High-Pressure NMR Study of *cis*-1,*n*-Disubstituted[*n*]paracyclophanes. Effect of Increased Pressure on the Hindered Internal Rotation

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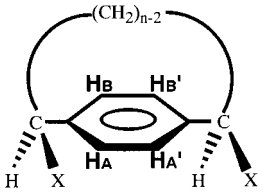
Abstract: The effect of hydrostatic pressure on the rate of internal rotation of title compounds has been examined by the DNMR method. Quartz pressure-resisting NMR cells were used to realize the high-pressure experiments up to 390 (line shape measurements) and 450 MPa (chemical shift measurements). Application of hydrostatic pressure was found to accelerate the rotation of the benzene ring, while pressure-induced low-frequency chemical shifts of bridge methylene protons indicated that there is a considerable shrinkage of the methylene bridge structure upon pressurization.

Introduction

Dynamic conformational behavior of macrocyclic molecules has been studied intensively in recent years by the DNMR method with the solvent and the temperature as the variables.[1] Among them, cyclophane molecules are considered to be of significant interest, especially in view of their pressure profile. This is because they have a void space surrounded by a conformationally flexible methylene bridge. It is easy to suppose that pressurization can cause a deformation of the methylene bridge and exerts some influence upon dynamic properties of the molecule. To this type of compound, however, less attention to the pressure effect seems to have been adopted.[2]

For *cis*-1,*n*-disubstituted[*n*]paracyclophanes ($n = 12$, 13) **1** chosen in this study, examination of the relevant NMR signals easily affords information concerning internal rotation of the benzene ring. Owing to the substituents at each of the α, α′



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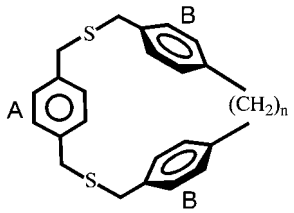
positions in the cyclophane molecule, the aromatic protons become nonequivalent when rotation of the benzene ring is frozen. When warming, the benzene ring is beginning to rotate rapidly through the loop of the polymethylene bridge and, above the coalescence temperature, T_C, the sets of protons ($H_AH_{A'}$ and $H_BH_{B'}$) are rendered to be indistinguishable. Thus at temperatures near the T_C, the rate of rotation of the benzene ring can be obtained by DNMR simulation on observed ring proton signals.[3]

It is well-known that the benzene ring in the molecule exerts a very large magnetic anisotropy effect (the ring current effect) to a proton in the neighborhood, the magnitude of which is governed by a geometric relation between the resonating proton and the ring. Therefore, concurrent observation of pressure-induced NMR chemical shift (pressure shift) of the methylene protons which are exposed to the ring current effect yields in principle information about the deformation of the methylene bridge caused by applied hydrostatic pressure.

In our previous high-pressure, high-resolution NMR (HPHR-NMR) works,[2a] a study on 2,11-dithia[3.3.*n*]paracyclophanes ($n = 1$, 2) **2** has shown that proton chemical shift (relative to the internal reference, cyclohexane) for the benzene ring **A** exhibits a marked low-frequency shift upon pressurization (−0.08 ppm/$\Delta P = 150$ MPa), while the ring protons of ring **B** give a high-frequency shift (+0.04−0.05 ppm).



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Reduction of a molecular partial volume under high pressure, being affected by changes in the dihedral angles in the bridges between rigid benzene rings accompanying some contraction of the macrocyclic structure, was considered to be responsible for the abnormal pressure shifts.

From studies on the *cis*-1,*n*-disubstituted[*n*]paracyclophanes ($n = 12$ and 13) at 1 atm,[3,4] on the other hand, a change in the size of the methylene loop by removing or adding one CH_2

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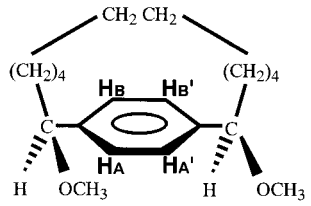
group was shown to affect the rotation rate by a factor larger than 10^2-10^3. We thus began to study pressure effects on the internal rotation of these cyclophanes with the expectation that pressurization leads to a slowdown of the rotation because it expectedly causes a contraction of the loop structure as is the case for the thiacyclophane system. A preliminary experiment on *cis*-1,12-diacetoxy- and *cis*-1,12-dihydroxy[12]paracyclophane was undertaken at temperatures near the T_C by following line shape of the ring proton resonance up to 200−300 MPa.[4] On the contrary to the expectation, it was found that increasing pressure accelerates the rotation of the benzene ring. In making the line shape analysis, however, the observed ring proton signals were simulated by assuming a simple two-site exchange system $H_A \rightleftarrows H_B$ (or $H_{A'} \rightleftarrows H_{B'}$) and by approximating J_{AB} (or $J_{A'B'}$) = 0.[3] There could be little doubt about the qualitative conclusion reached by this, but the approximate nature of the assumptions prevented us from obtaining an accurate reading of the pressure behavior of the cyclophane molecules. Thus a closer examination was demanded as the subject of upcoming research.

In the present study, our choice was *cis*-1,12-dimethoxy[12]-paracyclophane (**3**). This compound has sufficient solubility so that the S/N has been improved. At temperatures near T_C, rate of the rotation can be examined by employing a 90 MHz spectrometer while chemical shift parameters for the ring protons necessary for the line shape analysis are obtained at the same temperature and pressure by using a higher magnetic field (ν_0 = 400 MHz) NMR spectrometer. Because the rotation is nearly "frozen" on the time scale of the 400 MHz spectrometer, the simulation of 400 MHz ring proton spectra gives a more reliable chemical shift parameter, which is used in the simulation of the 90 MHz resonance to calculate the rotational rate. We also employed *cis*-1,13-dimethoxy[13]paracyclophane (**4**) and *cis*-1,13-dimethyl[13]paracyclophane (**5**) as reference compounds.



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The following criteria governed our choice of solvent: (i) the boiling point is higher than the T_C (ca. 405 K at 390 MPa for the 90 MHz spectrometer); (ii) the methylene proton signals in the loop are resolved fairly well so that their assignment can be made easily; (iii) there is no signal in the region of the ring proton and the methylene proton resonances; and (iv) there is sufficient solubility of the substituted cyclophanes even at high pressure.

Our final choice was 1,1,2,2-tetrachloroethane-d_2.

Results and Discussion

The pressure dependence of the ring proton line shape for **3** at 406.5 K is shown in Figure 1, where the simulations[5] by means of the DNMR-5 program (QCPE No. 569) were performed by assuming the $H_AH_{A'}H_BH_{B'} \rightleftarrows H_BH_{B'}H_AH_{A'}$ exchanging system with magnetically nonequivalent, coupled four spins. Results of simulations and NMR parameters are presented in Table 1.

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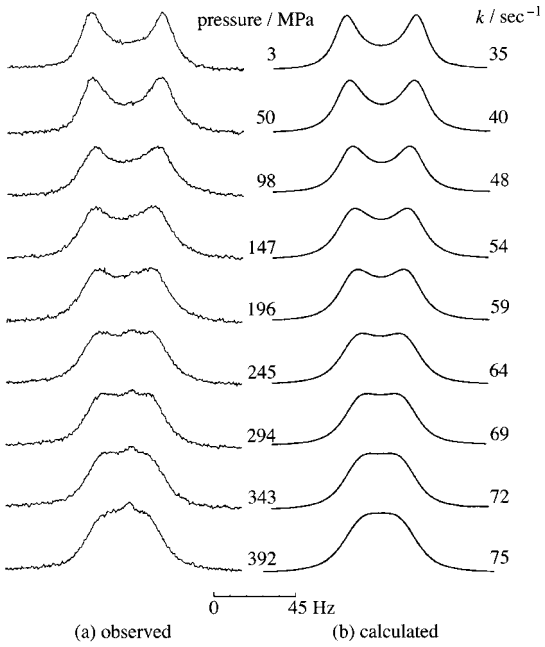

Figure 1. 90-MHz variable-pressure spectra of the ring protons of **3** at 406.5 K. A small peak at the center of the spectrum is considered to arise from the ring protons of the trans compound as an impurity.

Table 1. Effect of Pressure on the Hindered Internal Rotation in **3**

P/MPa	$(\delta_A - \delta_B)$/ppm	$w_{h/2}$[a]/ppm	ln *k*[b]
3[c]	0.445	0.039	3.56
—[d]	0.446	0.043	4.09
50[c]	0.436	0.056	3.69
—[d]	0.436	0.041	4.26
98[c]	0.430	0.042	3.87
—[d]	0.423	0.046	4.34
147[c]	0.423	0.051	3.99
—[d]	0.414	0.046	4.39
196[c]	0.415	0.041	4.08
—[d]	0.410	0.041	4.44
245[c]	0.409	0.057	4.16
294[c]	0.402	0.040	4.23
343[c]	0.396	0.041	4.28
392[c]	0.390	0.040	4.32

[a] Half-height width of the reference signal. [b] Estimated error limits are ±0.05. [c] Data at 406.5 K. [d] Data at 415.7 K.

Clearly, application of hydrostatic pressure accelerates the rotation of the benzene ring. This agrees qualitatively with our previous finding for the *cis*-1,12-diacetoxy- and *cis*-1,12-dihydroxy[12]paracyclophanes, where the simulations were made on the uncoupled two-site exchange approximation. In Figure 2a, logarithms of the rates are plotted against pressures. Although a general feature is a continued rise in ln *k* with increasing pressure, it is noted that the plot exhibits a decided curvature, the increase in ln *k* being diminished with increasing pressure. High-pressure experiments at 415.7 K were also conducted up to 200 MPa for **3** (Figure 3) and no particular temperature effects on the pressure behavior could be observed. As shown in Figure 2b, there may be a slight decrease in the pressure-induced acceleration as compared with that at 406.5 K. The lack of enough data at higher pressures renders the further pursuit of a quantitative elucidation of the temperature effects unprofitable.[6]

(6) Because of the partial decomposition of the sample caused by prolonged heating, we could not continue the HPHR-NMR measurements. The reliability of the data at this temperature is considered to be partly impaired.

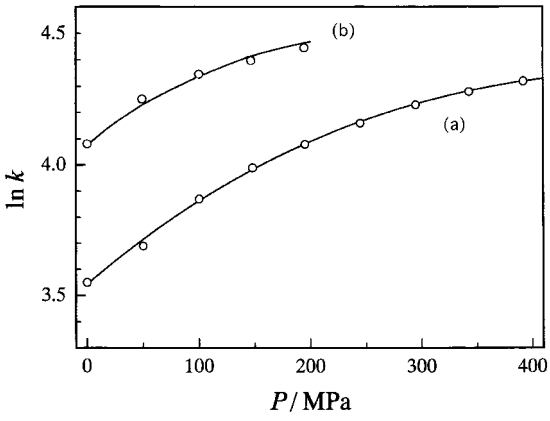

Figure 2. Pressure effect on the rate of internal rotation of **3** at 406.5 (a) and 415.7 K (b).

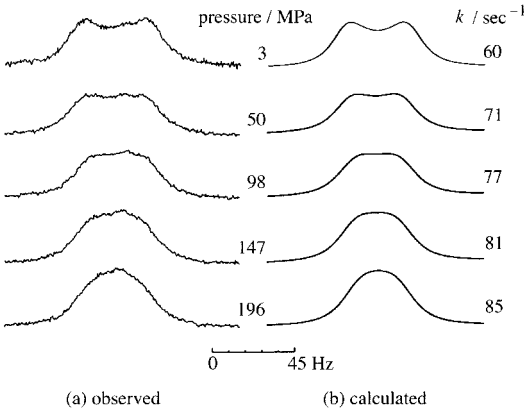

Figure 3. 90-MHz variable-pressure spectra of the ring protons of **3** at 415.7 K.

For **4** (in 1,1,2,2-tetrachloroethane-d_2 solvent) and **5** (in 1,1,2,2-tetrachloroethane-d_2 and hexane-d_{14} solvents), preliminary experiments up to 200 MPa were undertaken. The results were almost the same as the present observations except that **4** exhibited a smaller pressure-induced acceleration (by a factor of 1.5−2 smaller than that for **3**) and **5** showed a smaller curvature in the ln *k* vs pressure plot. There is, however, no satisfactory explanation for the *difference* in the pressure behavior among **3**, **4**, and **5**.

In general, pressure dependence of the reaction rate is expressed by the well-known equation,

$$\ln k = (\ln k_0) - (\Delta V^{\ddagger})(RT)^{-1}P \qquad (1)$$

where $\Delta V^{\ddagger}$, known as the activation volume,[7,8] is the difference in the partial molar volume between the original state and the transition state. Equation 1 predicts an increase in the rate by pressurization if the transition state occupies a smaller volume than the original state (a negative $\Delta V^{\ddagger}$). In a plot of ln *k* against pressure, a slope of the curve at a given pressure *P* affords $-\Delta V^{\ddagger}/RT$ at pressure *P*. In Table 2 are listed mean activation volumes at 406.5 K for four successive pressure ranges obtained from the slopes in the curve. It is noted that the activation volume is less negative the higher the pressure.

Table 2. Pressure Dependence of the Mean Activation Volume, $(\Delta V^{\ddagger})_{av}$ for **3**[a]

pressure range/MPa	$(\Delta V^{\ddagger})_{av}$/cm^3 mol^{-1}
0−100	−11
100−200	−7
200−300	−5
300−400	−3

[a] Mean activation volume in the pressure range between $P = m$ and n is calculated by the following: $(\Delta V^{\ddagger})_{av} = -RT(\ln k_n - \ln k_m)(P_n - P_m)^{-1}$.

The presently observed negative activation volume (acceleration by pressurization) is understood on the basis of a considerable difference in geometry of the cyclophane molecule between the original and the transition states of the rotating process:

(i) In the original state, the cyclophane molecule should have a nonplanar geometry, where a plane bearing the methylene loop is at a right angle to the benzene plane. This nonplanar shape is considered to be unfavorable to tight packing with the solvent molecules[2b,9] and leads to a larger partial molar volume, contributing to produce the negative activation volume. Since internal rotation of this type is a neutral reaction, the rate is not very solvent dependent. However, there may be weak polar interaction (such as the dipole−dipole interaction) between solvent dipoles, and group dipoles arose from methoxy substituents. From an examination of the molecular model, the methoxy groups are found to be more exposed to the solvation in the transition state than in the original state. Therefore, this type of specific solvent effect, if any, should again contribute to produce the negative activation volume.

(ii) On the basis of the molecular model obtained from a SPARTAN PM3 calculation, the volume of a void space surrounded by the methylene loop is estimated to be 10−15 cm^3 mol^{-1}. At the transition state, this void space is occupied by about half of the benzene ring, so that the intrinsic molecular volume is reduced. Furthermore, the resulting almost planar molecular shape is considered to facilitate the tight packing with the solvent molecules, which gives rise to a smaller partial molar volume. The pressure-induced acceleration of the rotation observed for nonpolar **5** in nonpolar solvent, hexane-d_{14}, justifies the above-mentioned view that a purely geometric factor governs mainly the pressure effect on the rotational rate of the cyclophane molecules.

In general, a curved ln *k* vs pressure plot is attributed to a change in the activation volume upon pressurization, i.e., nonzero pressure derivative of the activation volume.[7] The change in the activation volume, in turn, is related to the compressibility coefficient of activation,[7] $\Delta\beta^{\ddagger}$:

$$(\partial\Delta V^{\ddagger}/\partial P)_T = -\Delta\beta^{\ddagger} \qquad (2)$$

Because the transition state, as compared with the original state, has a close-packed structure and is associated with stronger solvation, both the intrinsic volume of the cyclophane molecule and the solvation volume should be less compressible at the transition state than at the original state. This gives rise to a negative $\Delta\beta^{\ddagger}$, leading to an increased (a less negative) activation volume with increasing pressure, i.e., a partially convex curve of ln *k* vs pressure plot.

We consider that another cause of the curvature should be, at least partly, attributed to possible shrinkage of the methylene loop structure induced by pressurization. For **3**, methylene proton resonances of the methylene bridge are comparatively

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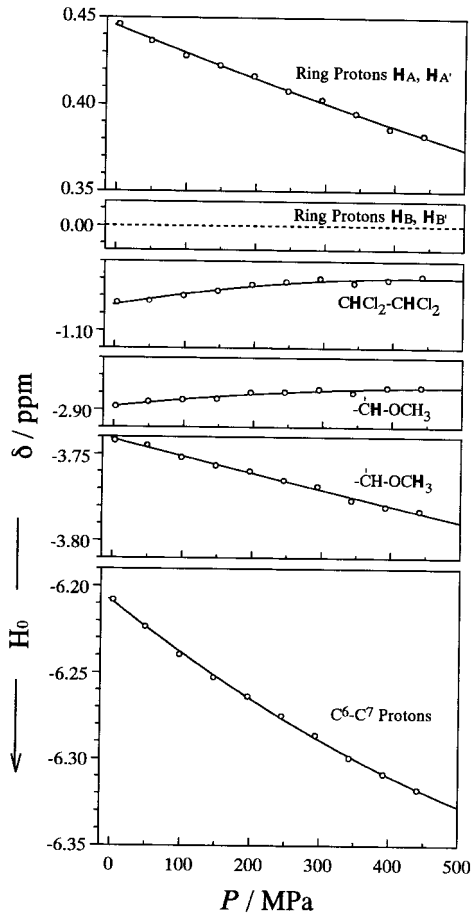

Figure 4. Pressure-induced chemical shifts for **3**.

well resolved so that the chemical shift of four protons at the top of the loop (protons on C^6 and C^7 give a slightly broadened singlet) can be followed throughout the full pressure range. Hereafter we refer to these protons as C^6-C^7 protons. Since they are located nearest to the 6-fold axis of the benzene ring and are exposed to the highest diamagnetic ring current effect, they displayed the lowest frequency chemical shift. When hydrostatic pressure was applied, this low-frequency shift, referenced to all other intramolecular proton signals, was found to increase even more. In Figure 4, it can be seen that the C^6-C^7 protons show the largest pressure-induced low-frequency shift, 0.11 ppm relative to the ring protons H_B, $H_{B'}$, upon pressurization up to 450 MPa. If the ring protons H_A, $H_{A'}$ are employed as the reference, this pressure-induced shift is 0.05 ppm[10]/450 MPa. On this ground, we estimate that the low-frequency shift attributable to the shrinkage of the methylene loop caused by compression to 450 MPa should be 0.05−0.1 ppm. Examining Johnson−Bovey's table for the **ring-current effect**,[12,13] we conclude that a pressurization up to 450 MPa causes a distortion of the paracyclophane molecule at the original state with a shrinkage of the methylene loop 0.1−0.4 Å along the 6-fold axis of the benzene ring. This shrinkage at the original state causes an increased potential energy of the transition state in **3**, where the benzene ring should be forced into a smaller space in the methylene loop. Resulting retardation of the pressure-induced acceleration contributes to the curved ln *k* vs pressure plot.

Conclusions

Hindered internal rotation of the benzene ring in *cis*-1,*n*-disubstituted[*n*]paracyclophanes is shown to be accelerated by increased hydrostatic pressure, while there is a considerable shrinkage of the methylene bridge structure upon pressurization. The pressure-induced acceleration is explained in terms of a negative activation volume of the rotation process. A negative activation compressibility and shrinkage of the methylene loop at high pressure are considered to lead to the curved ln *k* vs pressure plot.

Experimental Section

The technique used for the HPHR-NMR measurements is a modification of the high-pressure glass cell method.[14] A detailed description of this new HPHR-NMR technique will appear elsewhere. In HPHR-NMR experiments, pressures were measured on a 700 MPa Heise Bourdon pressure gauge. Temperatures were calibrated by the chemical shift of ethylene glycol[15] filled in a glass cell similar in shape and size to the high-pressure quartz cell employed in the high-pressure experiments.

Measurements of the Ring Proton Signal for Line Shape Analysis. For **3**, HPHR-NMR measurements were conducted on a JEOL JNM-FX-90Q spectrometer at 406.5 and 415.7 K. A solution consisting of 5 mol % of **3**, 2 mol % of 1,1,2,2-tetrachloroethane, and 93 mol % of 1,1,2,2-tetrachloroethane-d_2 was introduced into a CSX-type[14] quartz high-pressure cell[4] with o.d./i.d. = 3.8 mm/1 mm and a length of 37 mm (shoulder to shoulder), with a flexible 440 mm long capillary tail. The 1,1,2,2-tetrachloroethane was used as a reference to monitor the resolution of proton spectra. At each measurement, time averaging of 128−320 scans was made with external NMR lock field control. In addition, the ring proton signals were measured on a JEOL JNM-GX-400 spectrometer at the same temperature and pressure with time averaging of 32−128 scans and with internal lock to the solvent deuterium. These ring proton signals were then subjected to the DNMR-5 simulation to obtain the corresponding chemical shift parameters, $\delta_A-\delta_B$. Since the rotation of the benzene ring was nearly frozen on the time scale of the 400 MHz machine, the chemical shift parameters thus obtained are considered to be more reliable. These parameters were then employed in the DNMR-5 simulation on the 90 MHz ring proton spectra for the calculation of the rotational rates. Because the pressure variation of the coupling constants is negligibly small for a spin system on the rigid benzene ring,[16] the coupling constants, $J_{AA'} = J_{BB'} = 9.0$ Hz, $J_{AB} = J_{A'B'} = 2.0$ Hz, $J_{AB'} = J_{A'B} = 0.1$ Hz, were assumed to remain constant throughout the present pressure range and used for the simulation.

For **4** (1.5 mol % in 1,1,2,2-tetrachloroethane-d_2, 64 scans, internal lock) and **5** (1.5 mol % in 1,1,2,2-tetrachloroethane-d_2 and 1.5 mol % in *n*-hexane-d_{14}, 128 scans, internal lock), HPHR-NMR measurements of their ring proton signals were conducted on the JEOL JNM-GX-400 spectrometer with time averaging of 64−128 scans, where the field control was effected by internal lock to the solvent deuterium. The

(10) The ring protons H_A, H_A' displayed a pressure-induced low-frequency shift, 0.06 ppm, relative to the ring protons H_B, $H_{B'}$. This is most likely explained in terms of the steric overcrowding of methoxy substituents.[11]

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(15) Ammann, C.; Meier, P.; Merbach, A. E. *J. Magn. Reson.* **1982**, *46*, 319−321.

(16) A small change in the coupling constant, if any, proved to have little effect on the result of the simulation.

DNMR-5 simulations were performed, assuming that the coupling constants, $J_{AA'} = J_{BB'} = 9.0$ Hz, $J_{AB} = J_{A'B'} = 2.0$ Hz, and $J_{AB'} = J_{A'B} = 0.1$ Hz, remain constant throughout the pressure range.[16]

Measurements of Chemical Shifts at Various Pressures. To study the pressure dependence of chemical shifts for the protons in the rest of the molecule, HPHR-NMR measurements for **3** (5 mol % in 1,1,2,2-tetrachloroethane-d_2) were carried out on the 400-MHz spectrometer at 406.5 K up to 450 MPa, where the time averaging of 32 scans was made with the internal lock field control.

General Procedures for Cyclophane Synthesis. **3** was prepared from *cis*-1,12-dibromo[12]paracyclophane (**6**) adapting a procedure reported by Wasserman et al.[17] **4** was obtained by methylation of *cis*-1,13-dihydroxy compound **7**. **5** was prepared from 1,15-dimethyl-2,14-dithia-[15]paracyclophane (**8**) (a mixture of cis (*meso*) and trans (*dl*) compounds) according to the procedure reported by Misumi et al.[18] For preparations of **6** and **7**, a method reported by Nakazaki et al.[3] was adapted.

Routine ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-250 spectometer. Mass spectra were recorded on a Shimazu GCMS-QP2000A spectrometer. Melting points were measured on a micro hot plate apparatus and were uncorrected.

***cis*-1,12-Dibromo[12]paracyclophane (6).** [12]Paracyclophane was brominated with NBS in carbon tetrachloride[3] to yield a mixture of *cis*- and *trans*-1,12-dibromo[12]paracyclophanes. The mixture was recrystallized repeatedly from hexane−dichloromethane to give **6**, mp 171−173 °C [lit.[3] mp 172−173 °C].

***cis*-1,12-Dimethoxy[12]paracyclophane (3).** A mixture of 255 mg of **6**, 237 mg of silver nitrate, and 4.9 mL of methanol was refluxed for 2 h with stirring. After being cooled to room temperature, the reaction mixture was filtrated. Ether extract of the filtrate was washed with saturated aqueous $NaHCO_3$ and with saturated aqueous NaCl. After drying with anhydrous Na_2SO_4, evaporation of ether under reduced pressure gave 109 mg of yellow raw product. Purification by silica gel column chromatography (hexanes−ether, 15/1) afforded 84 mg of **3** as pale yellowish needles: mp 32−35 °C; ^{1}H NMR (250 MHz,$CDCl_3$) δ 0.75−1.08 (m, 16H), 1.56−1.93 (m, 4H), 3.29 (s, 6H), 4.15 (dd, 2H, J = 9.1 Hz, 3.8 Hz), 7.06 (s, 2H), 7.47 (s, 2H); ^{13}C NMR (63 MHz, $CDCl_3$, reference $CDCl_3$,) δ 22.24, 26.37, 27.28, 36.36, 56.61, 84.00, 126.12, 127.97, 141.41; MS *m*/*z* 304 (M^+), 289, 272, 164, 91. Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 78.93; H, 10.71.

***cis*-1,13-Dibromo[13]paracyclophane (9).** [13]Paracyclophane was brominated using a similar procedure as employed for [12]paracyclophane[3] and the resulted mixture of *cis*- and *trans*-dibromide, without separation, was used to prepare *cis*-1,13-diacetoxy[13]paracyclophane (**10**). Repeated recrystallizations of the mixture from hexane−dichloromethane gave **9** as white needles: mp 158−159 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.71−1.25 (m, 18H), 2.26−2.40 (m, 4H), 4.88 (dd, 2H, J = 11.6 Hz, 4.6 Hz), 7.38 (broad s, 4H); ^{13}C NMR (63 MHz, $CDCl_3$, reference $CDCl_3$) δ 25.94, 26.73, 27.47, 27.79, 40.50, 53.52, 127.95, 141.80; MS *m*/*z* 335, 337, 255, 91. Anal. Calcd for $C_{19}H_{28}Br_2$: C, 54.83; H, 6.78. Found: C, 54.89; H, 6.78.

***cis*-1,13-Diacetoxy[13]paracyclophane (10).** A mixture of 6.43 g of **9** (contaminated with trans compound), 6.33 g of anhydrous sodium acetate, and 64 mL of acetic acid was stirred at 110 °C for 20 h.[3] After cooling, reaction mixture was poured into saturated aqueous $NaHCO_3$ solution and the organic layer was extracted several times with ether. The ether extract was washed with saturated $NaHCO_3$ and saturated aqueous NaCl and dried over anhydrous Na_2SO_4. The ether solution was concentrated under reduced pressure. The residue (3.3 g) was subjected to silica gel column chromatography separation, which afforded **10** as white needles: mp 83−84 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.71−1.32 (m, 18H), 1.69−2.03 (m, 4H), 2.05 (s, 6H), 5.64 (dd, 2H, J = 10.3 Hz, 3.9 Hz), 7.32 (broad s, 4H); ^{13}C NMR (63 MHz, $CDCl_3$, reference $CDCl_3$) δ 21.45, 23.11, 26.35, 27.29, 27.79, 35.08, 76.14, 127.25, 139.94, 170.25; MS *m*/*z* 374 (M^+), 272, 91. Anal. Calcd for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 73.56; H, 9.33.

***cis*-1,13-Dihydroxy[13]paracyclophane (7).** A mixture of 98 mg of **10** and 5 mL of 1 N KOH solution in ethanol was refluxed for 10 h with stirring.[3] After cooling and dilution with distilled water, the organic layer was extracted with chloroform repeatedly. Chloroform extract was washed with saturated aqueous NaCl and dried over anhydrous Na_2SO_4. Evaporation under reduced pressure gave 68 mg of crude **7** as white crystals: mp 189−191 °C. This crude product, without further purification, was used for the preparation of **4**. ^{1}H NMR (250 MHz, $CDCl_3$,) δ 0.80−1.23 (m, 18H), 1.55−1.78, 1.91−1.99 (m, 4H), 1.82 (d, 2H, J = 2.7 Hz), 4.62−4.69 (m, 2H), 7.34 (broad s 4H); ^{13}C NMR (63 MHz,$CDCl_3$, reference $CDCl_3$) δ 23.27, 26.42, 27.39, 27.46, 27.86, 38.09, 75.15, 126.57, 143,80; MS *m*/*z* 290 (M^+), 272, 254, 135, 91.

***cis*-1,13-Dimethoxy[13]paracyclophane (4).** To 124 mg of sodium hydride was added a solution of 68 mg of **7** in 5 mL of dry THF, followed by 220 μL of methyl iodide, under argon atmosphere. The mixture was stirred at 50 °C for 3 h under argon atmosphere. After cooling, the reaction was quenched by adding ethyl acetate and distilled water to the reaction mixture. The mixture was extracted with ether and the extract was washed with saturated aqueous NaCl solution and dried over anhydrous Na_2SO_4. Ether was evaporated under reduced pressure and the residue was subjected to silica gel column chromatographic purification (hexanes−ether 9/2) to afford 67 mg of **4** as pale yellowish needles: mp 63−65 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.81−1.26 (m, 18 H), 1.60−2.00 (m, 4H), 3.22 (s, 6H), 4.07 (dd, 2H, J = 10.2, 3.7 Hz), 7.06 (broad s, 2H), 7.47 (broad s, 2H); ^{13}C NMR (63 MHz, $CDCl_3$, reference $CDCl_3$) δ 23.29, 26.35, 27.34, 27.48, 27.74, 36.51, 56.43, 84.41, 126.12, 128.14, 141.34; MS *m*/*z* 318 (M^+), 303, 286, 165, 91. Anal. Calcd for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76. Found: C, 79.34; H, 10.63.

1,15-Dimethyl-2,14-dithia[15]paracyclophane (Mixture of *cis* (*meso*) and *trans* (*dl*) Compounds) (8). *p*-Bis(1-hydroxyethyl)benzenes (mixture of *meso* and *dl* compounds) were converted to *p*-bis(1-mercaptoethyl)benzenes (mixture of *meso* and *dl* compounds), which were subjected to the coupling reaction with 1,11-dibromoundecane according to the following procedure.[18]

To 500 mL of a 0.15 M solution of potassium hydroxide in ethanol was added with stirring under refluxing 130 mL of benzene solution containing 4.00 g of *p*-bis(1-mercaptoethyl)benzenes and 6.33 mL of 1,11-dibromoundecane. Addition of the benzene solution was carried out under nitrogen atmosphere and required 10 h. After the addition was completed, stirring was continued for 2 h. Crude product was purified by silica gel column chromatography (hexanes−ethyl acetate, 30/1) to give 4.75 g of **8** (mixture of *meso* and *dl* compounds) as white crystals: mp 52−58 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.05−1.70 (m, 18H), 1.53 (d, 6H, J = 7.1 Hz), 2.15−2.40 (m, 4H), 3.94 (q, 2H, J = 7.1 Hz), 7.29 (s, 4H), 7.31 (s, 4H); ^{13}C NMR (63 MHz, $CDCl_3$, reference $CDCl_3$) δ 22.95, 23.13, 27.13, 27.17, 27.20, 27.80, 28.14, 28.39, 28.68, 28.90, 30.92, 31.04, 44.13, 44.56, 127.31, 127.35, 143.30; MS *m*/*z* 350 (M^+), 132, 91.

1,15-Dimethyl-2,14-disulfonyl[15]paracyclophane (Mixture of *cis* (*meso*) and *trans* (*dl*) Compounds) (11). A mixture of 21 mL of acetic acid, 2.22 g of **8**, and 7.2 mL of 30% hydrogen peroxide was heated slowly to 120 °C.[18] At this temperature, stirring was continued for 4 h. After the mixture was cooled to 0 °C, 2.25 g of **11** (mixture of cis and trans (*dl*) compounds) was obtained as white crystals: mp 222−225 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.10−1.46 (m, 14H), 1.70−1.84 (m, 10H), 2.50−2.70 (m, 4H), 4.19 (q, 2H, J = 7.1 Hz), 4.20 (q, 2H, J = 7.1 Hz), 7.52 (s, 4H); ^{13}C NMR (63 MHz, $CDCl_3$, reference $CDCl_3$) δ 13.56, 13.68, 19.96, 20.59, 26.84, 27.53, 26.88, 27.57, 26.97, 49.54, 49.77, 62.56, 63.52, 129.52, 129.55,136.28, 136.38; MS *m*/*z* 414 (M^+), 350, 286, 132, 91.

***cis*-1,13-Dimethyl[13]paracyclophane (5).** In a 500 mm long quartz tube (inside diameter = 10 mm, sealed on one side) was placed 1.04 g of **11**. Pyrolysis[18] of **11** was carried out by heating the quartz tube at 630 °C in an electric furnace, which required 75 min. The reaction mixture was extracted with hexane. Evaporation of hexane under reduced pressure, followed by purification by silica gel column chromatography (hexane), gave 171 mg of colorless oil, a mixture of

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cis- and *trans*-1,13-dimethyl compounds. Repeated recrystallizations from methanol−hexane afforded a small amount of **5** as white crystals: mp 56−57 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.76−1.19 (m 18 H), 1.25 (d, 6H J = 7.0 Hz), 1.32−1.71 (m, 4H), 2.54−2.75 (m, 2H), 7.10 (s, 4H); ^{13}C NMR (63 MHz, $CDCl_3$, reference $CDCl_3$) δ 23.29, 26.12, 26.37, 27.48, 27.63, 27.96, 38.43, 40.22, 127.20, 144.66; MS *m*/*z* 286 (M^+), 146, 91. Anal. Calcd for $C_{21}H_{34}$: C, 88.04; H, 11.96. Found: C, 87.82; H,11.95.

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