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Hemisphere-shaped calixarenes and their analogs: synthesis, structure, and chiral recognition ability

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ABSTRACT

The hemisphere-shaped calixarene **1a** and its split-hemisphere-shaped isomer **1b** were synthesized from [2.1.2.1]metacyclophane (MCP) **3** by pinacol rearrangement and subsequent intramolecular acetalization. Their structures were revealed by X-ray crystallography and ^{1}H NMR spectroscopy. The temperature-dependence of the intramolecular acetalization to provide **1a** and **1b** was examined. The results indicated that **1a** is the dominant product at high temperatures, and the values of ΔH° and ΔS° were estimated to be -18.3 ± 0.37 kJ mol^{-1}, -59.1 ± 1.12 kJ mol^{-1} K^{-1}, respectively. The dinitro derivative **7** and tetranitro derivatives **8** were obtained by *ipso*-nitration at the upper rims of **1a**. The optical resolution and chiral recognition ability of racemic mixture **7** were investigated by HPLC systems.

1. Introduction

The development of new macrocyclic compounds is still an attractive topic in organic synthesis because of the potential applications of these compounds as host molecules for molecular recognition[1] and in molecular machines, such as rotaxanes or catenans.[2] Calixarenes and their analogs are one of the well-known macrocyclic compounds because of their convenient preparation and functionalization capacities.[3] One of the characteristic properties of calixarenes is their conformational variety. For example, calix[4]arenes can assume four types of conformations, namely, the cone, partial-cone, 1,3-alternate, and 1,2-alternate conformations. There are some reports of fixing their conformers by introducing bulky functional groups at the lower rims,[3e] and the rigid cone or 1,3-alternate conformers could achieve specific molecular recognition properties.[4] However, it would still be difficult to stop wobbling motions since the aromatic moieties of calixarenes are merely connected by methylene bridges at two positions. Although cyclodextrins[5] and cucurbiturils[6] are conformationally fixed, they have a limited capacity to introduce functional groups.

In this study, we present a new type of hemisphere-shaped calixarene **1a** and its split-hemisphere-shaped isomer **1b**.[7] These compounds are prepared from tetrahydroxy-tetramethoxy[2.1.2.1]metacyclophane (MCP) **3** by pinacol rearrangement and subsequent intramolecular acetalization. This is the first example of pinacol rearrangement producing a macrocyclic compound that could be regarded as a new functionally capable molecular architecture adopting a rigid conformation. In addition, the nitration of **1a** gives a dinitro derivative **7** that possesses a C_2-symmetric structure similar to chiral ligands. The optical resolution and chiral recognition ability of racemic mixture **7** are also examined using HPLC systems.

2. Results and introduction

2.1. Preparation of tetrahydroxy-tetramethoxy[2.1.2.1]MCP 3 by pinacol coupling reaction

Previously, we reported the development of a pinacol coupling method to yield [2.2]MCP with pinacol units.[8] As an application of pinacol coupling to the development of calixarene analogs, tetrahydroxy-tetramethoxy[2.1.2.1]MCP **3** was synthesized from diformyl-diphenylmethane **2** by using aluminum powder and sodium hydroxide (Scheme 1).[7] Since the ^{1}H NMR spectrum of **3** was exhibited unidentified broad peaks, we performed ketal condensation of **3** using 2,2-dimethoxy propane in order to freeze its molecular movements. The bis-ketal derivative **4** was formed with a 55% yield. The structure of **4** was determined by ^{1}H NMR spectroscopy and X-ray crystallography (Fig. 1). The X-ray crystallographic data of **3** indicated its 1,2-alternate conformation alternated at the ethylene bridges. Both sides of the pinacol units were protected by the dimethylketal structure, and the pinacol units formed *dl*-type bonds. Two *dl*-type pinacol units were placed at plane-symmetric positions and **4** formed a *meso*-structure. This suggested that the stereostructure of **3** would assume a *meso*-type structure similar to **4**.

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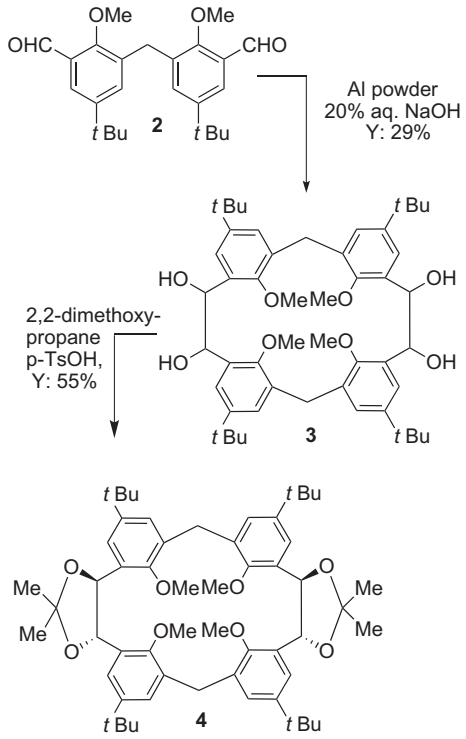


Scheme 1.

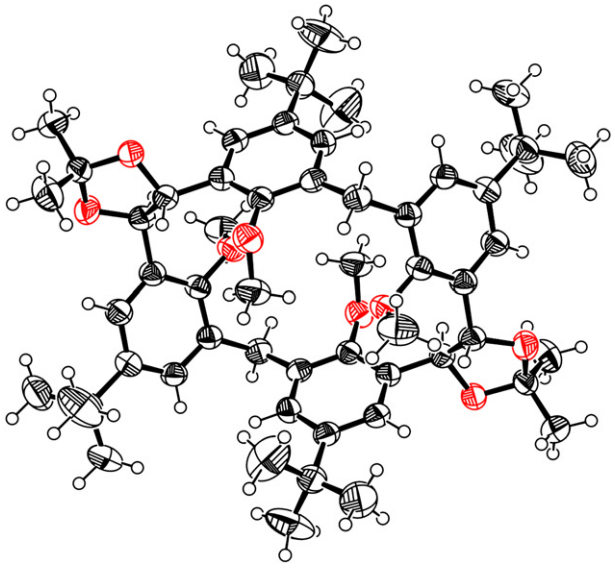
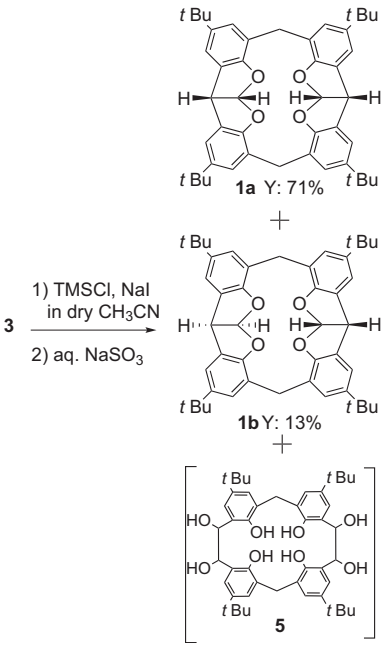


Fig. 1. X-ray crystal structure of **4**.

2.2. Synthesis of a hemisphere-shaped calixarene 1a and its isomer 1b

Treatment of **3** with trimethylsilyl chloride and sodium iodide provided two unexpected products **1a** and **1b** instead of the expected product **5**.[7] Compounds **1a** and **1b** were isolated by recrystallization and silica gel column chromatography at a ratio of 6/1 (Scheme 2). The ^{1}H NMR spectrum of **1a** was almost identical to that of **1b**; however, instead of a singlet peak for the methylene bridge positions of **1b**, a pair of doublets for the bridge protons of **1a** was identified.



Scheme 2.

X-ray crystallography revealed that **1a** had a calix[4]arene skeleton (Fig. 2).[7]

Compound **1a** formed a fixed cone-type structure that shows a hemispherical shape and an inclusion complex with an acetonitrile molecule from the recrystallization solvent at the center of its cavity. The methyl group of acetonitrile determined the direction of the calixarene cavity.

These results suggest that a CH–π interaction existed between the methyl group of acetonitrile and the benzene ring of **1a**, although the distances between the acetonitrile and benzene planes were approximately 3.60–3.66 Å. The diameters of the upper and lower rims of **1a** were measured to be 8.0 Å between the *ipso*-positions of the *tert*-butyl groups and 3.9 Å between the oxygen atoms at the internal position of calix[4]arene. These results promise host/guest properties of **1a** due to its cation–π interaction[9] with ammonium cations. Compound **1a** was comprised two 5a,10b-dihydrobenzofuro[2,3-*b*]benzofuran[10] units. The rigid structure of **1a** was verified by its dynamic NMR spectra, which showed no remarkable variation up to 160 °C in DMSO-d_6.

On the other hand, **1b** was expected to be a stereoisomer of **1a** based on the similarity of its ^{1}H NMR spectrum to that of **1a**. In the ^{1}H NMR spectrum of **1b**, the singlet peak of the ethylene bridge protons indicated an alternate structure of the aromatic rings at the ethylene bridges. This suggested that **1b** assumes a 1,2-alternate conformation.

X-ray crystallography of **1b** revealed that it had a fixed 1,2-alternate structure characterized by a split-hemisphere shape (Fig. 3). The cavity of **1b** was determined to have an elliptical form with major and minor axes of 7.46 and 4.77 Å, respectively. The crystal obtained by recrystallization included two acetones and a water molecule with one molecule of **1b**. However, the temperature factors of solvent molecules were remarkably large and there were no significant CH–π or hydrogen bonding interactions between **1b** and the solvent molecules. This suggests that **1b** may not show the same remarkable molecular recognition properties as **1a**.

2.3. Reaction mechanism for the synthesis of 1a and 1b

Although the details of the reaction mechanism to prepare **1a** and **1b** have been under investigation, a type of pinacol rearrangement and an intramolecular acetalization are expected to

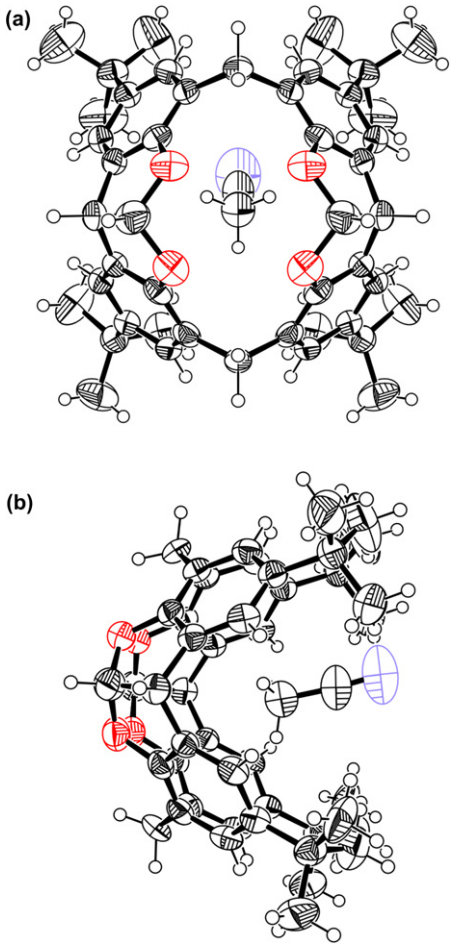


Fig. 2. Crystal structure of **1a** viewed from below (a) and from the side (b).

proceed toward 1,2-dihydroxyl diphenol ethane moieties in **3** (Scheme 3). The pinacol rearrangement of **3** is suggested to give a formyl calixarene **6** as an unstable intermediate, after which the formyl group at the methylene bridge reacts with two hydroxyl groups at the phenol moieties by intramolecular acetalization. These processes were verified when the rearrangement reaction of 1,2-dihydro-1,2-bis(2-phenoyl)ethane was reported to produce benzofura[2,3-*b*]- and [3,2-*b*]benzofuran.[11]

These reactions were examined at various temperatures to investigate the influence on the isomer fractions of **1a** and **1b** (Table 1).

The results indicated that as the temperature increased, the fractions of **1a** increased, whereas that of **1b** decreased. The temperature-dependence of the isomer ratio is likely to rely on intramolecular acetalization—a reversible reaction which provides **1a** or **1b**—but not on pinacol rearrangement—an irreversible reaction which provides an unstable intermediate **6**. The van't Hoff plot of the temperature-dependence of isomer fractions of **1a** to **1b** was examined (Fig. 4).

The thermodynamic parameters were determined as $\Delta H^{\circ}=-18.3\pm0.37$ kJ mol^{-1}, and $\Delta S^{\circ}=-59.1\pm1.12$ kJ mol^{-1} K^{-1}. These results suggest that while **1a** is preferred by the entropy factor, the enthalpy factor is partial to **1b**.

2.4. *ipso*-nitration of 1a and the structure of their nitro derivatives

On the basis of their rigid structures, we attempted to functionalize **1a** for molecular recognition. Previously, we reported the selective *ipso*-nitration of *tert*-butyl[2.2.2]MCP by using fuming

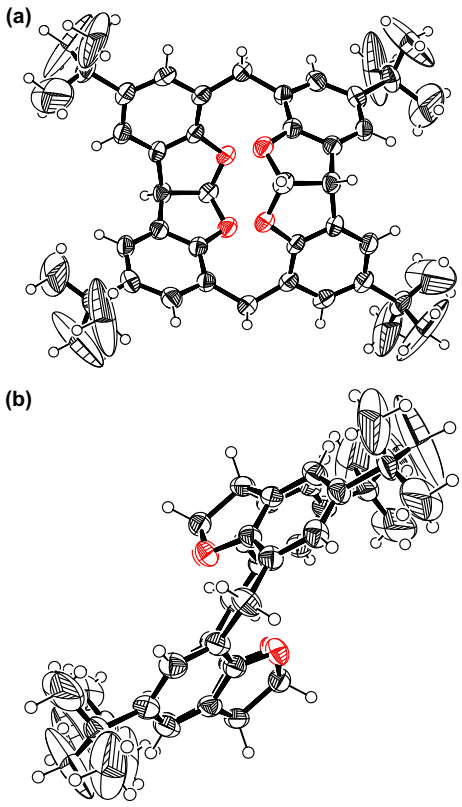
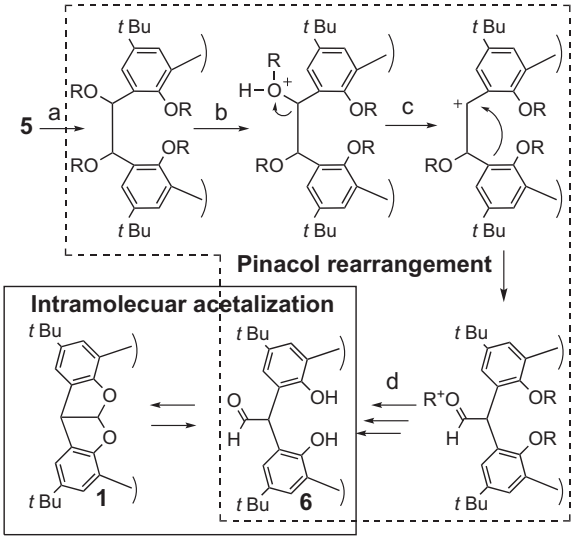


Fig. 3. Crystal structure of **1b** viewed from above (a) and from the side (b).

nitric acid or copper nitrate.[12] Scheme 4 shows the nitration of the upper rims in **1a** using fuming nitric acid or copper nitrate. In the case of **1a**, treatment with fuming nitric acids selectively provided the dinitro derivative **7**, and that with copper nitrate gave the tetranitro derivative **8**.

The chemical structures of **7** and **8** were determined by IR and ^{1}H NMR spectroscopy. NO_2 symmetrical- and antisymmetrical stretching vibrations were observed at 1339 and 1523 cm^{-1} in both IR spectra. In the case of **7**, a signal for *tert*-butyl protons was observed at 1.26 ppm with an intensity ratio of 18 protons. This in-



Scheme 3.

Table 1
Temperature-dependence of the isomer fractions of **1a** and **1b** in intramolecular acetalization

Temperature (°C)	Isomer fraction (%)	
	1a	**1b**
40	42.5	57.5
50	49.0	51.0
60	53.5	46.4
70	57.0	43.0
80	63.1	36.9

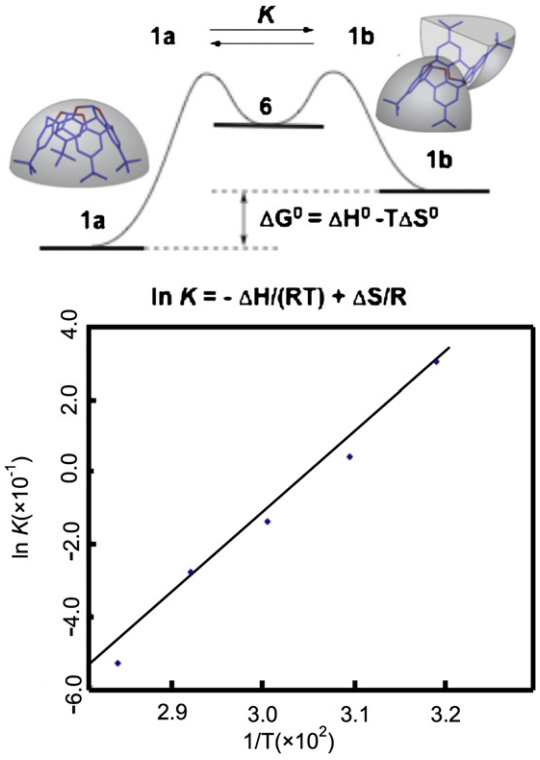
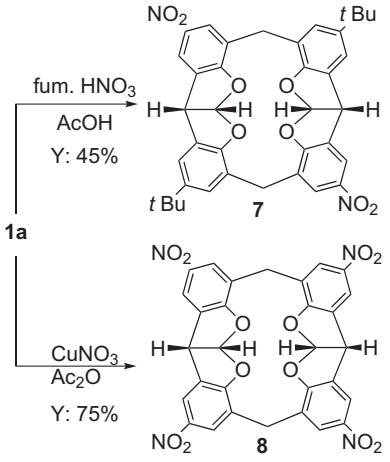


Fig. 4. van't Hoff plot of intramolecular acetalization.

dicates that two *tert*-butyl groups are substituted with two nitro groups. Although there were three possible orientations of the two nitro groups, the C_2-symmetric dinitro derivative, as shown in Scheme 4, was suggested by the pattern of the bridge and acetal peaks (which was not significantly different from that of the parent compound **1a**). This suggests that **7** possesses a C_2-symmetric structure similar to that of chiral binaphthyls.[13] Although the tetranitro derivative **8** showed no *tert*-butyl peak, its ^{1}H NMR spectrum exhibited nearly the same pattern of bridge and acetal peaks as that of **1a**. This suggests that **8** keeps a hemisphere-shaped structure and that all of the *tert*-butyl groups were substituted with nitro groups.



Scheme 4.

2.5. Optical resolution of 7 and its chiral recognition ability

There are many reports of chiral recognition using calixarenes[3a,13] that have chiral functional groups. On the other hand, reports of using calixarenes possessing a C_2-symmetric structure for chiral recognition are limited,[14] although some C_2-symmetric molecules were used as enantioselective tools like binaphthyls.[15] The optical resolution of the racemic mixture **7** and its potential for chiral recognition were examined using HPLC systems.

Fig. 5 shows that the racemic mixture **7** was separated by HPLC on the chiral packed column (CHIRALPAC IA) into two species whose retention times were 10.8 and 8.98 min. Their peak intensities were almost the same, and the CD spectra were opposite in sign. This suggests that the enantiomers of **7** were separated by the chiral HPLC system.

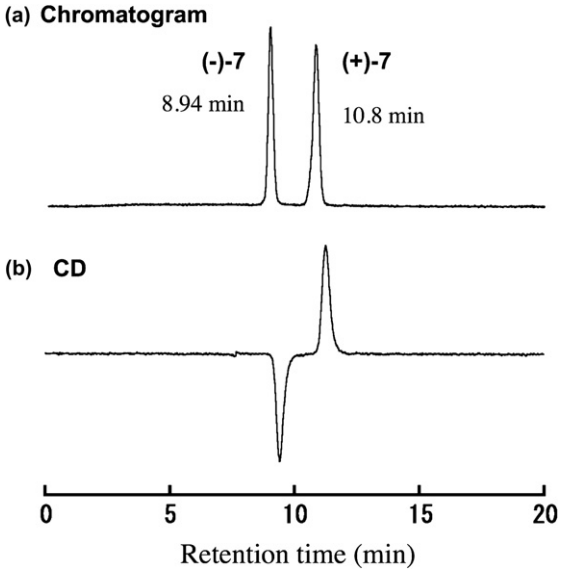


Fig. 5. Chromatogram (a) and CD spectra (b) for dinitro derivative **7** using a chiral packed column (CHIRALPAK IA, Daicel chemical industry). Mobile phase: hexane/chloroform=1/1, column temperature: 25 °C, flow rate: 0.5 mL min^{-1}, Detector: 315 nm.

To determine the chiral recognition ability of the C_2-symmetric molecule **7**, we investigated the interaction between chiral molecules and **7** by using non-chiral HPLC systems.

Several types of chiral molecules, such as *S*-mandelic acid, (−)-menthol, (*S*)-(−)-2-methyl-1-butanol, L-methyl lactate, and (−)-α-pinene (Fig. 6) were dissolved in a mobile phase (methanol/H_2O v/v: 85/15); these mobile phases were then used for HPLC analyses of (+)-**7** and (−)-**7** by using ODS as the stationary phase. If the retention times of **7** are decreased in the presence of a chiral molecule, it suggests that there are some intramolecular interactions between **7** and that molecule. If the retention time of enantioisomer (+)-**7** or (−)-**7** is different from the other, this would indicate the chiral recognition abilities of **7**.

For most of the chiral molecules in Fig. 6, there was neither a decrease nor a difference in the retention times of (+)-**7** and (−)-**7**

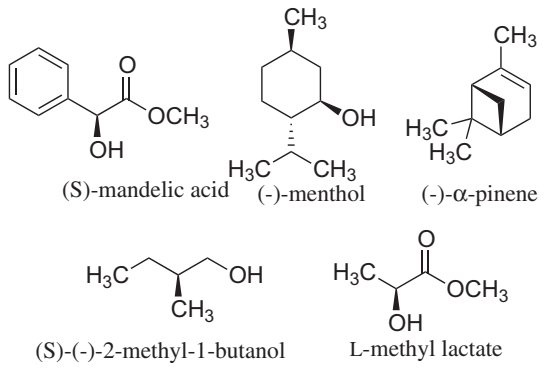


Fig. 6. Chiral molecules in mobile phase (0.1 M in methanol/H_2O 85/15 v/v).

in the chromatograms (about 36 min). However, some decrease and a difference in the retention times were observed in the presence of (−)-α-pinene. In the case of 0.1 M (−)-α-pinene in the mobile phase, the peaks of (+)-**7** and (−)-**7** were resolved at 29.06 min and 28.56 min of retention times, respectively (Fig. 7). Although the difference in the retention times between (+)-**7** and (−)-**7** are unremarkable, it supports the notion that (+)-**7** and (−)-**7** interacted with (−)-α-pinene with different strengths. The mechanism of intermolecular interaction between **7** and α-pinene is currently under investigation; it is expected that since (−)-α-pinene does not have a hydroxyl group, its hydrophobic interaction toward **7** would be improved more than for other molecules. Along its side, the hemisphere-shaped structure of **7** would be rigid and there would be no wobbling motion in ring structure. The rigid structure of **7** may be an important factor for chiral recognition ability. Incidentally, this result is evidence of the enantiospecific interaction of the C_2-symmetrical dinitro hemisphere **7** with (−)-α-pinene, and to our knowledge is the first example of chiral recognition ability in a C_2-symmetric calixarene analog.

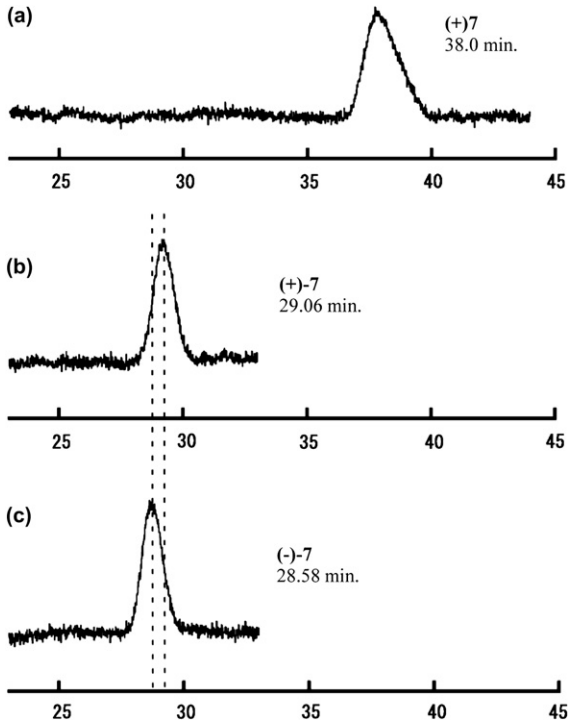


Fig. 7. Chromatograms of (+)**7** without any chiral molecules (a), (+)-**7** with (−)-a-pinene (0.1 M) (b) and (−)-7 with (−)-a-pinene (0.1 M) (c) using Inertsil ODS-3, Mobile phase: methanol/H_2O=85/15 v/v, Column temperature: 30 °C, Flow rate: 1.0 mL/min, Detector UV: 288 nm, Internal reference: naphthalene.

3. Conclusion

In conclusion, we have developed a novel hemisphere-shaped calixarene analog **1a** and its split-hemisphere isomer **1b** by a single-step reaction of pinacol rearrangement followed by intramolecular acetalization from tetrahydroxy-tetramethoxy[2.1.2.1] MCP **3**. Although these new macrocyclic architectures were synthesized at the same time, selective preparation of **1a** or **1b** was also possible by controlling the reaction temperature: **1a** was predominantly obtained over 50 °C, but **1b** was obtained as the major product under 50 °C. The X-ray crystallography data of **1a** indicated that it could form a CH−π complex with non-polarized molecules, such as acetonitrile.

The *ipso*-nitration of **1a** is a convenient procedure to introduce nitro groups at the upper rims, which in turn can be converted to other functional groups, such as amino, peptide, or azo groups. The C_2-symmetric dinitro derivative **7** was produced as the dominant product from **1a** using fuming acid. The optical resolution of **7** and its application to chiral recognition were examined by HPLC. As a result, **7** demonstrated a chiral recognition ability with (−)-α-pinene, which was the only molecule among the many chiral molecules tested without any hydrophilic groups (e.g., hydroxyl and/or carboxylic groups). This suggests that the interaction of **7** with (−)-α-pinene is mainly due to hydrophobic interactions, upon which the C_2-symmetrical structure at the upper rims recognizes the chirality of (−)-α-pinene. If the affinity for chiral molecules of the dinitro derivative **7** is greater than its hydrophobic effect, **7** could show more pronounced chiral recognition abilities with other chiral molecules. These results suggest that the rigid hemisphere-shaped calixarene analog **1a** has great potential as a new macrocyclic molecular architecture for chiral recognition.

4. Experimental

4.1. Preparation of 1,2,16,17-tetrahydroxy-5,12,20,27-tetra-*tert*-butyl-8,15,23,30-tetramethoxy [2.1.2.1]metacyclophane 2 and di-ketal derivative 3 and bis-ketal derivative 4

Aluminum powder (4.13 g, 150 mol, 150 mesh) was added to a solution of dialdehyde **2**[16] (1.0 g, 2.5 mmol) in 330 mL of methanol. The mixture was subjected to mechanical stirring, and then, 20% aqueous sodium hydroxide solution was added dropwise for a period of 2 h. After stirring for 1.5 h, the mixture was filtered, and the filtrate was extracted with ethyl acetate. The extract was washed with water, dried with magnesium sulfate, and evaporated to yield the crude product that was column chromatographed and recrystallized from hexane/chloroform, to yield [2.1.2.1]MCP **3** (584 mg, yield, 29%) as a mixture of isomers. To [2.1.2.1]MCP **3** (80 mg, 0.10 mmol) and dimethoxypropane (30 mL), *p*-toluenesulfonic acid (10 mg, 0.05 mmol) was added. After the mixture was stirred at rt for 10 h, it was quenched by adding triethylamine (1 mL), and then evaporated in vacuo. After toluene (17 mL) was added to the residue and evaporated in vacuo, it was chromatographed with chloroform and recrystallized from hexane/chloroform to yield bis-ketal derivative **4** (48 mg, 55%) as a colorless prism.

Compound **3**: mp 264–271 °C; FABMS: *m*/*z* 796 (M^+) for $C_{50}H_{68}O_8$. Anal. Calcd for $C_{50}H_{68}O_8$: C, 75.34; H, 8.60. Found: C, 75.53; H, 8.47%; IR (KBr): 3452, 2961, 1481, 1211, 1013 cm^{-1}.

Compound **4**: mp 299–302 °C; ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ=1.32 (s, 36H; ^{t}BuH), 1.68 (s, 12H, CH_3), 2.87 (s, 12H, CH_3O), 3.15 (d, ^2J(H,H)=14 Hz, 2H, CH_2), 4.22 (d, ^2J(H,H)=14 Hz, 2H, CH_2), 5.10 (s, 4H, CH), 7.33 (d, ^4J(H,H)=2 Hz, 4H, ArH), 7.52 (d, ^4J(H,H)= 2 Hz, 4H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ=8.7, 27.3,

31.5, 34.5, 45.8, 61.2, 79.4, 108.8, 122.5, 127.8, 129.6, 132.7, 146.4, 153.8; FABMS: m/z 876 (M^+) for $C_{56}H_{76}O_8$. Anal. Calcd for $C_{56}H_{76}O_8$: C, 76.68; H, 8.73. Found: C, 76.93; H, 8.69%; IR (KBr): 2923, 1401, 1361, 1255, 1200, 920 cm^{-1}.

4.2. X-ray crystallographics of 4

Crystallographic data: $C_{56}H_{76}O_8$, triclinic, space group $P-1$, a=10.585(4) Å, b=12.668(4) Å, c=9.841(4) Å, α=97.61(3), β=99.46(3), δ=92.88(3), U=1286.7(8) $Å^3$, D_c=1.132 Mg m^{-3}, Z=1, T=298.1 K, colorless rod, 0.30, 0.30, 0.10 mm^3. Data collection was carried out using a Rigaku AFC7R diffractometer, and the SIR92 and SHELXL97 programs were used for the structure solution and refinement. The number of reflections collected was 7146 of which 5902 independent [R(int=0.049)], giving $R1$=0.0710 and $wR2$=0.2260 for the observed unique reflections [$F^2>2\sigma(F^2)$]. The maximum and minimum residual electron densities on the final difference Fourier map were 0.28 and −0.25 e $Å^{-3}$, respectively. Supplementary data have been deposited with the CCDC in the CIF format with the deposition number CCDC 277666.

4.3. Preparation of 9,9′,2,2′-tetra-*tert*-butyl-[1,1](4,7)[5a,10b]-dihydrobenzofuro[2,3-*b*]-benzofuranophane 1a and 1b

After stirring a mixture of [2.1.2.1]MCP **3** (100 mg, 0.13 mmol) and sodium iodide (194 mg, 1.3 mmol) in 25 mL of dry acetonitrile solution for 1 h, the solution of trimethylsilyl chloride (0.17 mL, 1.3 mmol) in dry acetonitrile was added dropwise to the mixture and stirred for 48 h at reflux condition. The reaction mixture was poured into water and extracted with chloroform. The extract was washed with 200 mL of 5% aqueous sodium sulfite solution and water and then dried with magnesium sulfate anhydride. After the mixture was evaporated in vacuo, the residue was chromatographed to yield the two isomers of 9,9′,2,2′-tetra-*tert*-butyl-[1,1](4,7)[5a,10b]dihydrobenzofuro[2,3-*b*]benzofuranophane **1a** (60 mg, 71%) and **1b** (11 mg, 13%).

Compound **1a**: colorless prism (acetonitrile), mp 368.0–369.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ=1.23 (s, 36H, ^{t}BuH), 1.90 (s, 3H, acetonitrile), 3.40 (d, ^2J(H,H)=13 Hz, 2H, CH_2), 4.44 (d, ^2J(H,H)=13 Hz, 2H, CH_2), 4.95 (d, ^3J(H,H)=6 Hz, 2H, CH), 7.01 (d, ^3J(H,H)=6 Hz, 2H, CH), 7.07 (d, ^4J(H,H)=2 Hz, 4H, ArH), 7.08 (d, ^4J(H,H)=2 Hz, 4H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ=30.7, 31.6, 34.3, 51.3, 112.0, 118.5, 122.8, 127.7, 144.0, 153.7; FABMS: m/z 668 (M^+) for $C_{46}H_{52}O_4$. Anal. Calcd for $C_{46}H_{52}O_4$, CH_3CN, $1/2H_2O$: C, 80.19; H, 7.85; N, 1.95. Found: C, 80.18; H, 7.87; N, 2.13%; IR (KBr): 2956, 1488, 1184, 971 cm^{-1}.

Compound **1b**: colorless rod (acetone), mp 368.8–369.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): d=1.31 (s, 36H, ^{t}BuH), 4.04 (s, 4H, CH_2), 4.76 (d, ^3J(H,H)=7 Hz, 2H, CH), 6.37 (d, ^3J(H,H)=8 Hz, 2H, CH), 7.02 (d, ^4J(H,H)=2 Hz, 4H, ArH), 7.25 (d, ^4J(H,H)=2 Hz, 4H, ArH); ^{13}C NMR (100 MHz, CDCl3, 25 °C, TMS) δ=29.7, 31.5, 35.0, 49.9, 116.3, 118.7, 120.0, 126.2, 127.5, 144.5, 154.7; FABMS: m/z 668 (M^+) for $C_{46}H_{52}O_4$. Anal. Calcd for $C_{46}H_{52}O_4$: C, 82.60; H, 7.84. Found: C, 82.35; H, 7.76%; IR (KBr): 2958, 1488, 1187, 967 cm^{-1}.

4.4. X-ray crystallographics of 1a

Crystallographic data: $C_{48}H_{55}NO_4$, orthorhombic, space group $Pnma$, a=11.365(5) Å, b=21.338(6) Å, c=16.49(2) Å, β=115.693(10)°, U=3999(5) $Å^3$, D_c=1.179 Mg m^{-3}, Z=4, T=298.1 K, colorless rod, 0.50, 0.30, 0.10 mm^3. Data collection was carried out using the Rigaku AFC7R diffractometer, and the SIR92 and SHELXL97 programs were used for the structure solution and refinement. The reflections collected were 4708 of which 2934 independent [R(int=0.049)], giving $R1$=0.0770 and $wR2$=0.2440 for observed unique reflections [$F^2>2\sigma(F^2)$]. The maximum and minimum residual electron densities on the final difference Fourier map were 0.41 and −0.22 e $Å^{-3}$, respectively. Supplementary data have been deposited with the CCDC in the CIF format with the deposition number CCDC 277667.

4.5. X-ray crystallographics of 1b

Crystallographic data: $C_{46}H_{52}O_4$, $+2C_3H_6O_1$, $2O_2$, monoclinic, space group C_2/c, a=17.560(3) Å, b=18.965(4) Å, c=15.7349(19) Å, U=4722.0(15) $Å^3$, D_c=1.149 Mg m^{-3}, Z=2, T=298.1 K, colorless rod, 0.50, 0.30, 0.30 mm^3. Data collection was carried out using the Rigaku AFC7R diffractometer, and the SIR92 and SHELXL97 programs were used for the structure solution and refinement. The reflections collected were 5438 of which 2130 independent [R(int=0.0279)], giving $R1$=0.1099 and $wR2$=0.3020 for observed unique reflections [$F^2>2s(F^2)$]. The maximum and minimum residual electron densities on the final difference Fourier map were 0.384 and −0.717 e $Å^{-3}$, respectively. Supplementary data have been deposited with the CCDC in the CIF format with the deposition number CCDC 778463.

4.6. Preparation of 9,2,-di-*tert*-butyl-9′,2′-dinitro-[1,1](4,7)[5a,10b]dihydrobenzofuro[2,3-*b*]benzofuranophane 7 by using fuming nitric acid

After dissolving **1a** (20 mg, 2.7×10^{-2} mmol) in 4 mL of a mixture of acetic acid and dichloromethane (v/v=1/1), the fuming nitric acid (0.5 g, 8 mmol) was added dropwise to the solution under cooling by ice water and then stirred for 7 h at 0 °C. The reaction mixture was poured into water and extracted with 100 mL of dichloromethane. The extract was washed with 200 mL of 10% aqueous sodium hydrogen carbonate solution and water and then dried with magnesium sulfate anhydride. After the mixture was evaporated in vacuo, the residue was recrystallized from acetonitrile to yield 9,2,-di-*tert*-butyl-9′,2′-dinitro-[1,1](4,7)[5a,10b]dihydrobenzofuro[2,3-*b*]benzofuranophane **7** (8.1 mg, 46%): yellow powder (acetonitrile), mp 400 °C decomp.; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ=1.26 (s, 18H, ^{t}BuH), 3.53 (d, ^2J(H,H)=13 Hz, 2H, CH_2), 4.47 (d, ^2J(H,H)=18 Hz, 2H, CH_2), 5.09 (d, ^3J(H,H)=6 Hz, 2H, CH), 7.15 (d, ^3J(H,H)=6 Hz, 2H, CH), 7.19 (d, ^4J(H,H)=2 Hz, 2H, ArH), 7.11 (d, ^4J(H,H)=2 Hz, 2H, ArH), 7.96 (d, ^4J(H,H)=2 Hz, 2H, ArH), 8.05 (d, ^4J(H,H)=2 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS) δ=29.8, 31.6, 34.6, 50.4, 113.1, 118.4, 119.4, 121.7, 124.0, 126.1, 126.2, 126.7, 129.2, 142.9, 146.5, 153.2, 161.0; FABMS: m/z 647 (M^++1) for $C_{38}H_{34}N_2O_8$. Anal. Calcd for $C_{38}H_{34}N_2O_8$, H_2O: C, 68.66; H, 5.46; N, 4.21. Found: C, 68.82; H, 5.22; N, 4.46%; IR (KBr): 2962, 1597, 1523, 1484, 1460, 1338, 1264, 985 cm^{-1}. The enantiomers (+)-**7** and (−)-**7** were isolated by HPLC method using CHIRALPAC IA (DAICEL chemical industry, 4.6 id×250 mm). The specific rotation of (+)-**7** and (−)-**7** was determined as +66.2 (c 0.460, chloroform) and $[\alpha]_{D^{20}}$ −66.4 (c 0.514, chloroform), respectively.

4.7. Preparation of 9,9′2,2′-tetranitro-[1,1](4,7)[5a,10b]dihydrobenzofuro[2,3-*b*]benzofuranophane 8 by using copper(II) nitrate

After dissolving **1a** (60 mg, 9.0×10^{-2} mmol) in 5 mL of acetic anhydride, the copper (II) nitrate trihydrate (1.6 g, 0.9 mmol) was added to the solution under nitrogen atmosphere and then stirred for 24 h at rt. The reaction mixture was poured into water and 100 mL of dichloromethane was added to the reaction mixture. The white powder was precipitated at an interface between water and dichloromethane and the precipitate was separated through decantation. After the precipitate was washed with methanol and water and dried in vacuo, the residue was recrystallized from DMSO to yield 9,9′2,2′-tetranitro-[1,1](4,7)[5a,10b]dihydrobenzofuro[2,3-*b*]

benzofuranophane **8** (42 mg, 75%): colorless needle (DMSO), mp 400 °C decomp.; ^{1}H NMR (400 MHz, DMSO, 25 °C, TMS): δ=3.96 (d, ^2J(H,H)=18 Hz, 2H, CH_2), 4.18 (d, ^2J(H,H)=18 Hz, 2H, CH_2), 5.43 (d, ^3J(H,H)=6.5 Hz, 2H, CH), 7.34 (d, ^3J(H,H)=6.5 Hz, 2H, CH), 8.48 (s, 8H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$, 50 °C, TMS) δ=27.4, 48.9, 114.4, 119.7, 122.8, 126.4, 128.9, 142.8, 160.0; FABMS: *m*/*z* 625 (M^++1) for $C_{30}H_{16}N_4O_{12}$. Anal. Calcd for $C_{30}H_{16}N_4O_{12}$, 8/5H_2O: C, 55.15; H, 2.96; N, 8.58. Found: C, 55.52; H, 3.21; N, 8.09%; IR (KBr): 1523, 1338, 1268, 1206, 1089, 1049, 964 cm^{-1}.

4.8. Chromatography

The chromatograph included a JASCO 1580 pump, a JASCO MD-1510 UV/vis photodiode array detector, and a JASCO CD-1595 circular dichroism detector. Given the high sensitivity of the UV detector, a 5 μl sample was injected through a Reodyne Model 7125 injector. The column temperature was maintained using a column jacket with a circulator having a heating and cooling system. A personal computer with JASCO-Borwin (Ver 1.5) software, which was connected to the detector, was used for system control and data analysis. Chromatographic grade solvent was used to prepare mobile phase solutions. In examining the optical resolution of **7**, CHIRALPAC IA (DAICEL chemical industry, 4.6 id×250 mm) was used as the packed column and hexane/chloroform mixture (1/1) was used as the mobile phase at a flow rate of 0.5 mL min^{-1}. In studying chiral recognition properties, Intersil ODS-3 (GL Science, 4.6 id×250 mm) was used as the packed column and a methanol/water mixture (9/1) was used as the mobile phase at a flow rate of 0.5 mL min^{-1}.

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Supplementary data

Syntheses of **1a**, **1b**, **3**, **4**, **7**, **8**, Chromatography, Experiments for temperature-dependence of isomer fraction of **1a** and **1b**. ^{1}H NMR spectra of **1a**, **1b**, **4**, **7**, **8**, ^{13}C NMR spectra of **1a**, **1b**, **4**, **7**, IR spectra of **7**, **8**, and X-ray crystallographic structure of **1a**, **1b**, **4**. Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2011.04.025.

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