5.90 (q, 1 H, J = 7.1 Hz), 5.93 (q, 1 H, J = 7.1 Hz), 7.30 (m, 10 ArH); ^{13}C NMR δ 15.0, 15.8, 17.7, 44.8, 49.9, 50.5, 52.7, 126.9, 127.8, 128.0, 128.3, 128.5, 128.6, 138.3, 139.1, 164.4, 167.8; $[\alpha]_D$ −366.4° (c 2, $CHCl_3$).

(3*S*,6*S*)-1,4-*N*,*N*-((*S*)-1-Phenyleth-1-yl)-3,6-dimethylpiperazine-2,5-dione (7). LHMDS (20 mL of 1 M solution in THF, 20 mmol) was slowly added to a solution of **6a** (6.72 g, 20 mmol) in dry THF (60 mL) at 0 °C. After 2 h, the reaction mixture was cooled to −78 °C and methyl iodide (2.84 g, 20 mmol) in dry THF (20 mL) was added. After 2 h, 2 M HCl (10 mL) was added, and the mixture was extracted with ethyl acetate. After the extract was dried and the solvent was removed, the residue was purified by silica gel chromatography to give 7 as a white solid (6.4 g, 92% yield); mp 185 °C; IR (Nujol) 1660; ^{1}H NMR δ 1.58 (d, 6 H, J = 7.1 Hz), 1.62 (d, 6 H, J = 7.1 Hz), 3.82 (q, 2 H, J = 7.1 Hz), 5.8 (q, 2 H, J = 7.1 Hz), 7.25 (m, 10ArH); ^{13}C NMR δ 17.2, 21.7; 51.3, 52.6, 126.7, 127.6, 128.4, 138.6, 167.8; $[\alpha]_D$ −232.4° (c 2.16, $CHCl_3$). Anal. Calcd for $C_{22}H_{26}N_2O_2$: C, 75.4; H, 7.48. Found: C, 75.5; H, 7.46.

(3*R*,6*R*)-1,4-*N*,*N*-((*S*)-1-Phenyleth-1-yl)-3,6-dimethylpiperazine-2,5-dione (8a) and (3*R*,6*S*)-1,4-*N*,*N*-((*S*)-1-Phenyleth-1-yl)-3,6-dimethylpiperazine-2,5-dione (8b). Starting from **6b**, the alkylation reaction was performed as described for **6a**. A mixture of **8a** and **8b** was obtained in 90% yield and a diastereomeric ratio of 90:10. Diastereomers **8a** and **8b** were separated by silica gel chromatography (cyclohexane–ethyl acetate (85:15)). Isomer **8a**: white solid; mp 175 °C; ^{1}H NMR δ 0.87 (d, 6 H, J = 7.1 Hz), 1.58 (d, 6 H, J = 7.1 Hz), 4.09 (q, 2 H, J = 7.1 Hz), 5.85 (q, 2 H, J = 7.1 Hz), 7.3 (m, 10 ArH); ^{13}C NMR δ 15.6, 20.2, 50.9, 53.0, 127.5, 127.7, 128.3, 139.4, 167.5; $[\alpha]_D$ −316.9° (c 2.04, $CHCl_3$). Isomer **8b**: ^{1}H NMR δ 1.1 (d, 3 H, J = 7.1 Hz), 1.45 (d, 3 H, J = 7.1 Hz), 1.65 (d, 3 H, J = 7.1), 1.7 (d, 3 H, J = 7.1 Hz), 3.9 (q, 1 H, J = 7.1 Hz), 4.20 (q, 1 H, J = 7.1 Hz), 5.8 (q, 1 H, J = 7.1 Hz), 5.85 (q, 1 H, J = 7.1 Hz), 7.30 (m, 10ArH). Anal. Calcd for $C_{22}H_{26}N_2O_2$: C, 75.4; H, 7.48. Found: C, 75.4; H, 7.45.

(*S*)-Alanine (1). To 10 mL of 57% hydriodic acid was added 7 (1.1 g, 3 mmol), and the mixture was refluxed for 1 h. Then the resulting solution was extracted with ethyl acetate, and the aqueous solution was evaporated under reduced pressure. The residue was dissolved in water (10 mL) and adsorbed on ion-exchange resin Amberlyst H 15. The resin was washed with distilled water and then eluted with 5 M NH_4OH to give (*S*)-alanine (0.48 g, 90% yield). ^{1}H NMR (D_2O, DCl) δ 1.50 (d, 3 H, J = 7 Hz), 3.8 (q, 1 H, J = 7 Hz); $[\alpha]_D$ +14.5° (c 1, 5 M HCl) (lit.[7] $[\alpha]_D$ +14.6 (5 M HCl)).

(*R*)-Alanine (2). The product was obtained in 90% yield starting from **8a** and following the procedure described for (*S*)-alanine (1): $[\alpha]_D$ −14.45° (c 1, 5 M HCl) (lit.[7] $[\alpha]_D$ +14.6° (5 M HCl) for the (*S*)-isomer).

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Registry No. 1, 56-41-7; 2, 338-69-2; 3, 36293-01-3; 4, 143746-58-1; 5a, 143746-59-2; 5b, 143837-97-2; 6a, 143746-62-7; 6b, 143837-99-4; 7, 143746-60-5; 8a, 143746-61-6; 8b, 143837-98-3; (*S*)-$PhCHMeNH_2$, 2627-86-3; $ClCH_2COCl$, 79-04-9; (±)-$H_3CCHClCOCl$, 76248-57-2.

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A Conformational Study of [3.3]Metacyclophanes through Variable-Temperature ^{1}H NMR and Optical Rotation[1]

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Conformational behavior of 2,2,11,11-tetradeuterio[3.3]metacyclophanes 1-d_4 and 2-d_4 has been studied by a variable-temperature (VT) ^{1}H NMR method. In order to simplify the interpretation of the ^{1}H NMR spectrum, four deuteriums were introduced at C-2 and C-11 positions of the trimethylene bridges of [3.3]metacyclophanes by reductive desulfurization of 2,11-bis(1,4-dithiabutane-1,4-diyl)[3.3]metacyclophanes 4 and 5 with tri-*n*-butyltin deuteride. Our previous conformational study of tetradeuterio-1,4-dioxa[4.3.3]cyclophane (3-d_4) revealed that the temperature-dependent phenomenon in the ^{1}H NMR spectrum of 1 was ascribed to the inversion the trimethylene bridges. The work also suggested the presence of benzene ring inversion. To confirm this, optically active [3.3]metacyclophanechromium tricarbonyl complexes (−)- and (+)-17 were prepared by means of the HPLC separation of racemic complex (±)-17 using a chiral stationary phase. Racemization occurred when (−)- and (+)-17 were decomplexed at 20 °C. This result as well as the fact that the energy barrier (ΔG^*) for the benzene ring inversion could not be detected by the VT NMR method indicated that the barrier is much lower than that of trimethylene bridge inversion (ΔG^* = 11–12 kcal/mol). The most stable conformer of 1-d_4 and 2-d_4 is a syn-(chair-chair), and the less stable conformer is estimated to be a syn(chair-boat) on the basis of the ^{1}H NMR data.

Introduction

[*m.n*]Metacyclophanes can generally adopt two different geometries, syn and anti.[5] Lehner et al. reported that the conformation of [*m.n*]metacyclophane in solution is sensitive both to chain length of the bridges and substitution. Thus [3.3]metacyclophane (m = n = 3, 1) preferentially adopts the syn geometry, but its lower and higher homologs (m = 2–4; n = 2,3) adopt the anti geometry.[6] Recently,

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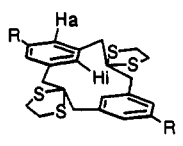
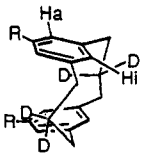
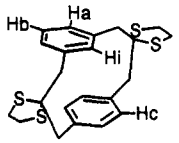
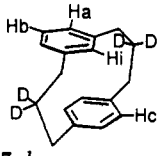
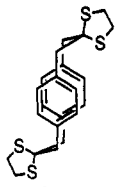
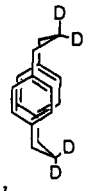
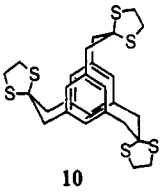
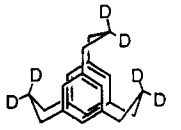
0022-3263/92/1957-6536$03.00/0

Table I. The Yields of the Deuteration Reaction of [3.3]Cyclophane Thioacetals with Tri-*n*-butyltin Deuteride in the Presence of AIBN in Refluxing Xylene

starting material	product	yield
		
4 (R = H) 5 (R = OMe)	1-d_4 (R = H) 2-d_4 (R = OMe)	79% 77%[2]
		
6	7-d_4	94%[20]
		
8	9-d_4	93%[3]
		
10	11-d_6	49%[4]

conformational studies have been focused on [3.3]metacyclophane (1)[2,7-9] and related systems[10-15] among the [*m.n*]metacyclophanes. The preferred syn geometry of 1 and related systems in both crystalline state[7-9,10a,c,15a] and in solution[2,7-15] has been established. Two inversion processes for the conformational isomerism of 1 and its related systems have been proposed: inversion of the benzene rings and the chair-boat type conformational isomerism of the trimethylene bridges between syn(chair-chair) (1-cc), syn(chair-boat) (1-bc), and syn(boat-boat) (1-bb) forms (Figure 1).

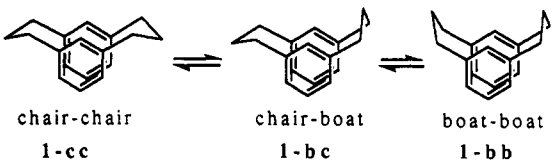
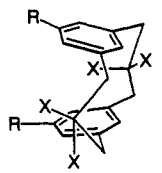
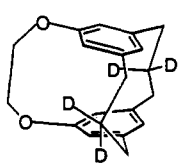


Figure 1. Conformational isomerism of [3.3]metacyclophane (1) via chair-boat inversion of the trimethylene bridges.



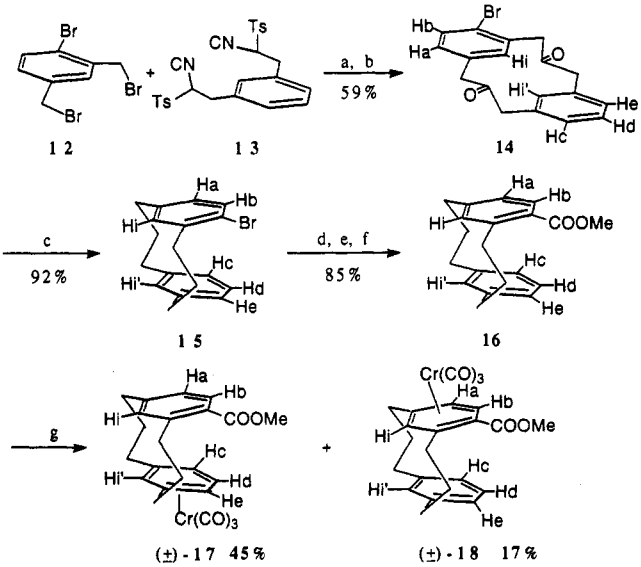
1; X=R=H
1-d_4; X=D, R=H
2-d_4; X=D, R=OMe



3-d_4

Interest in this laboratory[8,16] in the dynamic behavior of [3.3]cyclophanes has extended to conformational behavior and variable-temperature (VT) NMR.[2-4] Previously our conformational study of tetradeuterio-1,4-dioxa[4.3.3]cyclophane (3-d_4) revealed that the temperature-dependent phenomenon in the ^{1}H NMR spectrum of 1 was ascribed to the inversion of trimethylene bridges, which was consistent with the study by Semmelhack et al.[7] The work also suggested benzene ring inversion together with the inversion of the trimethylene bridges.[2] In order to seek unambiguous evidence for the benzene ring inversion process, we prepared optically active [3.3]metacyclophane derivatives; if benzene ring inversion does exist, racemization of the optically active isomer should occur or vice versa. We chose cyclophanechromium tricarbonyl complexes as optically active [3.3]metacyclophane derivatives since attached chromium tricarbonyl could freeze the

Scheme I. Synthetic Route to Racemic Cyclophanechromium Tricarbonyl Complexes (±)-17 and (±)-18[a]



[a] (a) *n*-Bu_4NI, NaOH, CH_2Cl_2/H_2O. (b) Concd HCl, CH_2Cl_2/Et_2O. (c) $H_2NNH_2{\cdot}H_2O$, KOH, $O(CH_2CH_2OH)_2$. (d) *n*-BuLi, Et_2O. (e) CO_2, H^+. (f) MeOH, concd H_2SO_4. (g) $Cr(CO)_6$, *n*-Bu_2O, THF.

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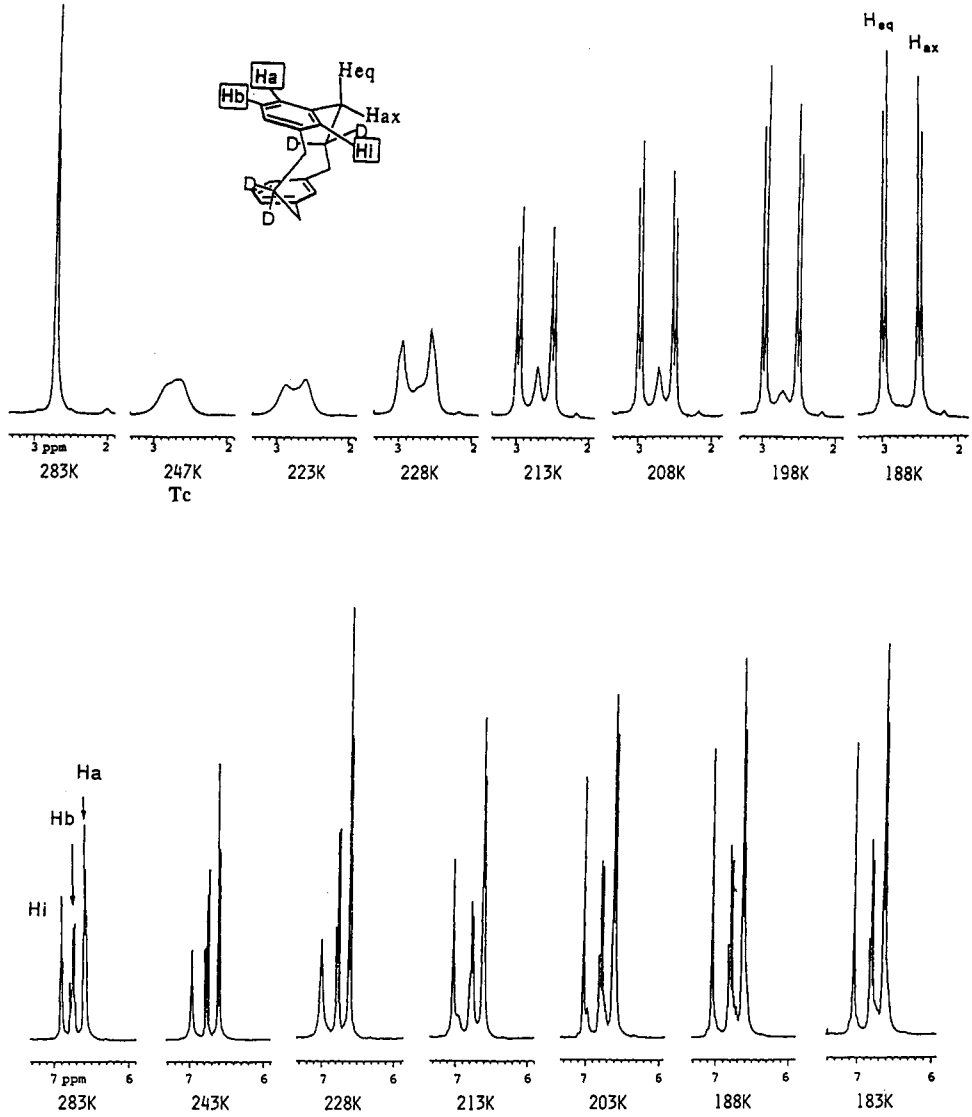

Figure 2. VT ^{1}H NMR spectra of the benzylic protons (upper) and aromatic protons (lower) of 1-d_4 (270 MHz, CD_2Cl_2).

benzene ring inversion and the chromium tricarbonyl moiety could be readily attached to and removed from benzene ring under mild conditions, as suggested by Mitchell et al.[20b]

In this paper, we herein describe the synthesis and conformational study of 2,2,11,11-tetradeuterio[3.3]metacyclophanes 1-d_4 and 2-d_4 by the VT ^{1}H NMR method as well as the racemization of optically active [3.3]metacyclophanechromium tricarbonyl complexes [(+)- and (−)-17] on removal of the chromium tricarbonyl.

Results and Discussion

Synthesis. Four deuteriums were introduced at C-2 and C-11 to simplify the interpretation of the ^{1}H NMR spectrum. Reductive desulfurization of 1,3-dithiolanes was done with tri-*n*-butyltin deuteride.[17] Treatment of thioacetal 4 with tri-*n*-butyltin deuteride in the presence of AIBN in refluxing xylene produced 1-d_4 in 79% yield. A summary of deuteration results is presented in Table I.

The synthetic route to the chromium tricarbonyl complexes (±)-17 and -18 is shown in Scheme I. 5-Bromo-[3.3]metacyclophane-2,11-dione (14) was prepared (59%) by the coupling between 12 and 13.[18] Wolff–Kishner reduction of the carbonyl groups of 14 afforded 15 (92%). Lithiobromine exchange of 15 with *n*-butyllithium, followed by carboxylation and esterification provided ester 16 (85%).[19] Complexation of 16 with chromium hexacarbonyl in refluxing *n*-Bu_2O/THF (10:1) produced π-arenechromium tricarbonyl complexes, (±)-17 (45%) and (±)-18 (17%).[20,21]

Dynamic ^{1}H NMR Study. Conformational behavior of 1-d_4 and 2-d_4 was studied by the VT ^{1}H NMR method. The dynamic NMR study of 1 was already reported by Semmelhack et al.,[7] but we wish to report here our own result.

The benzylic protons of 1-d_4 exhibit strong temperature-dependent phenomenon (Figure 2, 270 MHz, CD_2Cl_2). They appear as a singlet (2.71 ppm) at 10 °C, which

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broadens as the temperature is lowered. The broad band is gradually split into two peaks below −26 °C (T_c), then resolves into an AB quartet [2.50 (d, J = 13.7 Hz, H_{ax}) and 2.97 ppm (d, J = 13.7 Hz, H_{eq})] and a broad peak (2.71 ppm) at −60 °C. The intensity of the broad peak, however, decreases as the temperature is lowered and it finally disappears at −85 °C.

The aromatic protons of 1-d_4 appear at 6.59 (d, J = 7.4 Hz, 4 H, Ha), 6.75 (t, J = 8.2, 6.6 Hz, 2 H, Hb), and 6.90 ppm (s, 2 H, Hi) at 10 °C. After the temperature is lowered, all aromatic proton signals broaden and shift slightly to downfield, but no significant changes are observed. The internal aromatic proton signal (Hi) resolves into two peaks (7.02 and 6.95 ppm) of unequal intensities at −65 °C. The low-intensity signal disappears at about −85 °C, corresponding to the spectral change of the benzylic protons as shown in Figure 2. The major conformer of 1-d_4 is assigned to a syn(chair-chair) 1-cc since chemical shifts and geminal coupling constants of the benzylic protons are similar to those of the chair-chair conformer of 3-d_4 (H_{ax} 2.46, J = 13.8; H_{eq} 2.95 ppm, J = 13.7 Hz).[2] The new low-intensity signals may be ascribed to a minor isomer, probably a syn(chair-boat) 1-bc, on the basis of the relative stability order of three conformers (1-cc > 1-bc > 1-bb) as determined by the molecular mechanics calculations by Semmelhack et al.,[7] as well as our experimental results in 3-d_4.[2] The activation energy ($\Delta G^{\ddagger}$) for the conversion of a chair form to a boat form in trimethylene bridges of 1-d_4 is estimated to be 11.6 (11.5[7]) kcal/mol.[22]

The low-temperature ^{1}H NMR spectrum of 2-d_4 having higher solubility in CD_2Cl_2 than 1-d_4 was studied to obtain more detailed information on the minor conformers. Sharp singlets for the aromatic protons [6.13 (s, 4 H, Ha), and 6.49 ppm (s, 2 H, Hi)] at 15 °C in $CD_2Cl_2/CFCl_3$ (1:1) broaden as the temperature is lowered. At −50 °C, a new signal appears as a shoulder of the Hi peak at a slightly higher field. At −70 °C, two sets of the aromatic proton signals due to the major isomer [6.16 (Ha), 6.60 (Hi) ppm] and a minor one [6.11 (Ha″), 6.16 (Ha′), 6.58 (Hi′) ppm] are clearly observed (Figure 3).

In contrast, benzylic proton signals [2.67 ppm (br s) at 15 °C] are observed as the superposition of a pair of two broad signals due to a major isomer and a broad signal due to a minor one at −50 °C. At −70 °C, the major isomer signals become an AB quartet [2.47 (d, J = 13.7 Hz, H_{ax}) and 2.93 ppm (d, J = 13.7 Hz, H_{eq})], while the minor isomer signals appear as much broader peaks. The major isomer of 2-d_4 is assigned to a syn(chair-chair) on the basis of the chemical shifts and geminal coupling constants of the benzylic protons. An NOE experiment of 2-d_4 at −70 °C supports our assignment; irradiating the inner aromatic proton (Hi) gave a moderate enhancement (17%) of the benzylic protons at higher field but no effect was observed in the lower field absorption. Again, clear assignment of the minor conformer, however, cannot be made because of the broadening of the benzylic protons. The ^{1}H NMR parameters of the major and minor conformers of 1-d_4 and 2-d_4 are compiled in Table II (found in the supplementary material).

Lowering of the intensities of the minor isomer signals may be explained by the preferential crystallization of the minor isomer, as pointed by Semmelhack et al.[7] Broadening of the benzylic proton signals even at −70 °C in both cases suggests the possibility of the presence of another

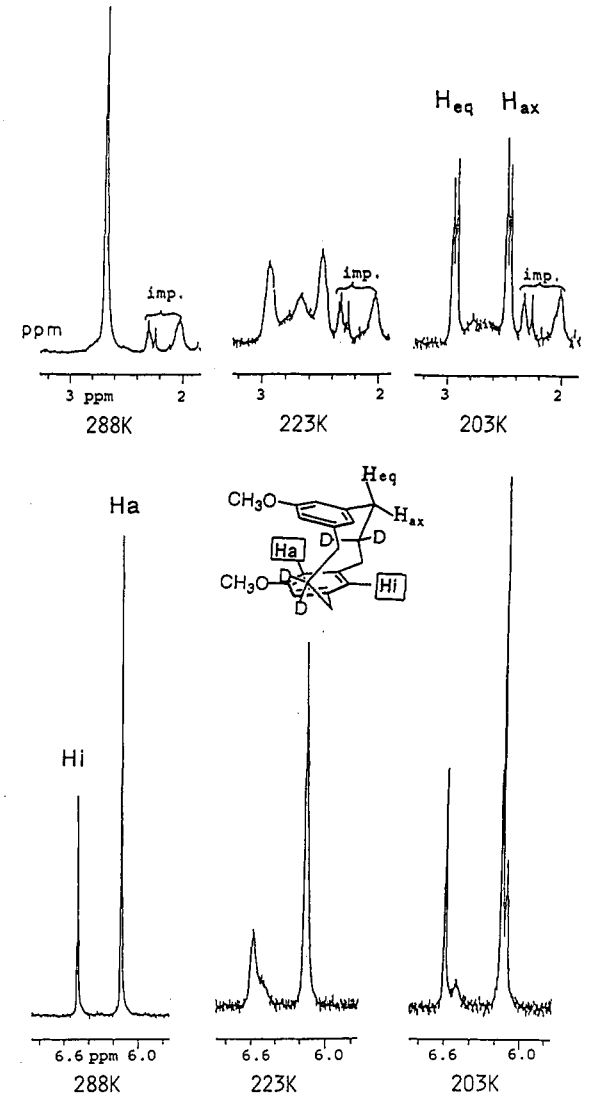

Figure 3. VT ^{1}H NMR spectra of the benzylic protons (upper) and aromatic protons (lower) of 2-d_4 (400 MHz, $CD_2Cl_2/CFCl_3$ = 1:1).

dynamic process, i.e., interconversion of the minor conformers via an anti conformer (benzene ring inversion). But we could not obtain the evidence to support this interconversion by the VT NMR method since the $\Delta G^{\ddagger}$ for the interconversion is beyond the detection limit of the method. So further study is needed into this point.

Optical Resolution and Chiroptical Properties. Taking into account the oxidative and photochemical instability of the chromium complex of 17, the HPLC resolution of 17 on chiral stationary phases should be the most effective method. A few examples of the HPLC separations of racemic metal carbonyl complexes into enantiomers have been reported[23] but this is the first application of the method to the resolution of racemic cyclophanes.

Racemic 17 was completely resolved into the enantiomers at room temperature on a column packed with Daicel CHIRALCEL OD [cellulose tris(3,5-dimethylphenyl-

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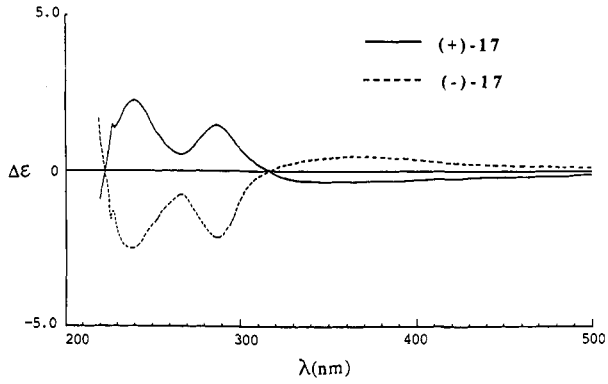

Figure 4. Circular dichroism spectra of (+)- and (−)-17 in methanol.

carbamate)][24] using hexane/2-propanol (9:1), as an eluent. The first fraction is levorotatory, the second is dextrorotatory. (±)-17 was separated by a preparative CHIRALCEL OD column (25 mm × 250 mm) with the same solvent system. The optical purities of the separated (−)- and (+)-17 were determined by HPLC on a CHIRALCEL OD column and found to be 100 and 98.6% ee, respectively. Their optical rotations at 589 nm (D) in acetone were $[\alpha]_D^{RT(20)} = -43°$ (c = 0.198, acetone) and $[\alpha]_D^{RT(20)} = +41°$ (c = 0.167, acetone), respectively. Their absolute configurations have not been determined.

The circular dichroism (CD) spectrum of (+)-17 is a mirror of (−)-17, verifying enantiomeric relationships (Figure 4). The two intensive Cotton effects of (−)-17 ($\Delta\epsilon$ = −2.58, −2.08) and (+)-17 ($\Delta\epsilon$ = +2.17, +1.64) at the wavelengths of 238 and 287 nms are assigned to the π-π^* transition of 17 (UV ϵ = 8300, 1900), while another weak broad Cotton effect at ca. 325 nm [(−)-17, $\Delta\epsilon$ = +0.46, (+)-17, $\Delta\epsilon$ = −0.42, UV ϵ = 1100] is ascribed to the intramolecular charge transfer band (chromium-π-bonded arene).[25]

Racemization. Decomplexation of (−)-17 by oxidation with ceric ammonium nitrate (CAN) was carried out in acetone at 20 °C. After the addition of CAN, the solution was filtered and the filtrate was diluted. Its optical rotation was determined and found to be zero. The same result was obtained for (+)-17 under similar conditions. The optically active [3.3]metacyclophane derivative (−)-16 should exist in the solution, if benzene ring inversion is prohibited. However, the optically active (−)-16 could not be detected by the optical rotation. This observation offers the strong evidence that benzene ring inversion exists in solution at 20 °C.

Conclusion

The presence of benzene ring inversion was confirmed by the racemization experiments using the optically active chromium tricarbonyl complexes [(−)-17 and (+)-17]; racemization occurred when the optically active (−)- and (+)-17 were decomplexed at 20 °C. We conclude that two isomerization processes, the inversion of the benzene rings and trimethylene bridges, are responsible for the dynamic behavior observed in the ^{1}H NMR spectra of [3.3]metacyclophanes. The energy barrier for benzene ring inversion in 1-d_4 and 2-d_4 is estimated to be much lower than that of the inversion process of the trimethylene bridges since the former was not detected by the VT NMR method even at the lowest temperatures.

Semmelhack et al. suggested an order of thermodynamic stabilities for three conformers in [3.3]metacyclophane (1) on the basis of the molecular mechanics calculations: syn(chair-chair) > syn(chair-boat) > syn(boat-boat).[7] A similar order of the thermodynamic stabilities was observed in the frozen ^{1}H NMR spectrum of 3-d_4 as reported earlier.[2] In [3.3]metacyclophanes 1-d_4 and 2-d_4, the most stable conformer is a syn(chair-chair) and the less stable conformer is estimated to be a syn(chair-boat).

A detailed study on the assignment of minor isomer(s) in [3.3](2,6)pyridinophanes will be reported elsewhere, and a mechanistic study of the inversion processes based on semiempirical molecular orbital calculations is now in progress.

Experimental Section

General Comments. All melting points are uncorrected. ^{1}H NMR spectra were recorded at 60, 90, 270, and 400 MHz in $CDCl_3$, except where noted. For optical resolution of the racemic 17 by HPLC, CHIRALCEL OJ [cellulose tris(4-methylbenzoate)][26] and CHIRALCEL OD[24] of Daicel Chemical Industries, Ltd. were used for analytical purposes, in which the CHIRALCEL OD gave the best resolution. Therefore CHIRALCEL OD column (20 mm × 250 mm) was used for preparative puposes. Optical rotations are uncorrected and were determined with a 1-dm thermostated cell. CD spectra were recorded in MeOH at room temperature.

2,2,11,11-Tetradeuterio-6,15-dimethoxy[3.3]metacyclophane (2-d_4). For the reaction apparatus and synthetic procedure of 6,15-dimethoxy[3.3]metacyclophane-2,11-dione (38%), refer to refs 18b and 4: colorless plates (benzene/EtOH); mp 219.0–220.0 °C; R_f (SiO_2, CH_2Cl_2) 0.24; IR (KBr) $\delta_{C=O}$ 1694 cm^{-1}; ^{1}H NMR (90 MHz) δ 3.51 (s, 8 H, $-CH_2COCH_2-$), 3.83 (s, 6 H, OMe), 5.54 (s, 2 H, Hi), 6.73 (s, 4 H, Ha); MS m/z M$^+$ 324. Anal. Calcd for $C_{20}H_{20}O_4$: C, 74.06; H, 6.21. Found: C, 73.98; H, 6.28.

For the synthetic procedure of 5, refer to refs 3 and 4. 5 (80%): Colorless prisms (benzene); mp 233.5–235.0 °C; ^{1}H NMR (270 MHz) δ 3.25 (s, 8 H, $-CH_2CCH_2-$), 3.43 (s, 8 H, $-SCH_2CH_2S-$), 3.81 (s, 6 H, OMe), 5.45 (br s, 2 H, Hi), 7.01 (s, 4 H, Ha); MS m/z M$^+$ 476. Anal. Calcd for $C_{24}H_{28}O_2S_4$: C, 60.47; H, 5.92. Found: C, 60.64; H, 5.87.

A mixture of 5 (722 mg, 1.51 mmol), n-Bu_3SnD (6.0 mL, 22.3 mmol), AIBN (175 mg), and xylene (33 mL) was refluxed for 12 h under nitrogen and then allowed to cool to room temperature. The mixture was searpated by silica gel chromatography; elution with hexane afforded xylene and then the column was eluted with diethyl ether. The ether eluate was concentrated, and the residue was further purified by preparative TLC (SiO_2) with benzene to afford 2-d_4 as colorless crystals (352 mg, 77%). 2-d_4: Mp 52.0–53.0 °C; R_f (SiO_2, benzene), 0.49; ^{1}H NMR (270 MHz) δ 2.67 (s, 8 H, $-CH_2CD_2CH_2-$), 3.63 (s, 6 H, OMe), 6.16 (s, 4 H, Ha), 6.50 (s, 2 H, Hi); MS m/z M$^+$ 300; IR (KBr) δ_{C-D} 2198, 2140, 2098 cm^{-1}. Anal. Calcd for $C_{20}H_{20}D_4O_2$: C, 79.96; H + $^1/_2$D, 8.05. Found: C, 79.71; H + $^1/_2$D, 7.98.

2,2,11,11-Tetradeuterio[3.3]metacyclophane (1-d_4). 4 was prepared from [3.3]metacyclophane-2,11-dione.[18a] 4: Colorless needles ($CHCl_3$), mp 233.0–233.5 °C; ^{1}H NMR (270 MHz) δ 3.27 (s, 8 H, $-CH_2CCH_2-$), 3.45 (s, 8 H, $-SCH_2CH_2S-$), 5.74 (br s, 2 H, Hi), 7.15 (br s, 2 H, Ha), 7.46 (br s, 4 H, Hb); MS m/z M$^+$ 416. Anal. Calcd for $C_{22}H_{24}S_4$: C, 63.42; H, 5.81. Found: C, 63.36; H, 5.75.

A mixture of 4 (191 mg, 0.458 mmol), n-Bu_3SnD (1.6 mL, 5.95 mmol), AIBN (70 mg), and xylene (25 mL) was refluxed for 12 h with stirring under nitrogen. After cooling, similar purification

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procedure (column chromatography and preparative TLC on SiO_2 with hexane) afforded **1-d_4** (87 mg, 79%) as colorless crystals (EtOH): mp 79.0–79.5 °C; IR (KBr) ν_{C-D} 2194, 2134, 2092 cm^{-1}; R_f (SiO_2, hexane) 0.17; MS m/z M^+ 240; ^1H NMR (270 MHz, CD_2Cl_2) δ 2.71 (s, 8 H, $-CH_2CD_2CH_2-$), 6.59 (d, J = 7.4 Hz, 4 H, Ha), 6.75 (t, J = 8.2 Hz, 6.6 Hz, 2 H, Hb), 6.90 (s, 2 H, Hi). Anal. Calcd for $C_{18}H_{16}D_4$: C, 89.94; H + $^1/_2$D, 8.38. Found: C, 90.04; H + $^1/_2$D, 8.14.

2,2,11,11-Tetradeuterio[3.3]metaparacyclophane (7-d_4). 6: Colorless needles (benzene); mp 260.5–261.5 °C; ^1H NMR (60 MHz) δ 3.13 (s, 4 H, $-CH_2CCH_2-$), 3.43 (s, 8 H, $-SCH_2CH_2S-$), 3.49 (s, 4 H, $-CH_2CCH_2-$), 5.40 (br s, 1 H, Hi), 7.07 (s, 4 H, Hc), 6.9–7.3 (m, 3 H, Ha, Hb); MS m/z M^+ 416. Anal. Calcd for $C_{22}H_{24}S_4$: C, 63.42; H, 5.81. Found: C, 63.45; H, 5.81. 7-d_4: Colorless needles by sublimation (70 °C, 15 Torr); mp 90.5–91.5 °C; IR (KBr) ν_{C-D} 2198, 2142, 2100 cm^{-1}; R_f (SiO_2, hexane) 0.45; MS m/z M^+ 240. ^1H NMR (270 MHz, CD_2Cl_2/CS_2 = 3:2) δ 2.68 (s, 4 H, $-CH_2CD_2CH_2-$), 3.35 (s, 4 H, $-CH_2CD_2CH_2-$), 5.52 (s, 1 H, ArH), 6.61 (s, 4 H, ArH), 6.65 (d, J = 7.8 Hz, 2 H, ArH), 6.95 (t, J = 7.8 Hz, 1 H, ArH). Anal. Calcd for $C_{18}H_{16}D_4$: C, 89.94; H + $^1/_2$D, 8.38. Found: C, 89.80; H + $^1/_2$D, 8.40.

5-(Methoxycarbonyl)[3.3]metacyclophane (16). 14 (3.06 g, 59%) was prepared from 12 (5.15 g, 15.0 mmol) and 13 (7.40 g, 15.0 mmol). 14: Colorless needles (benzene); mp 158.5–159.0 °C; IR (KBr) $\nu_{C=O}$ 1698 cm^{-1}; R_f (SiO_2, CH_2Cl_2) 0.42; MS m/z M^+ 342. ^1H NMR (270 MHz) δ 3.50 (s, 2 H, $-CH_2COCH_2-$), 3.52 (s, 2 H, $-CH_2COCH_2-$), 3.58 (s, 2 H, $-CH_2COCH_2-$), 3.59 (s, 2 H, $-CH_2COCH_2-$), 5.80 (s, 1 H, Hi'), 5.88 (d, J = 2.4 Hz, 1 H, Hi), 7.10 (d, J = 7.3 Hz, 1 H, Hc), 7.13 (dd, J = 8.3, 2.0 Hz, 1 H, Ha), 7.18 (d, J = 7.8 Hz, 1 H, He), 7.30 (t, J = 7.3, 7.8 Hz, 1 H, Hd), 7.58 (d, J = 8.3 Hz, 1 H, Hb). Anal. Calcd for $C_{18}H_{15}O_2Br$: C, 62.99; H, 4.41. Found: C, 63.16; H, 4.28.

A mixture of 14 (2.01 g, 5.86 mmol), KOH (10.29 g, 183 mmol), 100% $N_2H_4 \cdot H_2O$ (15 mL, 309 mmol), and triethylene glycol (55 mL) was heated at 120 °C for 2 h and then at 200 °C for 2 h. The reaction mixture was poured into ice (400 mL) and acidified with concd HCl. The resultant white powder 15 was collected by filtration and dried in vacuo (92%). 15: Colorless needles (EtOH), mp 112.5–113.5 °C; R_f (SiO_2, petroleum ether) 0.31; MS m/z M^+ 314; ^1H NMR (270 MHz) δ 2.01–2.18 (m, 4 H, $-CH_2CH_2CH_2-$), 2.66–2.84 (m, 8 H, $-CH_2CH_2CH_2-$), 6.48 (dd, J = 7.8, 8.3, 2.0, 2.4 Hz, 1 H, Ha), 6.61 (d, J = 7.3 Hz, 1 H, Hc), 6.75 (d, J = 7.3 Hz, 1 H, He), 6.83 (d, J = 2.0 Hz, 1 H, Hi), 6.83 (t, J = 7.3 Hz, 1 H, Hd), 6.91 (s, 1 H, Hi'), 6.97 (d, J = 7.8 Hz, 1 H, Hb). Anal. Calcd for $C_{18}H_{19}Br$: C, 68.58; H, 6.08. Found: C, 68.57; H, 6.05.

To a solution of 15 (604.9 mg, 1.92 mmol) in dry Et_2O (60 mL) was added a solution of butyllithium in hexane (1.5 M, 6.15 mmol) at 20 °C. The mixture was then refluxed for 25 min with stirring. After cooling powdered dry ice (70 g) was added and the mixture was stirred at 20 °C for 1 h. The mixture was extracted with an aqueous NaOH solution (50 mL × 4), and the combined aqueous portion was acidified with concd HCl. Then the resulting precipitate was collected by filtration, washed with water, and dried in vacuo to give the carboxylic acid as white powder (477.7 mg, 89%), which was used in the following reaction without further purification.

A mixture of the carboxylic acid (103 mg, 0.367 mmol), concd H_2SO_4 (1 mL), and MeOH (35 mL) was refluxed for 16 h with stirring. After cooling, the mixture was concentrated and the concentrate was extracted with CH_2Cl_2. The combined organic portion was washed with $NaHCO_3$ solution, dried ($MgSO_4$), filtered, and concentrated to dryness to give 16 as colorless crystals (103 mg, 95%). A sample for microanalysis was sublimed (65 °C, 0.5 Torr): mp 110.0–111.5 °C; IR (KBr) $\nu_{C=O}$ 1713 cm^{-1}; R_f (SiO_2, benzene/hexane = 1:1) 0.37; MS m/z M^+ 294. ^1H NMR (270 MHz) δ 2.05–2.11 (m, 4 H, $-CH_2CH_2CH_2-$), 2.73 -2.77 (m, 6 H, $-CH_2CH_2CH_2-$), 3.11 (m, 2 H, $-CH_2CH_2CH_2-$), 3.83 (s, 3 H, COOMe), 6.62 (d, J = 6.8 Hz, 1 H, Hc), 6.64 (d, J = 6.4 Hz, 1 H, 1 H, He), 6.69 (dd, J = 7.8, 8.3, 1.5, 2.0 Hz, 1 H, Ha), 6.80 (t, J = 7.3 Hz, 1 H, Hd), 6.87 (d, J = 1.5 Hz, 1 H, Hi), 6.93 (s, 1 H, Hi'), 7.46 (d, J = 7.8 Hz, 1 H, Hb). Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.37; H, 7.53.

Chromium Tricarbonyl Complexes (±)-17 and (±)-18. A mixture of 16 (208.4 mg, 0.708 mmol), chromium hexacarbonyl (1.146 g, 5.21 mmol), THF (1 mL), and n-Bu_2O (10 mL) was heated at gentle reflux under a slight positive pressure of nitrogen with stirring. After 4 h, the mixture was cooled, opened to the air, and filtered, and the filtrate was concentrated. The residue was purified by preparative TLC (Al_2O_3, benzene/hexane = 1:2) to give complex (±)-17 (137.0 mg, 45%) as yellow crystals (EtOH) and (±)-18 (35.2 mg, 12%) as an orange oil. (±)-17: Mp 185–186 °C; R_f (Al_2O_3, benzene/hexane = 1:2) 0.20; FABMS m/z M^+ 430; IR (KBr) ν_{Cr-Co} 1958, 1876, 1855 cm^{-1}; $\nu_{C=O}$ 1716 cm^{-1}; ^1H NMR (270 MHz) δ 1.77–3.08 (m, 12 H, $-CH_2CH_2CH_2-$), 3.86 (s, 3 H, COOMe), 4.62 (d, J = 5.9 Hz, 1 H, Hc), 4.64 (d, J = 5.9 Hz, 1 H, He), 5.08 (s, 1 H, Hi'), 5.13 (t, J = 6.3 Hz, 1 H, Hd), 6.87 (d, J = 7.3 Hz, 1 H, Ha), 7.19 (s, 1 H, Hi), 7.60 (d, J = 7.8 Hz, 1 H, Hb). Anal. Calcd for $C_{23}H_{22}O_5Cr \cdot C_2H_5OH$: C, 63.03; H, 5.88. Found: C, 62.72; H, 5.69. (±)-18: R_f (Al_2O_3, benzene/hexane = 1:2) 0.39; IR (KBr) ν_{Cr-CO} 1962, 1886 cm^{-1}; $\nu_{C=O}$ 1716 cm^{-1}; FABMS m/z M^+ 430; ^1H NMR (270 MHz) δ 1.82–3.65 (m, 12 H, $-CH_2CH_2CH_2-$), 3.82 (s, 3 H, COOMe), 4.68 (d, J = 6.8 Hz, 1 H, Ha), 4.84 (s, 1 H, Hi), 5.86 (d, J = 6.8 Hz, Hb), 6.78 (d, J = 6.8 Hz, 2 H, Hc and He), 6.95 (t, J = 7.3 Hz, 1 H, Hd), 7.10 (s, 1 H, Hi'). Anal. Calcd for $C_{23}H_{22}O_5Cr \cdot {}^1/_3C_{20}H_{22}O_2 \cdot {}^1/_2n$-$Bu_2O$: C, 68.11; H, 6.51. Found: C, 68.39; H, 6.32.

Resolution of (±)-17. Racemic 17 was resolved by preparative HPLC with CHIRALCEL OD (250 × 20 mm) using hexane/2-propanol (9:1) as an eluent. The flow rate was 5 mL/min and the fractions were detected through UV (λ = 253 nm). (±)-17 (87 mg) was dissolved in ca. 90 mL of EtOH/2-propanol (1:1). Each time 2.5 mL of the sample solution was injected and separated. The separation was achieved by 36 injections. All fractions containing pure enantiomers were combined to afford (−)-17 (35 mg, retention volume 407 mL) and (+)-17 (37 mg, retention volume 496 mL), respectively.

Racemization of (−)-17 and (+)-17 through Oxidative Decomplexation by Ceric Ammonium Nitrate (CAN). (i) (−)-17 (2.38 mg, 5.53 × 10^{-3} mmol) was dissolved in 1.2 mL of acetone, and the optical rotation of the solution was recorded at 20 °C. The measurement at the temperature was directly carried out with a thermostated polarimeter cell. To the cell was added 50 mL of the CAN solution (112 mg, 0.204 mmol in 500 mL of acetone, 0.410 M). The reaction mixture was immediately filtered. The filtrate was diluted to 2 mL and its optical rotation was measured under the above conditions. The initial optical rotation of −43° changed to 0° as soon as the CAN solution was added.

(ii) (+)-17 (2.00 mg, 4.60 × 10^{-3} mmol) was dissolved in 1.2 mL of acetone. By a similar experiment, the optical rotation changed from $[\alpha]_D^{RT(20)}$ = +41° to 0°.

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Supplementary Material Available: ^1H NMR parameters of 1-d_4 and 2-d_4, as well as their major and minor conformers (Table II) (1 page). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS: see any current masthead page for ordering information.