electron-donating ability of the multilayered [3.3]-MCPs. When colorless $CHCl_3$ solutions of the multilayered [3.3]-MCPs **2**−**6** (0.86−2.37 × 10^{-3} mol/L) and TCNE (1.25 × 10^{-2} mol/L) were mixed, a purplish-red to purple solution appeared. The CT absorption spectra of the multilayered [3.3]MCPs **2**−**6** and multilayered [3.3]MCP-di- and tetraones **22**−**24**, **26**, **27**, and **29** are shown in Figures S5 and S6, respectively, and the λ_{max} values of the CT bands are summarized in Table 1. Although the intensity of the λ_{max} values of the CT band increased as an increase of the ratio of multilayered MCP/TCNE (from 1:1 to 1:10), no shift of the λ_{max} of the CT band was observed in the MCPs **3** and **4**, suggesting the 1:1 complex formation in the solution (Figures S7 and S8).

In the two layered CPs, [3.3]PCP (the λ_{max} of the CT band 606 nm) shows a much stronger CT interaction than [3.3]MCP **2** (λ_{max} 509 nm) and the [3.3]MPCP (λ_{max} 460 nm), and this type of dependence of the CT interaction on the molecular geometry was already observed in the intramolecular CT CPs, such as the [3.3]cyclophanequinones[13a] and quinhydrones.[13b] It should be noted that the *anti*-[3.3]MCP-dione **1** (λ_{max} 443 nm) exhibits much weaker CT interaction than the *syn*-**2**, and this

SCHEME 4. Expected Correlated Inversion Process of the Benzene Rings in Three-Layered [3.3]MCPs 3, 31, and 22



suggests that the effective overlapping of the facing benzene rings is one of the most important factors for the strong CT interaction.

In a series of multilayered [3.3]MCPs **2**−**6**, the λ_{max} of the CT band gradually shifts to the longer wavelength region as the number of layers increases (**2**, 509; **3**, 550; **4**, 556; **5**, 575; and **6**, 588 nm). The effect of an increase in the layers becomes less significant, and the changes in the λ_{max} values from two to three, three to four, and four to five are 41, 6, and 9 nm, respectively. The corresponding change from five to six may be less than 13 nm because the *tert*-butyl group substituted MCP **6** may show a stronger donating ability than the parent six-layered MCP. An appreciable effect may no longer be expected for more than six. It is worth noting that the *tert*-butyl group substituted three-layered [3.3]MCP **31** showed the CT band at a significantly longer wavelength region (581 nm) as compared to that of the parent **3** (550 nm), and this is ascribed to the electron-donating ability of the *tert*-butyl groups.

In the multilayered [3.3]MCP-keones, the three-layered dione **22** with a syn−anti geometry shows a CT band at 506 nm, and this value is comparable to that of [3.3]MCP **2** with a syn geometry (509 nm). Similarly, the four-layered dione **23** (518 nm) and five-layered dione **24** (543 nm) show a similar magnitude of CT interaction comparable to the two-layered MCP **2** (509 nm) and three-layered MCP **3** (550 nm), respectively. These data suggest that the anti geometry with -CH_2-$COCH_2$−- bridges behaves as an electron insulator. In fact, the multilayered [3.3]MCP-tetraones **26**, **29**, and **30** hardly interacted with TCNE, but the *tert*-butyl group substituted **27** shows the transannular interaction comparable to that of **3**.

Thus, the electron-donating ability of the multilayered [3.3]-MCPs **2**−**6** gradually increases with an increase in the layers, but the magnitude becomes less significant as the number of layers increases. The anti geometry with the -CH_2COCH_2−-

TABLE 1. Charge-Transfer Bands of Multilayered [3.3]CPs-TCNE in $CHCl_3$

multilayered [3.3]CPs	TCNE complex λ_{max} (nm)	multilayered [3.3]CPs	TCNE complex λ_{max} (nm)
[3.3]PCP	489	five-layered [3.3]MCP **5**	575
	606	*t*-Bu six-layered [3.3]MCP **6**	588
[3.3]MPCP	460	two-layered [3.3]MCP dione **1**	443
	510	three-layered [3.3]MCP dione **22**	506
[3.3]MCP **2**	509	four-layered [3.3]MCP dione **23**	518
three-layered [3.3]MCP **3**	550	five-layered [3.3]MCP dione **24**	543
t-Bu three-layered [3.3]MCP **31**	581	*t*-Bu six-layered [3.3]MCP tetraone **27**	548
four-layered [3.3]MCP **4**	556	[3$_6$](1,2,3,4,5,6)CP[14b]	728

bridges included in the multilayered [3.3]MCPs serves as an electron insulator. The moderate electron-donating ability of the multilayered [3.3]MCPs as compared to that of the [3_n]CPs may be ascribed to the tilted overlap of the benzene rings.

Conclusion

We have successfully synthesized up to six-layered [3.3]-MCPs using a TosMIC method as a critical coupling reaction via repetitive processes. Structures in solution of all the MCPs could be assigned on the basis of the ^{1}H NMR data using the significantly shielded inner aromatic proton of the *anti*-[3.3]-MCP-dione **1** and moderately shielded inner aromatic proton of the *syn*-[3.3]MCP **2** as a diagnostic tool. The all-syn conformations are expected for multilayered [3.3]MCPs **2**−**6** in $CDCl_3$ solution, but the X-ray structural analysis revealed that the central [3.3]MCP unit of the four-layered MCP **4** takes anti geometry with the dihedral angle of the two benzene rings being 42.0°. The dihedral angle of the two benzene rings in the incorporated [3.3]MCP unit becomes larger (**3**, 34.5°) than that of the parent **2** (24°). These data indicate that [3.3]MCP unit is flexible to some extent and can change its conformation so as to be adapted to the environment such as crystal-packing forces. In the electronic spectra, rather simple and structureless absorption curves are observed, and the most significant spectral change is observed from two to three layers but becomes less effective even if more layered. In the CT bands of the multilayered [3.3]MCPs, the λ_{max} gradually shifts to the longer wavelength region, but the extent of the shift is much smaller as the number of layers increases. In the multilayered [3.3]MCP-ketones, the *trans*-[3.3]MCP-dione unit serves as an electric insulator. In fact, the CT interaction of the four- and five-layered [3.3]MCPs with one *trans*-[3.3]MCP-dione unit (**23** and **24**) shows almost a comparable magnitude of the interaction to the two- and three-layered MCPs (**2** and **3**). The tetraones of the four- and six-layered MCPs (**26** and **27**) do not form CT complexes. The CT data suggest the moderate electron-donating ability of the multilayered [3.3]MCPs with all-syn geometries as compared to that of multibridged [3_n]CPs (n = 2−6).[35]

The ^{1}H NMR study of the multilayered [3.3]MCPs showed that they were mobile in solution because of the sharp singlet of the benzylic protons of the [3.3]MCP-2,11-dione moiety as well as the averaged signals of the trimethylene bridges of the [3.3]MCP moiety. In connection with the conformational behavior of the parent [3.3]MCP **2**, much more complex dynamic conformational behavior would be expected for the multilayered [3.3]MCPs. For example, the simultaneous RI processes of the two outer benzene rings are required for the conformational isomerism of the three-layered MCPs **3** and **31** (Scheme 4). Similar correlated RI processes may be observed in the three-layered MCP-dione **22**. For the elucidation of the dynamic conformational behavior, the temperature-dependent NMR study of **31** and **22** is in progress.

We will continue the synthesis of more layered [3.3]MCPs as model compounds for the development of new electron-transfer systems through π electrons of the benzene rings. In the multilayered [3.3]MCPs with electron-donor and -acceptor moieties at each end of the layers, electron transfer from a donor to an acceptor may be observed. Furthermore, our efforts toward the synthesis of multilayered [3.3]PCPs is in progress, and these results will be reported elsewhere.

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Experimental Section

5,7-Bis(bromomethyl)[3.3]metacyclophane 11. A mixture of *n*-Bu_4NI (3.3 g), CH_2Cl_2 (1.0 L), and NaOH (30 g) dissolved in water (80 mL) was heated to reflux with stirring. To the mixture was added dropwise a mixture of bromide **7** (6.68 g, 17.6 mmol) and TosMIC adduct **8** (8.68 g, 17.6 mmol) in CH_2Cl_2 (700 mL) over a period of 8 h, and the mixture was refluxed for an additional 3 h. The cooled mixture was washed with water and concentrated to a volume of ca. 300 mL. To the concentrate was added concd HCl (50 mL), and the mixture was stirred for 2 h at room temperature. The mixture was washed with brine and concentrated to dryness to afford dark brown oil. To the oil was added MeOH (50 mL), and the mixture was sonicated and triturated. The precipitate was collected by filtration, washed with MeOH, and air-dried. Similar reactions were repeated 5 times on similar scales (total 88.0 mmol of **7** was used). Purification of the crude product by silica gel column chromatography with CH_2Cl_2 afforded ketoester **9** (12.3 g, 37%). −**9**: Colorless needles (EtOH/benzene), mp 196.5−197.5 °C; IR (KBr) ν 1716 (ester C═O), 1708 (ketone C═O) cm^{-1}; ^{1}H NMR (300 MHz) δ3.51 (s, 4H, CH_2COCH_2), 3.75 (s, 4H, CH_2COCH_2), 3.97 (s, 6H, OCH_3), 5.69 (s, 1H, Hi_1), 6.08 (s, 1H, Hi_2), 7.11 (dd, J = 7.6, 1.5 Hz, 2H, Ha), 7.30 (t, J = 7.5 Hz, 1H, Hb), 8.69 (s, 1H, Hc); MS (EI) m/z 380 [M$^+$]. Anal. Calcd for $C_{22}H_{20}O_6$: C, 69.46; H, 5.30. Found: C, 69.31; H, 5.33.

A mixture of the ketoester **9** (11.9 g), KOH (23 g), 100% NH_2-NH_2·H_2O (40 mL), and diethylene glycol (200 mL) was heated at 130 °C for 2 h and then 200 °C for 3 h. After cooling, the mixture was acidified by the addition of concd HCl. The precipitate was collected by filtration, washed with water, and dried at 120 °C for 4 h to give crude dicarboxylic acid as a brown powder (8.59 g), which was treated with MeOH (500 mL), concd H_2SO_4 (15 mL), and benzene (100 mL) at reflux for 1 day with gradual removal of the benzene−water azeotrope. The mixture was concentrated to a volume of ca. 100 mL, and the concentrate was diluted with water and extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with brine, dried with $MgSO_4$, and filtered. Removal of the solvent followed by purification of the residue by silica gel column chromatography with CH_2Cl_2 gave dimethyl [3.3]metacyclophane-5,7-dicarboxylate **10** (4.63 g, 42% overall). −**10**: Colorless needles (MeOH/CH_2Cl_2): mp 113−114 °C; IR (KBr) ν 1721 (C═O) cm^{-1}; ^{1}H NMR (300 MHz) δ2.0−2.2 (m, 4H, CH_2CH_2-CH_2), 2.6−2.8 (m, 4H, $CH_2CH_2CH_2$), 3.0−3.2 (m, 4H, CH_2-CH_2CH_2), 3.86 (s, 6H, OMe), 6.65 (dd, J = 7.6, 1.5 Hz, 2H, Ha), 6.82 (t, J = 7.3 Hz, 1H, Hb), 6.84 (s, 1H, Hi_2), 6.94 (br s, 1H, Hi_1), 8.13 (s, 1H, Hc); MS (EI) m/z 352 [M$^+$]. Anal. Calcd for $C_{22}H_{24}O_4$: C, 74.98; H, 6.86. Found: C, 74.60; H, 6.85.

A mixture of the ester **10** (2.06 g, 5.85 mmol), $LiAlH_4$ (1.00 g, 26.4 mmol), and THF (80 mL) was refluxed for 4 h with stirring. After cooling, AcOEt, H_2O, and diluted HCl were added successively to the mixture. The mixture was extracted with Et_2O, and the combined extracts were washed with brine, dried with $MgSO_4$, and filtered. Removal of the solvent and drying of the residue in vacuo at room temperature gave alcohol, which was used without further purification.

A mixture of the diol, PBr_3 (8.0 mL, 85 mmol), and benzene (70 mL) was stirred for 6 h at room temperature. The reaction mixture was washed with brine, dried with $MgSO_4$, and passed through a short silica gel column with benzene. Concentration of the eluate provided two-layered bromide **11** (1.85 g, 75% in two steps). −**11**: Colorless needles (hexane/CH_2Cl_2), mp 106−107 °C; ^{1}H NMR (300 MHz) δ2.0−2.3 (m, 4H, $CH_2CH_2CH_2$), 2.6−2.9 (m, 8H, $CH_2CH_2CH_2$), 4.38 (s, 4H, CH_2Br), 6.64 (s, 1H, Hi_2), 6.70 (dd, J = 7.4, 1.3 Hz, 2H, Ha), 6.79 (t, J = 7.4 Hz, 1H, Hb), 6.95 (s, 1H, Hc), 6.99 (s, 1H, Hi_1); MS (EI) m/z 420 (M$^+$, 7%),

422 [(M + 2)$^+$, 15%], 424 [(M + 4)$^+$, 7%]. Anal. Calcd for $C_{20}H_{22}Br_2$: C, 56.90; H, 5.25. Found: C, 57.15; H, 5.20.

5,7-Bis[2-isocyano-2-(tolylsulfonyl)ethyl][3.3]metacyclophane 13. A mixture of *n*-Bu_4NI (250 mg), NaOH (6.0 g) dissolved in 15 mL of water, and CH_2Cl_2 (25 mL) was cooled in an ice bath with stirring. To the mixture was added in one portion a CH_2Cl_2 (25 mL) solution of TosMIC **12** (3.61 g, 18.5 mmol). After 30 min, the bromide **11** (2.31 g, 5.47 mmol) dissolved in CH_2Cl_2 (20 mL) was added in one portion. The mixture was stirred for 1 h in the ice bath, then at room temperature for 3 h. The reaction mixture was washed with water and concentrated to a volume of ca. 20 mL. The concentrate was diluted with MeOH (ca. 100 mL) and stored in a freezer. The precipitate was collected by filtration and washed with MeOH. Silica gel chromatography of the crude product with CH_2Cl_2 afforded pure 5,7-bis[2-isocyano-2-(tolylsulfonyl)ethyl]-[3.3]metacyclophane **13** (2.51 g, 71%) as white powder. −**13**: White powder (MeOH/CH_2Cl_2). mp 125 °C (dec); IR (KBr) ν 2132 (NC), 1333, 1151 (SO_2) cm^{-1}; ^{1}H NMR (300 MHz) δ2.0−2.2 (m, 4H, $CH_2CH_2CH_2$), 2.49 (s, 6H, CH_3), 2.6−2.8 (m, 8H, CH_2-CH_2CH_2), 2.80 (dd, J = 14.0, 11.4 Hz, 2H, CH_2CH), 3.46 (dd, J = 14.0, 2.4 Hz, 2H, CH_2CH), 4.42 (dd, J = 11.5, 2.5 Hz, 2H, CH_2CH), 6.58 (s, 1H, Hi_2), 6.60 (dd, J = 7.6, 1.4 Hz, 2H, Ha), 6.74 (s, 1H, Hc), 6.77 (t, J = 7.5 Hz, 1H, Hb), 7.00 (s, 1H, Hi_1), 7.43 (dd, J = 8.3, 1.8 Hz, 4H, TsH), 7.88 (dd, J = 8.3, 1.7 Hz, 4H, TsH). Anal. Calcd for $C_{38}H_{38}N_2O_4S_2$: C, 70.12; H, 5.88; N, 4.30. Found: C, 70.01; H, 5.89; N, 4.26.

General Synthetic Procedures of Multilayerd [3.3]Metacyclophanes. To a refluxing mixture of *n*-Bu_4NI, NaOH dissolved in water, and CH_2Cl_2 was added dropwise a mixture of the TosMIC adduct and the bromide dissolved in CH_2Cl_2, and the mixture was refluxed for an additional hour. After cooling, the mixture was washed with water and concentrated, and the concentrate was treated with concd HCl at room temperature. The mixture was washed with brine and concentrated to dryness. To the residue was added acetone (tetraone) or MeOH (dione), and the mixture was sonicated. The resulting precipitate was collected by filtration to give the ketone.

A mixture of the ketone, 100% $NH_2NH_2\cdot H_2O$, KOH, and polyethylene glycol was heated at 130 °C and then at 200 °C with stirring. After cooling, the mixture was diluted with water, acidified with concd HCl, and extracted with CH_2Cl_2. The CH_2Cl_2 solution was washed with brine, dried with $MgSO_4$, and filtered. The filtrate was concentrated to dryness to give the multilayered [3.3]MCP.

Three-Layered [3.3]Metacyclophane 3. Three-Layered Tetraone 29. (8.2%): Colorless crystals (CH_2Cl_2), mp >300 °C; IR (KBr) ν 1694 (C═O) cm^{-1}; ^{1}H NMR (300 MHz) δ3.53 (s, 8H, CH_2COCH_2), 3.62 (s, 8H, CH_2COCH_2), 5.54 (s, 2H, Hi_2), 6.09 (s, 2H, Hi_1), 7.22 (dd, J = 7.3, 1.6 Hz, 4H, Ha), 7.37 (t, J = 7.6 Hz, 2H, R = Hb); HRMS (FAB) *m*/*z* calcd for $C_{30}H_{26}O_4$ 451.1909 [(M + H)$^+$], found 451.1850. Anal. Calcd for $C_{30}H_{26}O_4\cdot 0.45CH_2Cl_2$: C, 74.83; H, 5.55. Found: C, 74.64; H, 5.47.

Three-Layered [3.3]Metacyclophane 3. (44%): Colorless needles (dioxane), mp 268−270 °C; ^{1}H NMR (300 MHz) δ1.8−2.0 (m, 8H, $CH_2CH_2CH_2$), 2.4−2.7 (m, 16H, $CH_2CH_2CH_2$), 5.92 (s, 2H, Hi_2), 6.69 (d, J = 7.0, 4H, Ha), 6.70 (s, 2H, Hi_1), 6.85 (t, J = 7.6 Hz, 2H, Hb); ^{13}C NMR (75 MHz) δ 27.9, 32.6, 36.2, 125.5, 127.8, 133.9, 134.1, 135.1, 140.1; HRMS (FAB) *m*/*z* calcd for $C_{30}H_{34}$ 394.2661 [M$^+$], found 394.2663. Anal. Calcd for $C_{30}H_{34}$: C, 91.32; H, 8.68. Found: C, 91.30; H, 8.73.

5,7,14,16-Tetrakis(bromomethyl)[3.3]metacyclophane 25. The original synthetic procedures reported by Vögtle et al.[10g] were modified. A mixture of [3.3]MCP **2** (17.3 g, 73.0 mmol), paraformaldehyde (16.2 g), and acetic acid (36 mL) was heated to 95 °C under N_2 with mechanical stirring. To the mixture was added 30 wt % HBr in acetic acid solution (90 mL) in one portion, and then the mixture was stirred for 27 h. As the reaction proceeded, precipitate appeared, and the quantity was gradually increased. After the reaction mixture was allowed to cool to room temperature, the precipitate was collected by filtration, and the solid was dissolved in CH_2Cl_2 and concentrated. The concentrate was diluted with acetone/hexane (1:1), and insoluble solid was collected by filtration to give the tetrabromide **25** (27.5 g, 62%) as a white powder. −**25**: ^{1}H NMR δ 2.21−2.25 (m, 4H, $CH_2CH_2CH_2$), 2.92 (br s, 8H, CH_2-CH_2CH_2), 4.39 (s, 8H, CH_2Br), 6.99 (s, 2H, ArH), 7.04 (s, 2H, ArH).[10g,29b]

Four-Layered [3.3]Metacyclophane 4. Four-Layered Tetraone 26. (67%): Colorless crystals (CH_2Cl_2), mp >300 °C; IR (KBr) ν 1701 (C═O) cm^{-1}; ^{1}H NMR (300 MHz) δ2.0−2.1 (m, 4H, $CH_2CH_2CH_2$), 2.7−2.9 (m, 8H, $CH_2CH_2CH_2$), 3.30 (s, 8H, CH_2-$COCH_2$), 3.33 (s, 8H, CH_2COCH_2), 5.24 (s, 2H, Hi_1), 5.50 (s, 2H, Hi_2), 7.01 (dd, J = 6.9, 1.3 Hz, 4H, Ha), 7.02 (s, 2H, Hi_3), 7.19 (t, J = 7.3 Hz, 2H, Hb); HRMS (FAB) *m*/*z* calcd for $C_{42}H_{40}O_4$ 608.2927 [M$^+$], found 608.2903. Anal. Calcd for $C_{42}H_{40}O_4\cdot 0.05$ CH_2Cl_2: C, 82.39; H, 6.59. Found: C, 82.25; H, 6.67.

Four-Layered [3.3]Metacyclophane 4. (81%): Colorless crystals (dioxane), mp 212−214 °C. ^{1}H NMR (300 MHz) δ1.9−2.0 (m, 12H, $CH_2CH_2CH_2$), 2.4−2.5 (m, 8H, $CH_2CH_2CH_2$), 2.5−2.6 (m, 8H, $CH_2CH_2CH_2$), 2.6−2.7 (m, 8H, $CH_2CH_2CH_2$), 6.05 (s, 2H, Hi_2), 6.10 (s, 2H, Hi_3), 6.70 (d, J = 7.3 Hz, 4H, Ha), 6.71 (s, 2H, Hi_1), 6.85 (t, J = 7.6 Hz, 2H, Hb); ^{13}C NMR (75 MHz) δ 26.2, 28.1, 32.3, 32.7, 36.2, 125.5, 127.8, 133.9, 134.2, 134.5, 134.6, 135.2, 140.1; HRMS (FAB) *m*/*z* calcd for $C_{42}H_{48}$ 552.3756 [M$^+$], found 552.3737. Anal. Calcd for $C_{42}H_{48}$: C, 91.25; H, 8.75. Found: C, 90.98; H, 8.77.

Five-Layered [3.3]Metacyclophane 5. Five-Layered Dione 24. (32%): Colorless crystals (dioxane), mp 278−280 °C; IR (KBr) ν 1695 (C═O) cm^{-1}; ^{1}H NMR (300 MHz) δ1.8−2.1 (m, 12H, $CH_2CH_2CH_2$), 2.4−2.6 (m, 4H, $CH_2CH_2CH_2$), 2.5−2.7 (m, 16H, $CH_2CH_2CH_2$), 2.7−2.8 (m, 4H, $CH_2CH_2CH_2$), 3.16 (br s, 4H, CH_2-$COCH_2$), 3.18 (br s, 4H, CH_2COCH_2), 5.00 (s, 1H, Hi_6), 5.07 (s, 1H, Hi_5), 5.88 (s, 1H, Hi_2), 6.45 (s, 1H, Hi_3), 6.57 (s, 1H, Hi_4), 6.61 (s, 1H, Hi_7), 6.63 (d, J = 7.4 Hz, 2H, Hc), 6.66 (dd, J = 7.5, 1.4 Hz, 2H, Ha), 6.74 (s, 1H, Hi_1), 6.75 (t, J = 7.4 Hz, 1H, Hd), 6.83 (t, J = 7.5 Hz, 1H, Hb), 6.97 (s, 1H, Hi_8); HRMS (FAB) *m*/*z* calcd for $C_{54}H_{58}O_2$ 738.4437 [M$^+$], found 738.4484. Anal. Calcd for $C_{54}H_{58}O_2$: C, 87.76; H, 7.91. Found: C, 87.77; H, 7.88.

Five-Layered [3.3]Metacyclophane 5. (58%): Colorless crystals (CH_2Cl_2), mp 244−245 °C; ^{1}H NMR (300 MHz) δ1.8−2.1 (m, 16H, $CH_2CH_2CH_2$), 2.3−2.8 (m, 32H, $CH_2CH_2CH_2$), 6.03 (s, 2H, Hi_2), 6.08 (s, 2H, Hi_3), 6.19 (s, 2H, Hi_4), 6.68 (d, J = 7.4 Hz, 4H, Ha), 6.69 (s, 2H, Hi_1), 6.84 (t, J = 7.5 Hz, 2H, Hb); ^{13}C NMR (150 MHz) δ 26.3, 28.1, 32.5, 36.2, 125.5, 127.8, 134.2, 134.5, 134.6, 134.8, 134.9, 135.3, 140.1; HRMS (FAB) *m*/*z* calcd for $C_{54}H_{62}$ 710.4852 [M$^+$], found 710.4873. Anal. Calcd for $C_{54}H_{62}\cdot 0.15$ CH_2Cl_2: C, 89.86; H, 8.68. Found: C, 89.89; H, 8.74.

***tert*-Butyl Group Substituted Six-Layered [3.3]Metacyclophane 6. *tert*-Butyl Group Substituted Six-Layered Tetraone 27.** (20%): White powder (CH_2Cl_2), mp > 300 °C; IR (KBr) ν 1701 (C═O)cm^{-1}; ^{1}H NMR (300 MHz) δ 0.94 (s, 18H, *t*-Bu), 1.8−2.1 (m, 12H, $CH_2CH_2CH_2$), 2.4−2.7 (m, 24H, $CH_2CH_2CH_2$), 3.06 (br s, 16H, CH_2COCH_2), 4.79 (s, 2H, Hi_4), 4.96 (s, 2H, Hi_3), 6.50 (d, J = 1.2 Hz, 4H, Ha), 6.64 (s, 2H, Hi_2), 6.79 (s, 2H, Hi_1), 6.93 (s, 2H, Hi_5); HRMS (FAB) *m*/*z* calcd for $C_{74}H_{84}O_4$ 1036.6370 [M$^+$], found 1036.6364. Anal. Calcd for $C_{74}H_{84}O_4\cdot 0.2CH_2Cl_2$: C, 84.52; H, 8.07. Found: C, 84.44; H, 8.07.

***tert*-Butyl Group Substituted Six-Layered [3.3]Metacyclophane 6.** (8.1%): White powder ($CHCl_3$), mp > 300 °C; ^{1}H NMR (300 MHz) δ 1.08 (s, 18H, *t*-Bu), 1.8−2.0 (m, 20H, $CH_2CH_2CH_2$), 2.3−2.7 (m, 40H, $CH_2CH_2CH_2$), 6.00 (s, 2H, Hi_4), 6.03 (s, 2H, Hi_3), 6.10 (s, 2H, Hi_2), 6.12 (s, 2H, Hi_5), 6.56 (s, 2H, Hi_1), 6.58 (s, 4H, Ha); ^{13}C NMR (150 MHz) δ 26.3, 26.5, 28.3, 29.7, 31.1, 32.5, 32.6, 33.2, 34.2, 36.7, 122.2, 130.9, 133.2, 134.3, 134.5, 134.5, 134.7, 135.1, 135.2, 135.5, 140.0, 149.8; HRMS (FAB) *m*/*z* calcd for $C_{74}H_{92}$ 980.7199 [M$^+$], found 980.7137.

X-ray Crystallographic Study. All measurements were made with graphite-monochromated Mo Kα (λ = 0.71069 Å) radiation and a rotating anode generator. The crystal structures were solved

by direct methods [SIR92][36] (**23**) and [SIR97][37] (**3**, **4**, and **26**) and refined by the full-matrix least-squares method. The non-hydrogen atoms were refined anisotropically, and hydrogen atoms were refined isotropically. All the computations were performed using the teXan package.[38] Crystallographic data for the structural analyses of **3**, **4**, **23**, and **26** have been deposited within the Cambridge Crystallographic Data Centre (CCDC) as 293730, 293733, 293732, and 293731, respectively. Copies of this information may be obtained from The Director, CCDC, 12 Union Road, Cambridge, CB21EZ,UK(fax: +441223336033ande-mail: deposit@ccdc.cam.ac.uk) or http://www.ccdc.cam.ac.uk/deposit.

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Supporting Information Available: Experimental details; summary of crystallographic data and refinement details of **3**, **4**, **23**, and **26**; molecular stacking forms of **3**, **4**, **23**,and **26**; charge-transfer absorption bands of multilayered [3.3]MCPs-TCNE, multilayered [3.3]MCP-ketones-TCNE, three-layered [3.3]MCP **3**-TCNE, and four-layered [3.3]MCP **4**-TCNE in $CHCl_3$; ^1H NMR spectra of multilayered [3.3]MCPs and ketones; ^{13}C NMR spectra of multilayered [3.3]MCPs; and coordinates of the four-layered [3.3]-MCP **4** by PM3 calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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