Syntheses, Structures, and Transannular $\pi-\pi$ Interactions of Multibridged [3_n]Cyclophanes[1]

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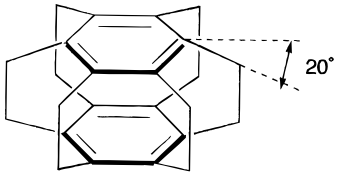
Abstract: The syntheses, conformational study, and transannular $\pi-\pi$ interaction of multibridged [3_n]cyclophanes including the ultimate member of this series, [3_6](1,2,3,4,5,6)cyclophane **1**, are described. The stepwise construction of trimethylene bridges starting from [3_3](1,3,5)cyclophane **6** led to the synthesis of **1** by way of four- and five-bridged cyclophanes **7** and **8**. The variable-temperature (VT) ^{1}H NMR study (CD_2Cl_2) and molecular mechanics calculations (MM3) of five-bridged **8** revealed the most stable conformer, the relative stability order of the three stable isomers, and energy barriers for the trimethylene bridge inversion. A similar VT ^{1}H NMR study (toluene-d_8) of **1** suggests the presence of the trimethylene bridge inversion process between two C_{6h} conformers. The charge transfer (CT) bands of the complexes of multibridged [3_n]cyclophanes with tetracyanoethylene (TCNE) show significant bathochromic shifts with the increase in the number of the bridges, and this is mainly attributed to the effective hyperconjugation between the benzyl hydrogens and the benzene rings. The CT band of the TCNE−**1** complex (728 nm) is the longest wavelength among those of the TCNE complexes of [*m.n*]cyclophanes and multibridged benzenophanes.

1. Introduction

The field of cyclophane chemistry was opened by the work of Cram and Steinberg in 1951.[5] Since then, various kinds of cyclophanes have been synthesized and their structures and properties have been studied.[6] One of the ultimate compounds, the highly strained [2_6](1,2,3,4,5,6)cyclophane **3** later named "superphane", was synthesized by Boekelheide et al. in 1979,[7] and the work opened the new field of superphane chemistry.[8] Since then syntheses, novel structures, and chemical properties



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of various superphanes, such as **3** by Hopf et al.,[9] [4_5](1,2,3,4,5)-ferrocenophane (superferrocenophane) by Hisatome et al.,[10] metal capped [3_4](1,2,3,4)cyclobutadienophane by Gleiter et al.,[11] and [2_4](2,3,4,5)thiophenophane (superthiophenophane) by Tashiro et al.,[12] have been reported.

Since our discovery of the first synthetic method of [3.3]-metacyclophane,[13] we have synthesized various [3.3]cyclophanes and studied their conformational behavior and transannular $\pi-\pi$ interactions.[14] Almost 10 years ago, we embarked on the synthesis of one of the ultimate molecules of this field, [3_6]-(1,2,3,4,5,6)cyclophane **1**, which is tentatively named as [3]-superphane.

We expect **1** to have fascinating chemical features involving the photochemical isomerization of **1** to propella[3_6]prismane

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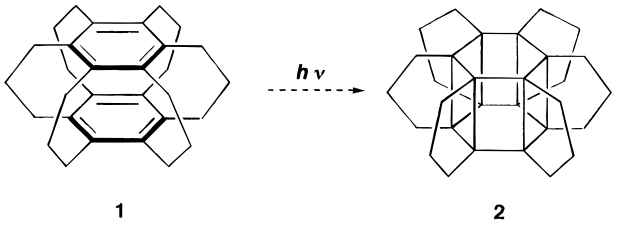
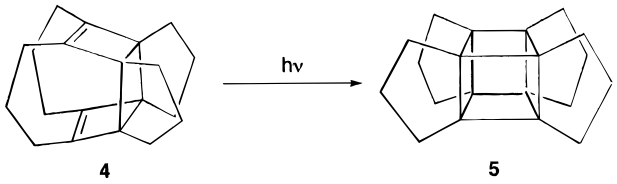
Scheme 1. Predicted Photochemical Isomerization of **1** to Propella[3_6]prismane **2**

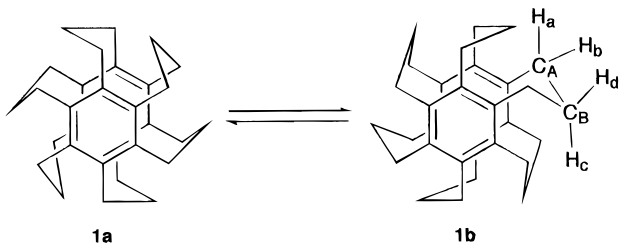


Scheme 2. Intramolecular [2 + 2] Photochemical Ring Closure Reaction of Tetrabridged Tricyclo[4.2.0.$0^{2,5}$]-octa-3,7-diene **4** to Propella[3_4]prismane **5**



2 (Scheme 1). In connection with this type of reaction, Osawa et al. proposed that the order of the frontier molecular orbitals (FMOs) of the bridged polycyclic diolefin, which is a final precursor for prismane formed in the photochemical reaction, is a crucial factor in diagnosing the intramolecular [$\pi^2 + \pi^2$] photochemical reaction of the diolefin. As long as the natural FMO order (π_+ (SS) < π_- (AS) < π_+* (SA) < π_-* (AA)) is maintained, the [$\pi^2 + \pi^2$] reaction takes place, while the reaction will be forbidden if this order is disturbed.[15b] According to this, the conversion of **1** to the hexaprismane skeleton **2** is evaluated to be a borderline case. The FMO order of diolefin is affected by several factors. The photochemical conversion of *syn*-tricyclo[4.2.0.$0^{2,5}$]octa-3,7-diene to cubane is forbidden, but bridging of the diene with trimethylene chains makes the reaction allowed, as was demonstrated by the Gleiter's remarkable intramolecular [2 + 2] photochemical reaction of tetrabridged tricyclo[4.2.0.$0^{2,5}$]octa-3,7-diene **4** to propella[3_4]-prismane **5.** In the former case, the natural FMO order is disturbed, while in the latter, it is maintained (Scheme 2).[16] In the prismane family, prismane,[17] cubane,[18] and pentaprismane[19] have been synthesized. However, the synthesis of hexaprismane has never been accomplished, even though its strain energy is estimated to be 177 kcal/mol (ab initio)[15b,21] or 156 kcal/mol (MM2),[15b,22] which is nearly comparable to that of cubane (157 kcal/mol).[23] It has been a challenging problem for organic chemists.[20]

Scheme 3. Predicted Most Stable C_{6h} Conformations and Correlated Inversion Process of the Six Trimethylene Bridges of **1**



Conformational behavior of **1** should also be interesting. From our previous conformational study of [3.3]para-[24] and metacyclophanes,[25] and three-bridged cyclophanes[26] by the variable-temperature (VT) NMR methods, we have predicted the correlated inversion process of the six trimethylene bridges for **1** (Scheme 3).

We report here the synthesis of **1** by the stepwise approach starting from [3_3](1,3,5)-cyclophane **6** and the conformational study of [3_5](1,2,3,4,5)cyclophane **8**[3] and **1**[4] based on the VT NMR method and theoretical calculations (AM1, PM3, MM3′92), as well as transannular $\pi-\pi$ interactions of multibridged [3_n]-cyclophanes.

2. Results and Discussion

2.1. Synthesis. Boekelheide et al. synthesized superphane **3** according to the principle of *o*-xylene dimerization, which introduces simultaneously two ethanobridges into a cyclophane by a gas-phase pyrolysis. The synthesis of **3** was accomplished in a 10-step process with an overall yield of 4% by this both convenient and efficient method.[7] Alternatively, Hopf et al. employed a transannular carbene insertion reaction between a pseudogeminally substituted methyl and a tosylhydrazide as a construction method of an ethano bridge for the synthesis of **3**.[9] Introduction of a propano bridge into a cyclophane has generally been a more difficult problem than that of an ethano bridge because of the availability of much fewer conventional synthetic methods. The most general TosMIC [(*p*-tolylsulfonyl)methyl isocyanide] method[27] was useful for the synthesis of tribridged cyclophane **6**[26] but did not seem to be promising for further elaboration of additional bridges because the reaction of the *pseudogem*-bis(halogenomethyl) group and TosMIC might be made increasingly difficult by an increased spatially constrained reaction space. Therefore we have focused on the reaction between two pseudogeminally substituted kinds of functional groups.

Our efforts toward the synthesis of **1** have been made via two approaches: (a) a stepwise introduction of additional trimethylene bridges starting from three-bridged cyclophane **6** (Scheme 4), and (b) a direct approach via cyclotrimerization of cyclodeca-1,6-diene in the presence of a metal catalyst.[8e,16,28]

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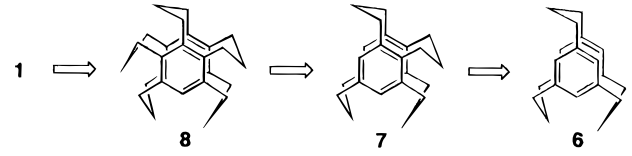
Scheme 4. Stepwise Synthetic Approach



Here we describe the synthesis of **1** via route a by way of [3$_4$]-(1,2,3,5)cyclophanes **7** and five-bridged cyclophane **8**.

2.1.1. The First Generation. As critical coupling reactions for the construction of a trimethylene bridge, we first tried an intramolecular Friedel−Crafts reaction of [3$_3$](1,3,5)cyclophane-1-propanoic acid since these types of reactions were used as the key reaction to the synthesis of Hisatome's superferrocenophane.[10] But, an application of this reaction failed to give the desired ketone **11**, probably due to much lower reactivity of the benzene ring than that of the cyclopentadienyl ring of the ferrocene.[29] Then we thought that the intramolecular coupling between two pseudogeminally substituted kinds of functional groups may be promising. There was only one precedent for such a reaction; Cram et al. reported that the treatment of *pseudogem*-acetyl(chloromethyl)[2.2]paracyclophane with *t*-BuOK in the presence of $AgNO_3$ in THF provided 1-keto-[3.2.2](1,2,5)cyclophane.[30]

On the basis of the background described above, we first applied Cram's method to our system. The coupling between *pseudogem*-acetyl(chloromethyl)[3$_3$](1,3,5)cyclophane **10a** was examined. After testing various reaction conditions for the reaction, we incidentally found that the refluxing of a mixture of **10a**,**b** in 30% HBr in AcOH afforded the desired 1-keto[3$_3$]-(1,3,5)cyclophane **11** and/or its secondary product **12**, depending on the reaction temperature.[2,3] We carried out this reaction with the intention of converting the alcohol **10b** obtained from **10a** by an aqueous workup, to the corresponding bromide which would be more reactive than the chloride, but fortunately, we obtained the coupling product **11** produced by the acid-catalyzed alkylation reaction of an enol by the bromomethyl group.[2] Addition of hydrogen bromide to the carbonyl group of **11** followed by the dehydration of the resultant bromohydrin provided the bromo-olefin **12**. As shown in Scheme 5, we successfully synthesized up to five-bridged **8** from three-bridged **6** by this method,[3] which we call the first generation of the coupling method. Although the use of this coupling method enabled us to prepare **7** and **8**, preparation of the multigram quantities of **8** seemed to be very difficult because of the modest yields and the poor reproducibility due to the instability of the coupling precursors **10a** and **15a**.

2.1.2. The Second Generation. We have developed an alternative method using intramolecular aldol condensation between an acetyl group and a pseudogeminally substituted formyl group.[4] This reaction proceeds in very high-yield, and the resulting enones can be readily reduced to give trimethylene bridges, as outlined in Scheme 6. As can be seen, the successful synthesis of **1** depended on high-yield intramolecular aldol condensation reactions, and this method has proved to be a very efficient construction method of a trimethylene bridge.

Three-bridged cyclophane **6** was treated with Ac_2O in the presence of $AlCl_3$ to give monoacetyl compound **9** along with a *pseudogem*-diacetyl compound[2] which was separated out by silica gel column chromatography. Formylation of **9** with Cl_2CHOCH_3 in CH_2Cl_2 in the presence of $AlCl_3$ quantitatively provided the pseudogeminally substituted compound **18**. The regioselectivity of the formylation and acetylation of **9** may be attributed to the favorable proton transfer from σ complexes to the acceptor sites, carbonyl oxygen of the acetyl group at the pseudogeminal position, which is similar to the exclusive or predominant pseudogem directing effects of the basic oxygen-containing functional groups in [2.2]paracyclophanes.[31]

Intramolecular aldol condensation of **18** under alkaline conditions (3 N aqueous NaOH) afforded enone **19**, which was readily hydrogenated in the presence of catalytic amounts of 10% Pd/C to give ketone **11**. Reduction of **11** by the mixture of $LiAlH_4$ and $AlCl_3$[32] afforded four-bridged **7**. In a similar manner, **7** was converted into five-bridged cyclophane **8** in good yield. Formylation of the acetyl compound **23** quantitatively provided the pseudogeminally substituted compound **24**. Its intramolecular aldol condensation under alkaline conditions provided six-bridged enone **25** in high yield. The PtO_2-catalyzed hydrogenation of **25** afforded ketone **26** quantitatively.

The carbonyl group of **26** was found to be extremely inert toward reducing agents such as $LiAlH_4-AlCl_3$ or triethylsilane[33] as compared with the corresponding carbonyl groups of lower homologues **11** and **22**. Then we examined the reduction of the carbonyl group of **26** via hydroxyl compound **27**. Reduction of the carbonyl group of **26** by $LiAlH_4$ in refluxing THF or by *n*-Bu_4NBH_4[34] in CH_2Cl_2 resulted in the complete recovery of the starting ketone **26**. Finally we chose SmI_2[35] in THF since this reagent is a potentially powerful reducing agent toward a variety of functional groups and the reducing power is enhanced in the presence of base or acid.[36] In fact, the reduction of **26** to alcohol **27** was accomplished with SmI_2 in THF in the presence of 1 N aqueous KOH. The resultant alcohol **27** was readily reduced by $LiAlH_4-AlCl_3$ to give the desired **1** as colorless crystals decomposed above 358 °C (69% yield from **26**). Thus the synthesis of **1** has been accomplished in 16 steps from three-bridged **6** with an overall yield of 3.8% or 7% based on the recovered starting materials in the acetylations (Scheme 6).

In the ^{1}H NMR spectrum of **1** [270 MHz, $CDCl_3$, 22 °C: δ 2.41−2.51 (m, 12H, $CH_2CH_2CH_2$), 3.19 (t, 24H, $CH_2CH_2CH_2$)], two groups of proton signals are observed for trimethylene bridges. The ^{13}C NMR spectrum of **1** (90 MHz, $CDCl_3$, 22 °C, TMS) shows three singlets at δ 20.5 (t, $CH_2CH_2CH_2$), 28.2 (t, $CH_2CH_2CH_2$), and 135.4 (s, aromatic). The multiplicity of the signals (in parentheses) is determined by the off-resonance proton decoupled ^{13}C NMR spectrum. The proposed, highly symmetrical structure of **1** and its dynamic nature are reflected in these NMR data. Elemental analysis and mass spectral data [MS (70 eV): M^+ m/z = 396] are also in agreement with the calculated values expected for **1**.

2.2. Structure in Solution. In the previous papers, we have reported the conformational study of [3.3]paracyclophane,[24] [3.3]metacyclophanes,[25a−d] [3.3](2,6)pyridinophanes,[25e] and three-

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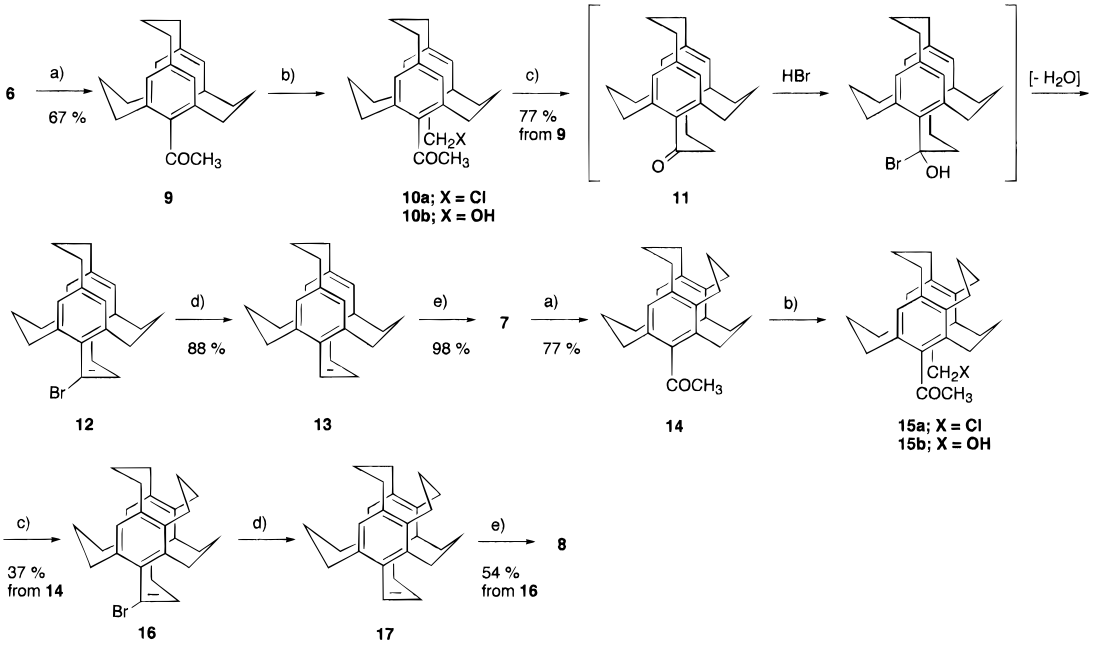
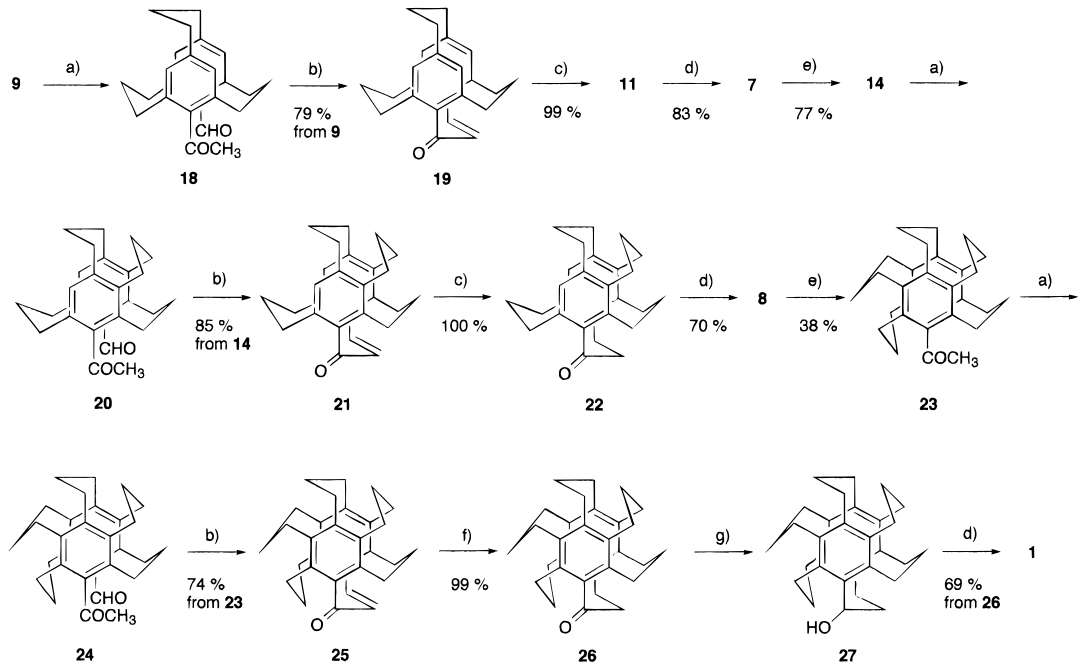
Scheme 5. Synthetic Route to [3_5](1,2,3,4,5)Cyclophane **8** from [3_3](1,3,5)Cyclophane **6**[a]



[a] (a) $(CH_3CO)_2O$, $AlCl_3$, CS_2. (b) CH_3OCH_2Cl, $AlCl_3$, room temperature. (c) 30% HBr in AcOH, ca. 140 °C. (d) H_2, 10% Pd/C, KOH, EtOH, THF. (e) H_2, PtO_2, AcOH.

Scheme 6. Synthetic Route to [3_6](1,2,3,4,5,6)Cyclophane **1** from 5-Acetyl[3_3](1,3,5)cyclophane **9**[a]



[a] (a) CH_3OCHCl_2, $AlCl_3$, CH_2Cl_2. (b) 3 N aqueous NaOH, THF, CH_3OH. (c) H_2, 10% Pd/C, THF−CH_3OH. (d) $AlCl_3$, $LiAlH_4$, THF; (e) $(CH_3CO)_2O$, $AlCl_3$, CS_2. (f) H_2, PtO_2, $CHCl_3$−CH_3OH. (g) SmI_2, 1 N aqueous KOH, THF.

and five-bridged [3_n]cyclophanes **6**[26] and **8**.[2] The most stable conformers of [3_n]cyclophanes are summarized in Figure 1. In the multibridged [3_n]cyclophanes ($n > 2$), the molecular motion is limited to the flipping process of the trimethylene bridges. Its energy barrier is estimated to be ca. 10−12 kcal/mol for the isolated trimethylene bridge.[24−26] In a previous communication, we briefly reported the conformational analysis of five-bridged cyclophane **8** by the VT NMR methods.[2] Figure 2 denotes the summary of both experimental and calculated values (MM3)[37] for the relative stability of the stable isomers **8a**−**c** and energy barriers for the trimethylene bridge flipping processes of **8**. Experimentally, two isomers **8a**,**8b** are observed in CD_2Cl_2 in a 1.0:1.2 ratio, which are equal to the difference of the free energies being 0.07 kcal/mol at −90 °C. The energy barrier for this conformational process is estimated to be 9.6 kcal/mol with $T_c = -70$ °C.[38] The MM3-predicted population of three

(37) The semiempirical MO calculations (PM3) also give a similar result. The computations were performed with MM3-92 and MOPAC93 programs, graphically facilitated by ANCHOR II from Fujitsu Limited and Kureha Chemical Industries. (a) MM3-Program was obtained from Technical Utilization Corp. The program was developed by N. L. Allinger and co-workers, University of Georgia. (b) Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209−220. (c) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902−3909. (d) Stewart, J. J. P., Fujitsu Limited, Tokyo, Japan, 1993.

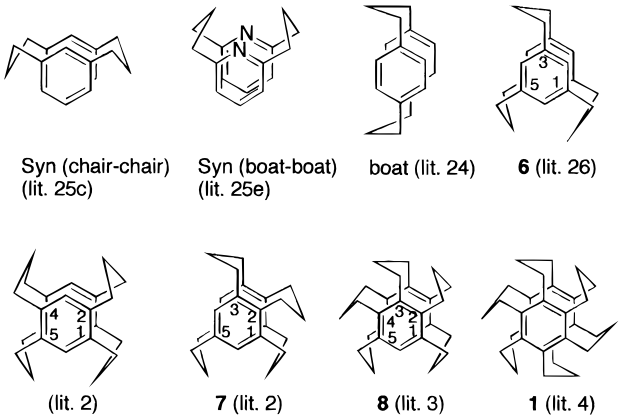
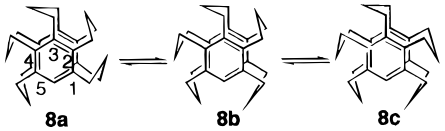


Figure 1. Summary of the most stable conformers of [3$_n$]cyclophanes ($n = 2-6$).



Relative stabilities (kca/mol)			
Experimental results	0.07	0.00	—
Calculated results	0.69	0.00	1.31
Energy Barrier (kcal/mol)			
Experimental results	9.6	—	
Calculated results	9.5	5.4	

Figure 2. Relative thermodynamical stability of the stable conformers of [3$_5$](1,2,3,4,5)cyclophane **8** and the energy barrier for the flipping of the trimethylene bridges estimated by the VT ^{1}H NMR method and MM3 calculations.

isomers **8a**:**8b**:**8c** is 13:85:2 at −90 °C. **8b** is the most stable, and **8a** and **8c** are less stable by 0.69 and 1.31 kcal/mol, respectively (relative free energies at −90 °C). The MM3-estimated energy barriers for the flipping processes of the trimethylene bridges suggest that the observed energy barrier (9.6 kcal/mol) is ascribed to that for the flipping of the C-1 bridge.

Two groups of proton signals for the trimethylene bridges of **1** reflect its dynamic nature, which is a rapid flipping of the six trimethylene bridges, and exhibit strong temperature-dependent phenomena. In the VT ^{1}H NMR (toluene-d_8) experiment, two groups of proton signals for the trimethylene bridges of **1** at 20 °C [δ 2.41−2.51 (m, 12H, $CH_2CH_2CH_2$), 3.19 (t, 24H, CH_2-$CH_2CH_2CH_2$)] broaden as the temperature is lowered and are finally resolved into four multiplets with the relative intensities being 2:2:1:1 at −70 °C (Figure 3). The MM3-optimized structure of **1** suggests that the torsion angles defined by $H_{a\ or\ b}-C_A-C_B-H_{c\ or\ b}$ (Scheme 3) are 154° ($H_a-C_A-C_B-H_c$), 42° ($H_a-C_A-C_B-H_d$), 43° ($H_b-C_A-C_B-H_c$), and 69° ($H_b-C_A-C_B-H_d$). On the basis of Karplus's relationship between the dihedral angle,[39] which is defined by the HCC and the CCH planes, and the coupling constant of the vicinal proton, the coupling constant between H_b and H_d is predicted to be the smallest one among those of the other vicinal protons coupling. Spin decoupling of the signal at 3.09−3.32 ppm results in the change of the multiplet at 1.60−1.79 ppm to the doublet. The signals at 3.09−3.32, 2.70−2.85, 2.41−2.68, and 1.60−1.79 ppm are assigned to H_a, H_b, H_c, and H_d on the basis of the above results, respectively. Double spin decoupling of H_c and H_d at −70 °C

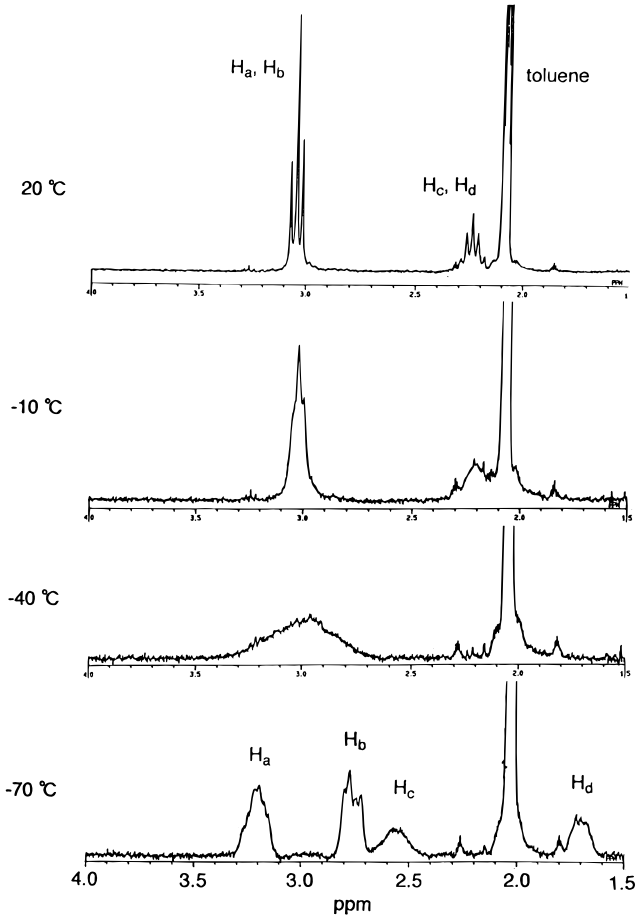


Figure 3. VT ^{1}H NMR spectra of **1** in toluene-d_8 (270 MHz).

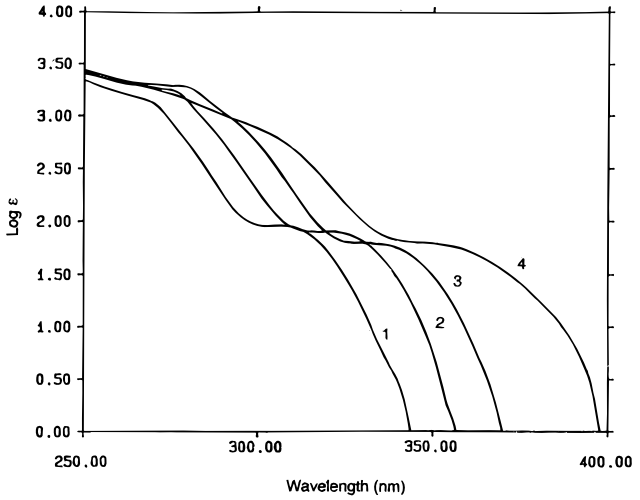


Figure 4. Electronic spectra of multibridged [3$_n$]cyclophanes in $CHCl_3$. Curves are identified by multibridged [3$_n$]cyclophanes as follows: curve 1, [3$_3$](1,3,5)cyclophane **6**; curve 2, [3$_4$](1,2,3,5)cyclophane **7**; curve 3, [3$_5$](1,2,3,4,5)cyclophane **8**; curve 4, [3$_6$](1,2,3,4,5,6)cyclophane **1**.

leads to loss of their vicinal coupling to H_a and H_b, and two multiplets of the benzylic protons (H_a, H_b) change to two doublets . The energy barrier for this process is estimated to be 10.9 kcal/mol with $T_c = -40$ °C.[40] The experimental results thus obtained indicate the presence of the expected dynamic process shown in Scheme 3 but fail to give information on the mechanism and transition state structure of the process. To make this point clear, theoretical calculations are in progress.

(38) $\Delta G^{\ddagger} = RT_c\,(22.96 + \ln T_c/\Delta\nu)$: $\Delta\nu = 96.7$ Hz, $T_c = 203$ K. Cadler, I. C.; Garrat, P. J. *J. Chem. Soc. B* **1967**, 660−662.

(39) Karplus, M. *J. Chem. Phys.* **1959**, *30*, 11.

(40) $\Delta G^{\ddagger} = RT_c\,(22.96 + \ln T_c/\Delta\nu')$, $\Delta\nu' = (\Delta\nu^2 + 6J^2)^{1/2}$SPCLN $\Delta\nu$ = 116 Hz, $J = 14.0$ Hz, $T_c = 233$ K.

Table 1. Electronic Spectral Data of Multibridged [2_n]- and [3_n]Cyclophanes and Position of the Longest Wavelength Absorption Bands in the Electronic Spectra of Their TCNE Complexes, Together with the Values for the Corresponding Methylated Benzene Analogues

[3_n]cyclophane	electronic absorption band λ_{max} (nm)[a]	TCNE complex λ_{max} (nm)[a]	[2_n]cyclophane	electronic absorption band λ_{max} (nm)[b]	TCNE complex λ_{max} (nm)[c]	methylated benzene analogues	TCNE complex λ_{max} (nm)[d]
[3_3](1,3,5)cyclophane **6**	261 (ϵ 1660) 305 (ϵ 91)	594	[2_3](1,3,5)cyclophane	258 (ϵ 1200) 312 (ϵ 96)	559	mesitylene	461
[3_4](1,2,3,5)cyclophane **7**	274 (ϵ 1778) 319 (ϵ 79)	632	[2_4](1,2,3,5)cyclophane	207 (ϵ 71 300) 222 (sh, ϵ 14 100) 248 (sh, ϵ 2030) 287 (sh, ϵ 370) 308 (ϵ 195)		1,2,3,5-tetramethyl-benzene	480
[3_5](1,2,3,4,5)cyclophane **8**	275 (ϵ 1950) 328 (ϵ 63)	684	[2_5](1,2,3,4,5)cyclophane	294 (ϵ 352) 313 (ϵ 200)	570	pentamethylbenzene	520
[3_6](1,2,3,4,5,6)cyclophane **1**	273 (ϵ 1698) 342 (ϵ 65)	728	[2_6](1,2,3,4,5,6)cyclophane **3**	296 (ϵ 421) 306 (sh, ϵ 394) 311 (sh, ϵ 324)	572	hexamethylbenzene	545

[a] Measured in chloroform. [b] References 7b and 42. [c] Reference 7b. [d] Reference 43.

2.3. Transannular $\pi-\pi$ Interactions. Cram and Bauer previously reported the CT spectra of the tetracyanoethylene (TCNE) complexes of a series of [*m.n*]paracyclophanes ($m = 2-6$, $n = 2-6$) and demonstrated that the [3.3]paracyclophane shows the strongest CT interaction.[41] In intramolecular CT cyclophanes such as [*m.n*]paracyclophanequinones ($m = n =$ 2,[42] 3,[14b] 4[43]), the [3.3]system also exhibits the strongest CT interaction because of less strain and more flexibility than the [2.2]system, as well as a more suitable transannular distance than the [4.4]system. Boekelheide et al. reported that the CT absorption bands of the TCNE complexes of multibridged [2_n]-cyclophanes shift very slightly to the longer wavelength region as an increase of the number of bridges, and the expected alkyl effects cannot be observed even in TCNE$-$[2_6](1,2,3,4,5,6)-cyclophane complex (λ_{max} 572 nm).[7] This observation suggested that the alkyl effect due to increased bridges is almost negligible because of the inhibition of the hyperconjugation of benzyl hydrogens due to significant bending of methylene groups out of the plane of the attached benzene ring (20°).[7] This molecular geometry is not suitable for effective $\pi-\sigma$ interaction.

Figure 4 shows the electronic spectra of multibridged [3_n]-cyclophanes ($n = 3-6$) in $CHCl_3$. The spectral data and their λ_{max} of the CT bands of TCNE complexes are summarized in Table 1, together with the values for the corresponding [2_n]-cyclophanes[7,44] and methylated benzenes.[45] In contrast to the case of [2_n]cyclophanes, the longest wavelength absorption bands of the TCNE$-$multibridged [3_n]cyclophane complexes gradually shift to longer wavelength region as an increase of the number of bridges ranged from 594 nm for the TCNE$-$**6** to 728 nm for the TCNE$-$**1** complex. This corresponds to the gradual increase of the first HOMO level as the number of bridges increases, while the first LUMO level does not depend on the number of the bridges, as suggested by the semiempirical MO calculations. The value (728 nm) for the TCNE$-$**1** complex is the longest wavelength among those of the TCNE complexes of the [*m.n*]cyclophanes and multibridged benzenophanes. The significant bathochromic shift of the CT bands as an increase of the trimethylene bridge is attributed not only to the enhanced transannular $\pi-\pi$ interaction between two faced benzene rings but also to the hyperconjugation between the benzyl hydrogens and the benzene rings due to the conformations favorable for $\pi-\sigma$ interaction. The bending of the benzylic methylene groups out of the plane of the attached benzene ring is expected to be 3$-$4° for **1** and 20° for **3** by AM1 calculations.

3. Conclusions

We have synthesized mutibridged [3_n]cyclophanes by using the newly developed intramolecular aldol condensation reaction between the acetyl group and the pseudogeminally substituted formyl group as the key reaction for constructing a trimethylene bridge. The conformational analysis of **8** by theoretical calculations and the VT ^{1}H NMR (CD_2Cl_2) method suggests that the energy barrier for the trimethylene bridge inversion is estimated to be 9.6 kcal/mol with $T_c = -70$ °C and the observed energy barrier is ascribed to that for the flipping of the C-1 bridge. VT ^{1}H NMR (toluene-d_8) of **1** suggests the energy barrier for the trimethylene bridge inversion process is estimated to be 10.9 kcal/mol with $T_c = -40$ °C. The longest wavelength absorption bands of multibridged [3_n]cyclophanes and the CT bands of their TCNE complexes gradually shift to the longer wavelength region as the number of the trimethylene bridges increases. The six-bridged **1** has the strongest π-donating ability due to the enhanced transannular $\pi-\pi$ interaction between two faced benzene rings and the hyperconjugation of the benzyl hydrogens with the benzene rings.

X-ray structural analyses of **1** and **8** as well as photoelectron spectral study of a series of multibridged [3_n]cyclophanes are in progress. Investigation of the photochemical properties of multibridged [3_n]cyclophanes is also in progress, and the results will be reported elsewhere.

4. Experimental Section

4.1. General Procedures. Melting points were measured on a Yanaco micro melting point apparatus MP-S3. ^{1}H and ^{13}C NMR spectra were measured on a JEOL JNM-GX 270 and 400. Chemical shifts were reported as δ values (ppm) relative to internal Me_4Si in $CDCl_3$ unless otherwise noted. Mass spectra (EIMS, ionization voltage 70 eV) and fast atom bombardment mass spectra (FABMS, *m*-nitrobenzyl alcohol) were obtained with a JEOL JMS-SX/SX 102A tandem mass spectrometer. Electronic spectra were recorded on a Hitachi U-3500 spectrometer. Infrared data were obtained on a Hitachi Nicolet

(41) Cram, D. J.; Bauer, R. H. *J. Am. Chem. Soc.* **1959**, *81*, 5971−5977.
(42) Cram, D. J.; Reeves, R. A. *J. Am. Chem. Soc.* **1958**, *80*, 3094−3103.
(43) Cram, D. J.; Day, A. C. *J. Org. Chem.* **1966**, 1227−1232.
(44) (a) Boekelheide, V.; Hollins, R. A. *J. Am. Chem. Soc.* **1973**, *95*, 3201−3208. (b) Gilp, W.; Menke, K.; Hopf, H. *Angew. Chem.* **1977**, *89*, 177; *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 195. (c) Schirch, P. F. T.; Boekelheide, V. *J. Am. Chem. Soc.* **1981**, *103*, 6873−6878.
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I-5040 FT-IR spectrometer. Elemental analyses were performed by the Service Centre of the Elementary Analysis of Organic Compounds affiliated with the Faculty of Science, Kyushu University. Analytical thin layer chromatography (TLC) was performed on Silica gel 60 F_{254} (Merck). Column chromatography was performed on Daiso gel IR-60 (40−63 μm), Merck silica gel 60 (40−63 μm), or Fuji Silysia BW-300.

All solvents and reagents were of reagent quality and were purchased commercially and used without further purification, except as noted below. Tetrahydrofuran (THF) was distilled from sodium and benzophenone. A solution of 0.1 mol/L SmI_2 in dry THF was prepared by a literature procedure.[34] [3.3.3]-(1,3,5)Cyclophane **6** was prepared by the reported procedures.[26]

4.2. Synthesis of Five-Bridged 8 by the Coupling Reaction Between a Pseudogeminally Substituted Acetyl Group and a Chloromethyl Group. 5-Acetyl[3.3.3](1,3,5)cyclophane 9. We describe here the improved procedure of the previously reported one.[2]

To a mixture of **6** (6.18 g, 22.4 mmol), $AlCl_3$ (6.66 g, 50.0 mmol), and CS_2 (375 mL) was added a solution of $(CH_3CO)_2O$ (2.37 g, 23.3 mmol) in CS_2 (35 mL) in one portion at room temperature with stirring. After the addition, the mixture was refluxed for 65 h with stirring. The reaction mixture was poured into ice water and extracted with CH_2Cl_2. The combined extracts were washed with brine, dried with $MgSO_4$, and filtered. After removal of the solvent, the residue was chromatographed on silica gel (240 g) with toluene to give recovered **6** (1.36 g, 22%), desired **9** (4.78 g, 67%, 86% based on recovered **6**), and a 5,14-diacetyl compound (0.88 g, 11%). All of the spectroscopic and physical properties of **9** and the 5,14-diacetyl compound were in complete agreement with the reported data.[2]

2-Bromo[3.3.3.3](1,2,3,5)cyclophane-1-ene 12. For the preparation of 5-acetyl-14-(chloromethyl)[3.3.3](1,3,5)cyclophane **10a** from the acetyl compound **9**, refer to the ref 2.

To a solution of the crude chloromethyl compound **10a** (234 mg, 0.638 mmol) in AcOH (10 mL) was added 30% HBr/AcOH (20 mL), and the mixture was refluxed for 4 h at 140 °C. After cooling, the mixture was poured into ice−water and extracted with CH_2Cl_2. The combined extracts were washed with brine, dried with $MgSO_4$, and filtered. The filtrate was passed through a short silica gel column [R_f (SiO_2, hexane/toluene = 5:1) 0.40], and the eluate was concentrated to give bromo-olefin **12** as white crystals (202 mg, 77% from **9**). **12**: colorless crystals (CH_2Cl_2/hexane), mp 233.0−235.0 °C; ^{1}H NMR δ 2.10−2.33 (m, 6H, $-CH_2CH_2CH_2-$), 2.60−2.98 (m, 12H, $-CH_2CH_2CH_2-$), 3.57 (d, 2H, J = 3.9 Hz, BrC=CHCH_2-), 6.69 (s, 4H, ArH), 6.70 (t, 1H, J = 3.9 Hz, BrC=C$H-$); MS (EI) *m/z* M^+ 392, $M^+ + 2$ 394. Anal. Calcd for $C_{24}H_{25}Br$: C, 73.28; H, 6.41. Found: C, 73.43; H, 6.40.

[3.3.3.3](1,2,3,5)Cyclophane-1-ene 13. A mixture of **12** (1.49 g, 3.79 mmol), 10% Pd/C (1.0 g), powdered KOH (250 mg), EtOH (200 mL), and THF (80 mL) was evacuated and filled with H_2 gas. The mixture was stirred under an atmosphere of H_2 gas (a balloon was used) for 2 d. The reaction mixture was filtered, and the filtrate was concentrated to dryness to give a white solid which was passed through a short silica gel column with CH_2Cl_2. Concentration of the eluate afforded crude **13** as white crystals (1.05 g, 88%). **13**: colorless crystals (CH_2Cl_2/hexane), mp 241.0−242.5 °C; R_f (SiO_2, hexane/toluene = 5:1) 0.54; ^{1}H NMR δ 2.09−2.31 (m, 6H, $-CH_2CH_2CH_2-$), 2.58−3.01 (m, 12H, $-CH_2CH_2CH_2-$), 3.55 (t, 2H, $-CH_2CH=CH-$), 6.06−6.11 (m, 1H, $-CH_2CH=CH-$), 6.55 (d, J = 11.7 Hz, 1H, $-CH_2CH=CH-$), 6.67 (s, 1H, ArH), 6.69 (s, 1H, ArH). Anal. Calcd for $C_{24}H_{26}$: C, 91.67; H, 8.33. Found: C, 91.61; H, 8.30.

[3.3.3.3](1,2,3,5)Cyclophane 7. A mixture of **13** (1.12 g, 3.56 mmol), PtO_2 (500 mg) in AcOH (200 mL), and THF (50 mL) was hydrogenated by stirring the mixture under a H_2 atmosphere for 12 h. The reaction mixture was filtered, and the filtrate was concentrated to dryness to give a white solid which was passed through a short silica gel column with CH_2Cl_2. Concentration of the eluate afforded **7** as white crystals (1.10 g, 98%); colorless crystals (hexane), mp 254.5−255.0 °C (lit.[2] 254.5−255.0 °C).

5-Acetyl[3.3.3.3](1,2,3,5)cyclophane 14. To a mixture of **7** (3.83 g, 12.1 mmol), $AlCl_3$ (3.60 g, 27.0 mmol), and CS_2 (200 mL) was added a solution of $(CH_3CO)_2O$ (1.29 g, 12.6 mmol) in CS_2 (20 mL) in one portion at room temperature with stirring. After the addition, the mixture was refluxed for 67 h with stirring. The reaction mixture was poured into ice water and extracted with CH_2Cl_2. The combined extracts were washed with brine, dried with $MgSO_4$, and filtered. After removal of the solvent, the residue was chromatographed on silica gel (200 g) with toluene to give recovered **7** (0.26 g, 7%) and desired **14** (3.36 g, 77%, 83% based on recovered **7**). **14**: white crystals (hexane/CH_2Cl_2), mp 168.5−169 °C; IR (KBr) ν 1697 (C=O) cm^{-1}; ^{1}H NMR δ 2.11−2.26 (m, 8H, $CH_2CH_2CH_2$), 2.22 (s, 3H, $COCH_3$), 2.58−2.78 (m, 16H, $CH_2CH_2CH_2$), 5.93 (s, 1H, ArH), 6.67 (s, 1H, ArH), 6.99 (d, J = 1.65 Hz, 1H, ArH); MS *m/z* M^+ 358. Anal. Calcd for $C_{26}H_{30}O$: C, 87.10; H, 8.43. Found: C, 86.89; H, 8.35.

2-Bromo[3.3.3.3.3](1,2,3,4,5)cyclophane-1-ene 16. To a mixture of $ClCH_2OCH_3$ (25 mL) and $AlCl_3$ (190 mg, 1.43 mmol) was added a solution of **14** (478 mg, 1.33 mmol) in $ClCH_2OCH_3$ (35 mL) at room temperature, and the mixture was stirred for 2 h at room temperature. The mixture was poured into ice−water and extracted with CH_2Cl_2, the combined extracts were washed with brine, dried with $MgSO_4$, and filtered, and the filtrate was concentrated to give crude 5-acetyl-14-(chloromethyl)[3$_4$](1,2,3,5)cyclophane **15a** as a blue-green oil, which was used in the next reaction without further purification. **15a**: white crystals (hexane/CH_2Cl_2), mp 128.0−129.0 °C; R_f (silica gel, CH_2Cl_2) 0.90; ^{1}H NMR δ 2.12−2.26 (m, 8H, $-CH_2CH_2CH_2-$), 2.22 (s, 3H, $COCH_3$), 2.85−3.21 (m, 16H, $-CH_2CH_2CH_2-$), 5.09 (s, 2H, $-CH_2Cl$), 6.60 (s, 1H, ArH), 6.67 (s, 1H, ArH).

To a solution of crude **15a** in AcOH (20 mL) was added 30% HBr/AcOH (40 mL) at room temperature and then refluxed for 18 h at 140 °C. After cooling, the mixture was poured into ice−water (50 mL) and extracted with CH_2Cl_2, and the combined extracts were washed with brine and dried with $MgSO_4$. Removal of the solvent and the separation of the crude product by pTLC (silica gel, toluene) provided **16** as white crystals (216 mg, 37% from **14**). **16**: colorless crystals (CH_2Cl_2/hexane), mp 245.0−247.5 °C; ^{1}H NMR δ 2.04−2.42 (m, 8H, $-CH_2CH_2CH_2-$), 2.59−3.32 (m, 24H, $-CH_2CH_2CH_2-$), 3.63 (d, J = 4.4 Hz, 2H, BrC=CHCH_2-), 6.64 (t, 1H, J = 4.4 Hz, 1H, BrCH=CH_2), 6.83 (s, 2H, ArH); MS *m/z* (relative intensity) M^+ 432 (98%), $M^+ + 2$ 434 (100%), $M^+ - {}^{79}Br$ 353 (48%). Anal. Calcd for $C_{27}H_{29}Br$: C, 74.82; H, 6.74. Found: C, 74.91; H, 6.77.

[3.3.3.3.3](1,2,3,4,5)Cyclophane 8. A mixture of **16** (216 mg, 0.50 mmol), 10% Pd/C (200 mg), KOH (40 mg), EtOH (50 mL), and THF (20 mL) was stirred under an atmosphere of H_2 gas for 3 d. The reaction mixture was passed through a Celite column, and the eluate was concentrated to give [3$_4$](1,2,3,4,5)cyclophane-1-ene **17** as pale yellow crystals (173 mg).

A mixture of **17** (173 mg, 0.49 mmol), PtO_2 (100 mg) in AcOH (50 mL), and THF (20 mL) was stirred under an

atmosphere of H_2 gas for 20 h. The reaction mixture was filtered through a celite column with AcOEt, and the eluate was concentrated. The concentrate was passed through a short silica gel column with CH_2Cl_2, and the eluate was evaporated to give white crystals (95.8 mg, 54% from **16**). **8**: colorless crystals (hexane/CH_2Cl_2), mp 265.0−266.5 °C; ^{1}H NMR δ 2.11−2.22 (m, 2H, −$CH_2CH_2CH_2$−), 2.33−2.56 (m, 8H, −$CH_2CH_2CH_2$−), 2.66−2.72 (m, 4H, −$CH_2CH_2CH_2$−), 3.05−3.26 (m, 16H, −$CH_2CH_2CH_2$−), 6.74 (s, 2H, ArH); ^{13}C NMR (100 MHz) 21.8, 22.4, 27.7, 28.2, 29.4, 32.0, 132.0, 134.3, 137.1, 137.4; MS *m/z* M^+ 356 (100%). Anal. Calcd for $C_{27}H_{32}$: C, 90.95; H, 9.05. Found: C, 90.99; H, 9.01.

4.3. Synthesis of Six-Bridged 1 by the Aldol Condensation Reaction between a Pseudogeminally Substituted Acetyl Group and a Formyl Group. 5-Acetyl-14-formyl[3.3.3]-(1,3,5)cyclophane 18. To a mixture of **9** (6.29 g, 19.7 mmol), $AlCl_3$ (5.78 g, 43.4 mmol), and CH_2Cl_2 (100 mL) was added dropwise a solution of Cl_2CHOCH_3 (3.39 g, 29.5 mmol) in CH_2Cl_2 (5 mL) in an ice−salt bath with stirring. After the mixture had been stirred in an ice−salt bath for 20 min, it was allowed to warm to room temperature and stirred for an additional 5 h. The reaction mixture was poured into ice water and extracted with CH_2Cl_2. The organic portion was washed with brine, dried with $MgSO_4$, and filtered. Removal of the solvent provided **18** (6.82 g), which was used in the next reaction without further purification. **18**: pale yellow crystals (CH_2Cl_2/MeOH), mp 220−221 °C; IR (KBr) ν 1673 (C═O) cm^{-1}; ^{1}H NMR δ 2.01−2.31 (m, 6H, $CH_2CH_2CH_2$), 2.26 (s, 3H, $COCH_3$), 2.58−2.86 (m, 10H, $CH_2CH_2CH_2$), 3.67−3.84 (m, 2H, $CH_2CH_2CH_2$), 6.64 (s, 2H, ArH), 6.70 (s, 2H, ArH), 10.50 (s, 1H, CHO); MS *m/z* M^+ 346. Anal. Calcd for $C_{24}H_{26}O_2$: C, 83.20; H, 7.56. Found: C, 82.94; H, 7.57.

[3.3.3.3](1,2,3,5)Cyclophane-1-ene-3-one 19. To **18** (6.71 g, 19.4 mmol) dissolved in a mixture of MeOH (150 mL) and THF (150 mL) was added 3 N aqueous NaOH (150 mL), and the mixture was stirred for 16 h at room temperature. As the reaction proceeded, precipitate appeared and the quantity was gradually increased. After removal of the solvent, the aqueous portion was neutralized with dilute HCl and extracted with $CHCl_3$. The combined extracts were washed with brine, dried with $MgSO_4$, and filtered. The filtrate was concentrated, and the concentrate was chromatographed on silica gel (200 g) with toluene to give **19** (5.09 g, 79% from **9**). **19**: pale yellow needles (toluene), mp 217−221 °C; IR (KBr) ν 1640 (C═O) cm^{-1}; ^{1}H NMR δ 2.11−2.25 (m, 6H, $CH_2CH_2CH_2$), 2.39−2.50 (m, 2H, $CH_2CH_2CH_2$), 2.66−2.84 (m, 10H, $CH_2CH_2CH_2$), 6.71 (s, 2H, ArH), 6.76 (s, 2H, ArH), 6.81 (d, J = 11.9 Hz, 1H, ArCH═C*H*), 7.66 (d, J = 12.2 Hz, 1H, Ar*CH*═CH); MS *m/z* M^+ 328. Anal. Calcd for $C_{24}H_{24}O$: C, 87.76; H, 7.37. Found: C, 87.84; H, 7.35.

[3.3.3.3](1,2,3,5)Cyclophane-1-one 11. A mixture of **19** (5.04 g, 15.3 mmol), 10% Pd/C (1.00 g), MeOH (200 mL), and THF (200 mL) was evacuated and filled with H_2 gas. The mixture was stirred under an atmosphere of H_2 gas (a balloon was used) for 6 d at room temperature. The Pd/C was filtered and the filtrate concentrated to give **11** (5.03 g, 99%), whose physical and spectroscopic data were in complete agreement with those of the reported values.[2]

[3.3.3.3](1,2,3,5)Cyclophane 7. A solution of $AlCl_3$ (5.82 g, 43.6 mmol) and **11** (4.79 g, 14.5 mmol) in dry THF (150 mL) was added dropwise to a mixture of $LiAlH_4$ (0.83 g, 21.8 mmol) and dry THF (100 mL) in an ice−salt bath under nitrogen with stirring. The mixture was allowed to warm to room temperature and then was refluxed for 12 h with stirring. The reaction mixture was poured into 6 N aqueous H_2SO_4 and extracted with toluene. The combined extracts were washed with brine, dried with $MgSO_4$, and filtered. Removal of the solvent provided a white powder which was purified by column chromatography on silica gel with toluene to give **7** (3.83 g, 83%), whose physical and spectroscopic data were in complete agreement with those of the reported values.[2]

5-Acetyl-14-formyl[3.3.3.3](1,2,3,5)cyclophane 20. To a mixture of **14** (3.36 g, 9.37 mmol), $AlCl_3$ (3.12 g, 23.4 mmol), and CH_2Cl_2 (50 mL) was added dropwise a solution of Cl_2CHOCH_3 (1.62 g, 14.1 mmol) in CH_2Cl_2 (5 mL) in an ice−salt bath with stirring. After the mixture had been stirred in an ice−salt bath for 10 min, it was allowed to warm to room temperature and stirred for an additional 5 h. The reaction mixture was poured into ice water and extracted with CH_2Cl_2. The organic portion was washed with brine, dried with $MgSO_4$, and filtered. Removal of the solvent provided **20** (3.92 g), which was used in the next reaction without further purification. **20**: pale yellow crystals (CH_2Cl_2/MeOH), mp 203−204 °C; IR (KBr) ν 1688 (C═O), 1687 (C═O) cm^{-1}; ^{1}H NMR δ 2.04−2.42 (m, 4H, $CH_2CH_2CH_2$), 2.17 (s, 3H, $COCH_3$), 2.52−2.83 (m, 10H, $CH_2CH_2CH_2$), 2.98−3.03 (m, 2H, $CH_2CH_2CH_2$), 3.14−3.34 (m, 6H, $CH_2CH_2CH_2$), 3.67−3.76 (m, 2H, $CH_2CH_2CH_2$), 6.71 (s, 2H, ArH), 6.74 (s, 2H, ArH), 10.53 (s, 1H, CHO); MS *m/z* M^+ 386. Anal. Calcd for $C_{27}H_{30}O_2$: C, 83.90; H, 7.82. Found: C, 83.67; H, 7.82.

[3.3.3.3.3](1,2,3,4,5)Cyclophane-1-ene-3-one 21. To the crude **20** (3.92 g) dissolved in a mixture of MeOH (120 mL) and THF (120 mL) was added 3 N aqueous NaOH (120 mL), and the mixture was stirred for 13 h at room temperature. As the reaction proceeded, precipitate appeared and the quantity was gradually increased. After removal of the solvent, the aqueous portion was neutralized with dilute HCl and extracted with $CHCl_3$. The combined extracts were washed with brine, dried with $MgSO_4$, and filtered. The filtrate was concentrated, and the concentrate was chromatographed on silica gel (80 g) with toluene to give **21** (2.94 g, 85% from **14**). **21**: yellow crystals (toluene), mp 253−256 °C; IR (KBr) ν 1645 (C═O) cm^{-1}; ^{1}H NMR δ 1.93−2.46 (m, 8H, $CH_2CH_2CH_2$), 2.62−2.99 (m, 10H, $CH_2CH_2CH_2$), 3.10−3.38 (m, 6H, $CH_2CH_2CH_2$), 6.79 (d, J = 11.9 Hz, 1H, ArCH═C*H*), 6.86 (s, 1H, ArH), 6.90 (s, 1H, ArH), 7.71 (d, J = 12.2 Hz, 1H, Ar*CH*═CH); MS *m/z* M^+ 368. Anal. Calcd for $C_{27}H_{28}O$: C, 88.00; H, 7.66. Found: C, 87.73; H, 7.70.

[3.3.3.3.3](1,2,3,4,5)Cyclophane-1-one 22. A mixture of **21** (2.89 g, 7.84 mmol), 10% Pd/C (500 mg), MeOH (100 mL), and THF (100 mL) was stirred under an atmosphere of H_2 gas for 4 d at room temperature. The Pd/C was filtered and the filtrate concentrated to give **22** (2.93 g, quantitative). **22**: white crystals ($CHCl_3$/toluene), mp 330−332 °C (sealed tube); IR (KBr) ν 1676 (C═O) cm^{-1}; ^{1}H NMR δ 2.01−2.26 (m, 4H, $CH_2CH_2CH_2$), 2.28−2.56 (m, 4H, $CH_2CH_2CH_2$), 2.62−3.52 (m, 20H, $CH_2CH_2CH_2$ and CH_2CH_2CO), 6.74 (s, 1H, ArH), 6.79 (s, 1H, ArH); MS *m/z* M^+ 370. Anal. Calcd for $C_{27}H_{30}O$: C, 87.52; H, 8.16. Found: C, 87.18; H, 8.12.

[3.3.3.3.3](1,2,3,4,5)Cyclophane 8. A solution of $AlCl_3$ (6.15 g, 46.1 mmol) and **22** (2.85 g, 7.69 mmol) in dry THF (150 mL) was added dropwise to a mixture of $LiAlH_4$ (0.44 g, 11.5 mmol) and dry THF (100 mL) in an ice−salt bath under nitrogen with stirring. The mixture was allowed to warm to room temperature and then was refluxed for 14 h with stirring. The reaction mixture was poured into 6 N aqueous H_2SO_4 and extracted with toluene. The combined extracts were washed with brine, dried with $MgSO_4$, and filtered. Removal of the solvent provided a white powder which was purified by column chromatography on silica gel with toluene to give **8** (1.93 g,

70%). Mp and spectroscopic data of this compound completely agreed with those prepared from **17**.

5-Acetyl[3.3.3.3.3](1,2,3,4,5)cyclophane 23. To a mixture of **8** (1.93 g, 5.41 mmol), $AlCl_3$ (1.83 g, 13.7 mmol), and CS_2 (180 mL) was added a solution of $(CH_3CO)_2O$ (0.562 g, 5.50 mmol) in CS_2 (20 mL) in one portion at room temperature with stirring. After the addition, the mixture was refluxed for 44 h with stirring. The reaction mixture was poured into ice water and extracted with CH_2Cl_2. The combined extracts were washed with brine, dried with $MgSO_4$, and filtered. After removal of the solvent, the residue was chromatographed on silica gel (210 g) with toluene to give recovered **8** (430 mg, 22%) and desired **23** (830 mg, 38%, 50% based on recovered **8**). **23**: pale yellow crystals (CH_2Cl_2/hexane), mp 214−216 °C; IR (KBr) ν 1692 (C═O) cm^{-1}; ^{1}H NMR δ 2.12 (s, 3H, $COCH_3$), 2.22−2.80 (m, 14H, CH_2CH_2CH_2), 3.05−3.22 (m, 16H, CH_2CH_2CH_2), 7.02 (s, 1H, ArH); MS *m/z* M$^+$ 398. Anal. Calcd for $C_{29}H_{34}O$: C, 87.39; H, 8.60. Found: C, 87.14; H, 8.60.

5-Acetyl-15-formyl[3.3.3.3.3](1,2,3,4,5)cyclophane 24. A solution of Cl_2CHOCH_3 (360 mg, 3.13 mmol) in CH_2Cl_2 (5 mL) was added dropwise in an ice−salt bath with stirring to a mixture of **23** (830 mg, 2.08 mmol), $AlCl_3$ (610 mg, 4.58 mmol), and CH_2Cl_2 (15 mL). After the mixture had been stirred in an ice−salt bath for 1 h, it was allowed to warm to room temperature and then was stirred for an additional 5 h. The reaction mixture was poured into ice water and extracted with CH_2Cl_2. The organic portion was washed with brine, dried with $MgSO_4$, and filtered. Removal of the solvent provided **24** (860 mg), which was used in the next reaction without further purification. **24**: yellow crystals (toluene), mp 290−292 °C; IR (KBr) ν 1694 (C═O), 1671 (C═O) cm^{-1}; ^{1}H NMR δ 2.08 (s, 3H, $COCH_3$), 2.11−2.65 (m, 12H, CH_2CH_2CH_2), 3.08−3.29 (m, 16H, CH_2CH_2CH_2), 3.54−3.63 (m, 2H, CH_2CH_2CH_2), 10.59 (s, 1H, CHO); MS *m/z* M$^+$ 426. Anal. Calcd for $C_{30}H_{34}O_2$: C, 84.47; H, 8.03. Found: C, 84.56; H, 8.02.

[3.3.3.3.3.3](1,2,3,4,5,6)Cyclophane-1-ene-3-one 25. To the crude **24** (860 mg, 2.02 mmol) dissolved in a mixture of MeOH (50 mL) and THF (50 mL) was added 3 N aqueous NaOH (50 mL) in one portion, and the mixture was refluxed for 59 h with stirring. After removal of the solvent, the aqueous portion was neutralized with dilute HCl and extracted with $CHCl_3$. The extracts were washed with brine, dried with $MgSO_4$, and filtered. The filtrate was concentrated and the residue chromatographed on silica gel (250 g) with $CHCl_3$ to give **25** (630 mg, 74% from **23**). **25**: yellow crystals ($CHCl_3$), mp 402 °C (dec, sealed tube); IR (KBr) ν 1647 (C═O) cm^{-1}; ^{1}H NMR δ 2.11−2.57 (m, 10H, $CH_2CH_2CH_2$), 2.72−3.28 (m, 20H, CH_2CH_2CH_2), 6.78 (d, J = 11.9 Hz, 1H, ArCH═C*H*), 7.74 (d, J = 11.9 Hz, 1H, ArC*H*═CH); MS *m/z* M$^+$ 408. Anal. Calcd for $C_{30}H_{32}O$: C, 88.19; H, 7.89. Found: C, 87.90; H, 7.87.

[3.3.3.3.3.3](1,2,3,4,5,6)Cyclophane-1-one 26. A mixture of **25** (320 mg, 0.783 mmol), PtO_2 (400 mg), MeOH (70 mL), and $CHCl_3$ (100 mL) was stirred under an atmosphere of H_2 gas for 41 h at room temperature. PtO_2 was filtered and the filtrate concentrated to give **26** (320 mg, 99%). **26**: colorless crystals (benzene), mp 377 °C (dec., sealed tube); IR (KBr) ν 1674 (C═O) cm^{-1}; ^{1}H NMR δ 2.01−2.60 (m, 10H, $CH_2CH_2CH_2$), 2.76−3.43 (m, 24H, CH_2CH_2CH_2 and CH_2CH_2CO); MS *m/z* M$^+$ 410. Anal. Calcd for $C_{30}H_{34}O$: C, 87.76; H, 8.35. Found: C, 87.58; H, 8.34.

1-Hydroxyl[3.3.3.3.3.3](1,2,3,4,5,6)cyclophane 27. To a solution of **26** (85.0 mg, 0.207 mmol) in dry THF (200 mL) was added a solution of 0.1 mol/L SmI_2 in dry THF (20.0 mL, 2.00 mmol) under argon at room temperature with stirring, followed by the addition of 1 N aqueous KOH (4.00 mL, 4.00 mmol). After the addition, the mixture was stirred for 30 min at room temperature. The color of the mixture changed from original dark blue to yellow in a few minutes. The reaction mixture was concentrated, and the residue was acidified with dilute HCl. It was extracted with $CHCl_3$, washed with brine, dried with Na_2SO_4, and filtered through a column of silica gel. The filtrate was concentrated to give **27** (70 mg), which was used in the next reaction without further purification. **27**: white powdery crystals (benzene); IR (KBr) ν 3416 (OH) cm^{-1}; ^{1}H NMR δ 1.94−2.16 (m, 6H, $CH_2CH_2CH_2$), 2.42−2.56 (m, 2H, $CH_2CH_2CH_2$), 2.69−3.09 (m, 16H, CH_2CH_2CH_2), 3.26−3.54 (m, 10H, CH_2CH_2CH_2), 4.19−4.31 (m, 1H, CH_2CH_2CHOH), 5.75−5.82 (m, 1H, CH_2CH_2CHOH); MS *m/z* M$^+$ 412. Anal. Calcd for $C_{30}H_{36}O\cdot 1/2H_2O$: C, 85.46; H, 8.85. Found: C, 85.53; H, 8.59.

[3.3.3.3.3.3](1,2,3,4,5,6)Cyclophane 1. To a mixture of **27** (410 mg, 0.994 mmol) and $LiAlH_4$ (190 mg, 5.00 mmol) in dry THF (500 mL) was added a solution of $AlCl_3$ in dry THF (50 mL) in an ice−salt bath under nitrogen with stirring. After the mixture had been stirred in an ice−salt bath under nitrogen for 30 min, it was allowed to warm to room temperature and then was stirred for 1 h. The mixture was refluxed for 13 h under nitrogen with stirring, and the cooled mixture was poured into water. It was concentrated and the concentrate extracted with $CHCl_3$. The combined extracts were washed with brine, dried with Na_2SO_4, and filtered. After removal of the solvent, the residue was chromatographed on silica gel (70 g) with $CHCl_3$ to give **1** (331 mg, 69% from **26**). **1**: colorless crystals (benzene), mp 358 °C (dec, sealed tube); ^{1}H NMR δ 2.41−2.51 (m, 12H, $CH_2CH_2CH_2$), 3.19 (t, J = 7.3 Hz, 24H, CH_2-CH_2CH_2); ^{13}C NMR ($CDCl_3$, off-resonance decoupled) δ 20.5 (t, $CH_2CH_2CH_2$), 28.5 (t, $CH_2CH_2CH_2$), 135.4 (s, aromatic); MS *m/z* M$^+$ 396. Anal. Calcd for $C_{30}H_{36}$: C, 90.85; H, 9.15. Found: C, 90.78; H, 9.04.

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Supporting Information Available: Figures showing relative thermodynamical stability for **8a**−**f** and double spin decoupling spectrum of **1** (2 pages). See any current masthead page for ordering information and Internet access instructions.

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