ACS OMEGA

http://pubs.acs.org/journal/acsodf

Article

Endo-Functionalized Cyclic Oligophenylenes: Synthesis and Complexation with a Chiral Phosphoric Acid

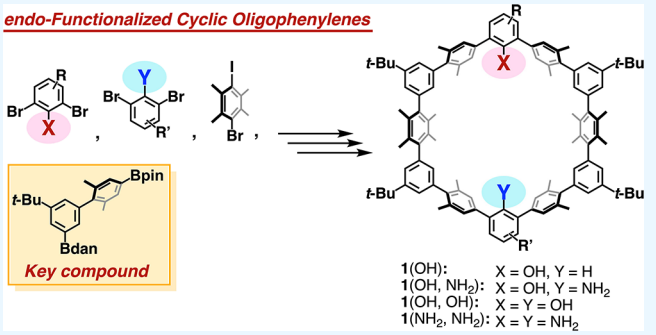
Kosuke Ono,* Yusei Tanaka, Kana Sugimoto, Shigemi Kinubari, and Hidetoshi Kawai

Cite This: *ACS Omega* 2022, 7, 45347−45352

Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: The synthesis of *endo*-functionalized cyclic oligophenylenes in which adjacent benzene rings are perpendicular to one another is described. Annulation precursors, OH- or NH_2-functionalized quinquephenyl diboronic acids, and septiphenyl dibromo compounds were systematically prepared by using a diprotected biphenyl-3,4′-diyl diboronic acid as a key compound. Four *endo*-functionalized cyclic oligophenylenes were synthesized by annulation of the precursors in dilute conditions through Suzuki−Miyaura cross-coupling. X-ray analysis of the macrocycle revealed the unique 1D channel packing structure formed by connecting the nanometer-sized cavity of the macrocycle. Furthermore, NH_2-functionalized macrocycles could bind a chiral phosphoric acid in the cavity in $CDCl_3$ solution.



INTRODUCTION

Functional groups in an enzyme binding pocket play a fundamental role in the selective recognition of substrates and catalytic transformation.[1] To mimic the active sites of enzymes, *endo*-functionalization of synthetic host molecules is one of the important topics in host−guest chemistry.[2]

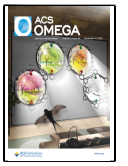
Cyclic oligophenylenes are one of the well-studied shape-persistent macrocycles, and functionalization of the macrocycles was also examined. For example, Cram's famous spherand where the inner space of the cyclic hexaphenylene framework was functionalized by six OMe groups showed the strong and selective binding of metal cations such as Li^+ and Na^+.[3] Schlüter et al. reported nanometer-sized hexagonal-shaped cyclic oligophenylenes containing 12 or 24 benzene rings whose alkyl chains were introduced to the frameworks for the solubility and exohedral functionalization of the macrocycle with chloro groups for potential use as anchor groups.[4] Cyclic oligophenylenes in which some benzene rings were replaced by heteroarenes such as pyridine or thiophene were also reported.[5] Since the advent of [*n*]cycloparaphenylenes (CPPs), various size CPPs were synthesized.[6] [10]CPP is known to include C_{60} and the related compounds, and [*n* +5]CPP can include smaller [*n*]CPP (*n* = 5, 6, 7, 8, 10) by $\pi-\pi$ interactions within the unique hoop structure.[6] Peripherally OMe-substituted CPPs associate weakly with electron-deficient guest molecules by electrostatic interactions.[7] Thus, the functionalization changes the electronic property of CPPs and expands the variety of guest molecules. However, compared to the exohedral or peripheral functionalization, endohedral functionalization of cyclic oligophenylenes, especially with different functional groups, has rarely been examined. *Endo*-functionalized cyclic oligophenylene with a well-defined cavity surrounded by aromatic rings is expected to exhibit characteristic molecular recognition through direct interactions between the introduced functional groups and the guest molecule. Furthermore, endohedral functionalization with different functional groups is interesting for potential applications for cooperative guest complexation, frustrated pairs, or *trans*-spanning ligands for transition metals, as reported in several phenylene-ethynylene macrocycles.[8]

Herein, we report the synthesis of four *endo*-functionalized cyclic oligophenylenes **1**(OH), **1**(OH, OH), **1**(NH_2, NH_2), and heterofunctionalized **1**(OH, NH_2) (Figure 1). Host−guest complexations of NH_2-functionalized macrocycles **1** with a chiral phosphoric acid via interactions between polar functional groups were also demonstrated.

RESULTS AND DISCUSSION

We designed hexagonal-shaped cyclic oligophenylenes **1** in which adjacent benzene rings are perpendicular to one another by using *o*-methylated *p*-phenylene units (Figure 1).[9] The macrocycle **1** has a well-defined nanometer-sized cavity surrounded by six *p*-phenylene rings. This nonplanar arrangement of the phenylene units and multiply introduced *tert*-butyl

Received: September 13, 2022
Accepted: November 7, 2022
Published: November 28, 2022



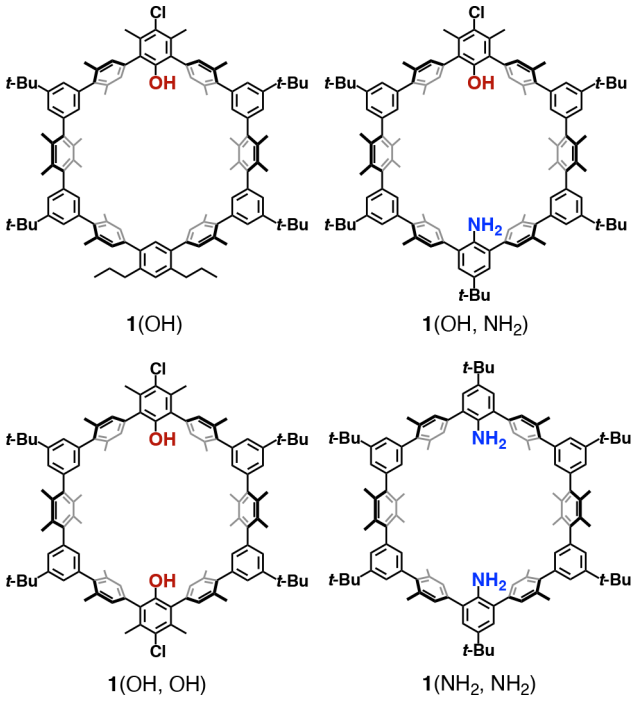


Figure 1. Chemical structures of *endo*-functionalized cyclic oligophenylenes **1**.

groups at the peripheral positions are expected to increase the solubility due to the inhibition of the π-stacking of macrocycles. This molecular design allows *endo*-functionalization of the macrocycle **1** by using appropriate *m*-phenylene units with the desired functional groups (Figure 1). We expected that introduced different functional groups such as OH and NH_2 in the macrocycle **1** could work independently toward guest molecules because these functional groups at the distal positions could not show intramolecular interactions, although phenol and aniline are known to interact each other in both solution and the solid state.[10]

Our synthetic strategy of cyclic oligophenylene **1** stems from an efficient preparation of annulation precursors, quinquephenyl diboronic acids **2**, and septiphenyl dibromo compounds **3** (Scheme 1, see also the Supporting Information (SI), Scheme S1). Diprotected biphenyl diboronic acid derivative **4** was designed as a key compound to provide facile access to these precursors and prepared by five steps in 76% yield starting from 3,5-dibromo-1-*tert*-butylbenzene (Scheme 1a). Borylation of one of two Br groups of 3,5-dibromo-1-*tert*-butylbenzene by using *n*-butyllithium (1 equiv) and triisopropyl borate followed by the protection of the resulting boronic acid by 1,8-diaminonaphthalene (= dan) gave compound **5** (98%). The other Br group was converted to the B(pin) group by using Pd catalyst (95%). Subsequently, Suzuki−Miyaura coupling of **6** with 2-bromo-5-chloro-1,3-dimethylbenzene gave compound **7** with a biphenyl framework (88%). Borylation of the Cl group using a Pd catalyst afforded the key compound **4** in 93%. It is noted that purification of the compounds **5**−**7** is only a MeOH washing, and a gram-scale synthesis of **4** is possible. Compound **4** has two boronic acid units, one of which is protected by dan group. The dan-protected boronic acids developed by Suginome is inactive in the general coupling conditions, and it can be deprotected easily by an acid treatment to activate.[11] Therefore, annulation precursors **2** and **3** can be efficiently prepared from the compound **4** by sequential Suzuki−Miyaura coupling reactions.

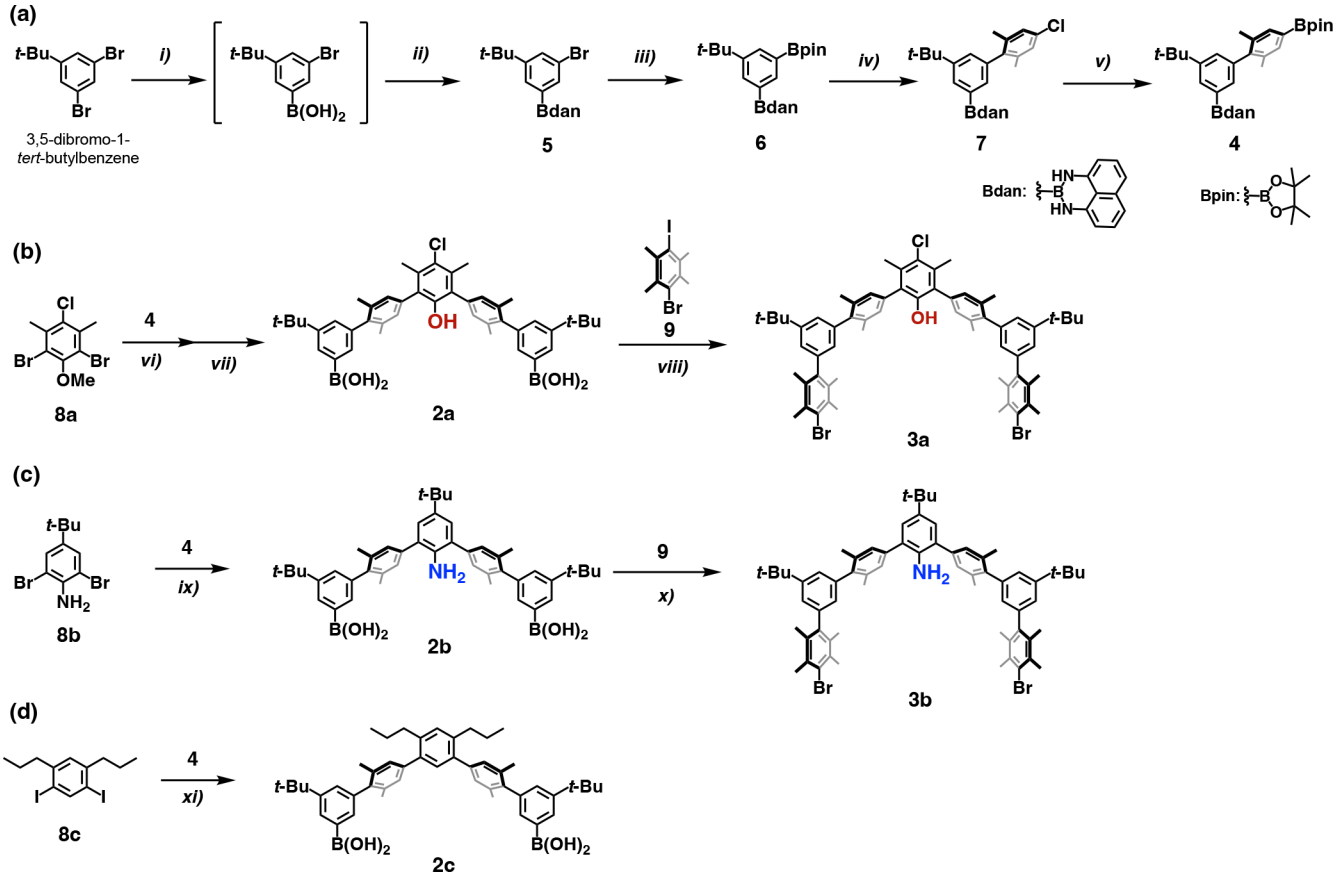
The synthesis of OH-functionalized precursor **3a** using the key compound **4** was as follows (Scheme 1b). The first coupling of **8a** with **4** gave quinquephenyl compound in 75% yield. Subsequent demethylation by BBr_3 and deprotection of the dan group by 6 N HCl gave the OH-functionalized quinquephenyl diboronic acid **2a** in 97% yield (two steps). The second coupling of compound **2a** with 4 equiv of 3-bromo-6-iododurene **9** gave the OH-functionalized dibromo septiphenyl compound **3a** in 68% yield. In this reaction, when 10 equiv of 3,6-dibromodurene was used instead of compound **9**, oligomeric compounds in which both sides of Br reacted with compound **2a** were formed as byproducts, and the isolated yield of desired compound **3a** dropped to 37%.[12] In the ^{1}H NMR spectrum of precursor **3a**, three peaks derived from OH were observed at 4.92, 4.98, and 5.04 ppm with an integral ratio of 1:2:1, respectively. This spectrum indicated the presence of three atropisomers in $CDCl_3$ solution (see the SI, Section 4). From the temperature-dependent ^{1}H NMR analysis of the $CDCl_3$ solution, the activation free energy $\Delta G^{\ddagger}$ (25 °C) = 69 kJ/mol of the rotation was estimated. This activation energy indicated that rapid exchange among the three atropisomers would occur under the heated coupling conditions (k = 40.1 s^{-1} at 58 °C in $CDCl_3$), and the presence of atropisomers does not seem to be a problem in the annulation reactions described below. Similarly, NH_2-functionalized quinquephenyl diboronic acid **2b** and septiphenyl dibromo compound **3b** were synthesized from **8b**, **4**, and **9** (Scheme 1c). Dipropyl-substituted precursor **2c** was also synthesized from **8c** and **4** in the same way (Scheme 1d). In the ^{1}H NMR spectrum of the dan-protected **2b**, **2c**, and the precursor **3b** in $CDCl_3$, one set of signals was observed in contrast to the precursor **3a**. Thus, annulation precursors were systematically prepared by using the key compound **4**.

With both precursors **2** and **3** in hand, we examined the cross-coupling annulation conditions to obtain **1**(OH) (Table 1, entries 1−4). Precursors **2c** and **3a** were reacted in a 1:1 ratio under the conditions that employed 10 mol % $Pd(PPh_3)_4$ as a catalyst, 6 equiv of Cs_2CO_3 as a base, and toluene as the reaction solvent.[13] The optimized reaction concentration of the substrates was studied by varying the value from 0.5 to 2.5 mM (Table 1, entry 1−4). The crude products were purified by gel permeation chromatography (GPC), and the isolated yields of the macrocycle **1**(OH) were compared. It was found that macrocycle **1**(OH) was isolated in 33% yield when the reaction was performed at 1.25 mM (Table 1, entry 2). Interestingly, when the same reaction was carried out by using 1,4-dioxane as the reaction solvent instead of toluene, only a trace amount of the product **1**(OH) was obtained and oligomeric byproducts were mainly observed in a GPC trace (Table 1, entry 3). The formation of oligomeric byproducts increased and the yield of **1**(OH) dropped to 24% at a higher concentration (2.5 mM) (Table 1, entry 4). At a lower concentration (0.5 mM), the yield dropped to 16%, even though a longer reaction time of 4 days was applied (Table 1, entry 1).

In the ^{1}H NMR spectrum of **1**(OH), the signal of OH was observed as one sharp signal at 4.82 ppm, which was shifted upfield by 0.1−0.2 ppm compared with that of the precursor **3a**. MALDI-TOF MS analysis showed the molecular ion peak at 1545.9409 ($[M + Na]^+$), and the isotopic patterns were in good agreement with the simulation (Figure S4).

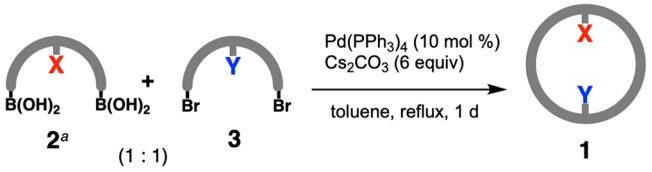
https://doi.org/10.1021/acsomega.2c05926
ACS Omega 2022, 7, 45347−45352

Scheme 1. (a) Preparation of Key Compound 4. (b)−(d) Preparation of Annulation Precursors 2a, 3a, 2b, 3b, and 2c



[I](1) 1 equiv of *n*-BuLi, THF, −78 °C; (2) $B(Oi\text{-}Pr)_3$; (3) 1 N HCl. [ii]1,8-Diaminonaphthalene, toluene, reflux, 98% in 2 steps. [iii]$(Bpin)_2$, $Pd(dppf)Cl_2$·DCM, KOAc, 1,4-dioxane, reflux, 95%. [iv]2-Bromo-5-chloro-1,3-dimethylbenzene, $Pd(PPh_3)_4$, $Ba(OH)_2{\cdot}8H_2O$, 1,4-dioxane, reflux, 88%. [v]$(Bpin)_2$, $Pd(OAc)_2$, SPhos, K_3PO_4, 1,4-dioxane, reflux, 93%. [vi]$Pd_2(dba)_3{\cdot}CHCl_3$, *t*-Bu_3PHBF_4, KOH, THF/H_2O (20:1), rt, 75%. [vii](1) BBr_3, DCM, 0 °C; (2) 6 N HCl, THF, rt, 97% in 2 steps. [viii]$Pd(PPh_3)_4$, Cs_2CO_3, toluene/MeOH (2:1), reflux, 68%. [ix](1) $Pd_2(dba)_3{\cdot}CHCl_3$, *t*-Bu_3PHBF_4, KOH, THF/H_2O (20:1), rt, 90%; (2) 6 N HCl, THF, rt, 96%. [x]$Pd(PPh_3)_4$, Na_2CO_3, DME/H_2O (3:1), reflux, 74%. [xi](1) $Pd(PPh_3)_4$, $Ba(OH)_2{\cdot}8H_2O$, 1,4-dioxane, reflux, 81%; (2) 6 N HCl, THF, rt, 95%.

Table 1. Synthesis of *Endo*-Functionalized Cyclic Oligophenylenes1 from 2 and 3



Entry	Substrates	Product	Concentration of substrates (mM)	Isolated yield of **1** (%)
1[b]	**2c**, **3a**	**1**(OH)	0.5	16
2	**2c**, **3a**	**1**(OH)	1.25	33
3[c]	**2c**, **3a**	**1**(OH)	1.25	trace
4	**2c**, **3a**	**1**(OH)	2.5	24
5[d]	**2b**, **3a**	**1**(OH, NH_2)	1.0	32
6[d]	**2a**, **3a**	**1** (OH, OH)	1.0	35
7[d]	**2b**, **3b**	**1** (NH_2, NH_2)	1.0	44

[a]Boronic acids were protected by pinacol before annulation. [b]Reaction time was 4 days. [c]Reaction solvent was 1,4-dioxane. [d]30 mol % $Pd(PPh_3)_4$ was used.

The structure of the framework of macrocycle **1** was also clarified by X-ray crystallographic analysis of **1**(OMe) (Figure 2; see also the SI, Section 7). As expected, a nanometer-sized inner space (12 Å × 14 Å) surrounded by six *p*-phenylene units was formed (Figure 2a). Interestingly, macrocycles **1** stack in a vertical orientation to lead the columnar structures meshed with adjacent ones tightly to form the nanochannel array (Figure 2b). The inner wall of the resulting nanochannels was decorated by OMe groups of the macrocycles. In the pores, there are highly disordered solvent molecules, and therefore, the macrocycle structure was refined by the Squeeze routine of PLATON to exclude the solvents. It is important to note that the columnar structures formed by meshed stacking of the cyclic oligophenylene framework, not the interaction with the OMe groups. Therefore, *endo*-functionalized macrocycles **1** would make it possible to construct various nanochannel structures modified by functional groups.

As the synthetic route for cyclic oligophenylene **1**(OH) was established, other *endo*-functionalized cyclic oligophenylenes **1**(OH, NH_2), **1**(OH, OH), and **1**(NH_2, NH_2) in which inner spaces are functionalized with two different or same functional groups were then synthesized from the corresponding combination of **2** and **3**. The annulation of the corresponding precursors under the optimized conditions gave the hetero-functionalized cyclic oligophenylene **1**(OH, NH_2) in 32% (Table 1, entry 5) and homodifunctionalized cyclic oligophenylenes **1**(OH, OH) and **1**(NH_2, NH_2) in 35% and 44%

https://doi.org/10.1021/acsomega.2c05926
ACS Omega 2022, 7, 45347−45352

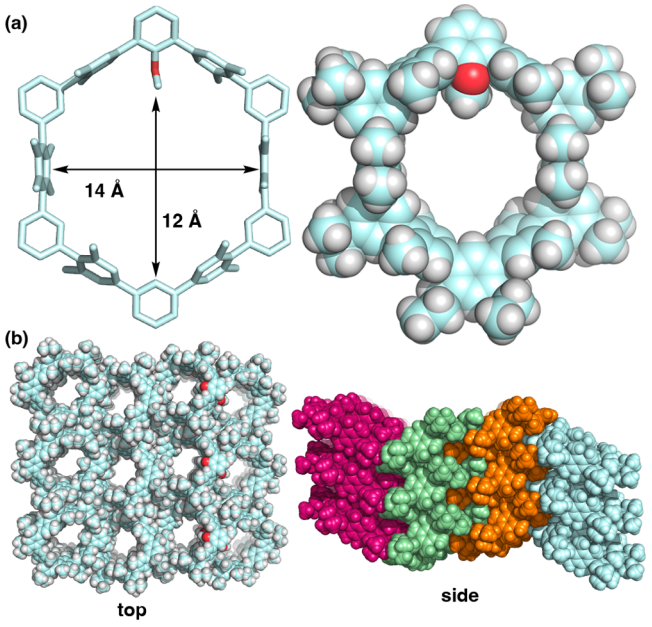


Figure 2. (a) Single-crystal structure of **1**(OMe). Left: stick model (*t*-Bu and *n*-propyl groups were omitted for clarity). Right: space-filling model. (b) Top and side view of packing structure of **1**(OMe).

yields, respectively (Table 1, entries 6 and 7). These macrocycles were characterized by NMR spectroscopy and MS measurements.

In the ^{1}H NMR spectrum in $CDCl_3$ of **1**(OH, NH_2), the signals of OH and NH_2 were observed at 4.87 and 3.59 ppm, respectively (Figure S17). These chemical shifts were almost the same as the 4.82 ppm of the OH signal in **1**(OH, OH) and the 3.65 ppm of the NH_2 signal in **1**(NH_2, NH_2), respectively. The chemical shifts remained unchanged from 0.5 mM to a saturated concentration of about 3.5 mM, independent of concentration. These observations indicate that the OH and NH_2 groups within the well-defined cavity of **1**(OH, NH_2) do not interact with each other either intra- or intermolecularly and prevent self-association in $CDCl_3$.[10] In the IR spectrum of the solid of **1**(OH, NH_2), the peaks corresponding to O−H stretching were observed at 3539 cm^{-1} and the peaks corresponding to N−H stretching was observed at 3473 and 3378 cm^{-1} (Figure S18). These frequencies were almost the same as the 3525 cm^{-1} of O−H stretching in **1**(OH, OH) and 3478 and 3383 cm^{-1} of N−H stretching in **1**(NH_2, NH_2). These results show that OH and NH_2 groups of **1**(OH, NH_2) do not interact each other even in the solid state.[10]

After screening of several polar guest molecules, such as boronic acids, carboxylic acids, phosphoric acids, or sulfonic acids, we examined the inclusion of a large chiral phosphoric acid (+)-**10** which is known as an organocatalyst[14,15] within the *endo*-functionalized cyclic oligophenylene **1**(OH, NH_2), **1**(NH_2, NH_2), or **1**(OH, OH) (Figure 3a). In the ^{1}H NMR spectrum of **1**(NH_2, NH_2) (0.5 mM) with 1.0 equiv of (+)−**10** in $CDCl_3$, all of the signals of (+)−**10** were shifted upfield compared with those of free (+)−**10** (Figure 3d,e). This result suggested that the (+)−**10** had been included within the macrocycle and experienced a shielding effect from the six *p*-phenylene units of **1**(NH_2, NH_2). The only set of signals from the guest molecule (+)−**10** observed in the presence of an excess amount of (+)−**10** indicates a rapid exchange between the free and included (+)−**10** on the NMR time scale. On the

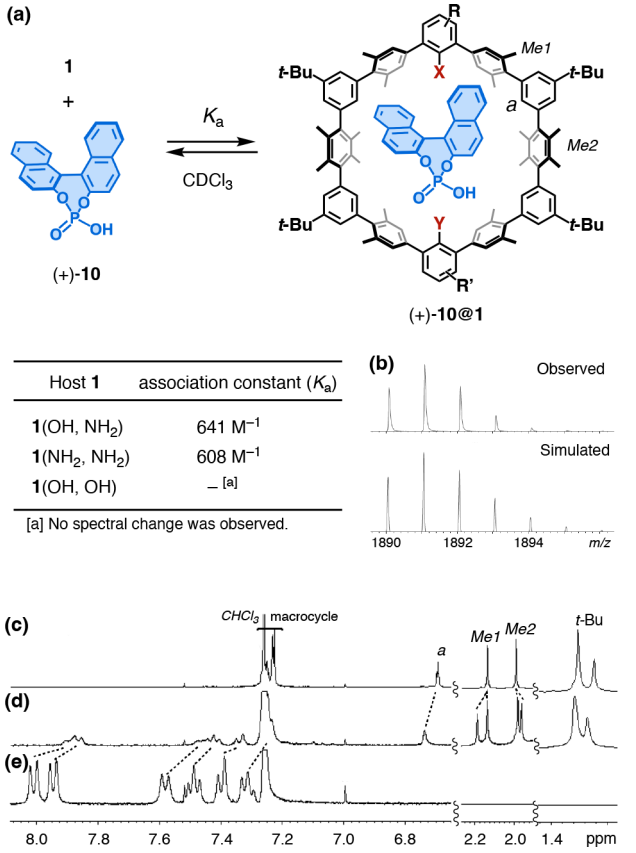


Figure 3. (a) Complexation of **1** with (+)−**10** and association constant with various hosts **1**(OH, NH_2), **1**(NH_2, NH_2), and **1**(OH, OH). (b) Molecular ion peak of [(+)-**10**@**1**(NH_2, NH_2) + K]$^+$ in the MALDI-TOF MS spectrum. Partial ^{1}H NMR spectra (400 MHz, 300 K, $CDCl_3$) of (c) **1**(NH_2, NH_2), (d) a 1:1 mixture of **1**(NH_2, NH_2) (0.5 mM), and (+)−**10**, and (e) (+)−**10**.

other hand, the signal H*a*, which is located inside the macrocycle, was shifted downfield compared with that of the free **1**(NH_2, NH_2), whereas the signals of *tert*-butyl groups outside did not show a significant change (Figure 3c,d). Furthermore, the methyl groups of host molecule *Me1* and *Me2* became diastereotopic and split into two signals upon association with the chiral guest (+)−**10** (Figure 3d). These ^{1}H NMR spectral changes strongly suggest that (+)−**10** was included inside **1**(NH_2, NH_2). Besides, MALDI-TOF MS analysis clearly showed the molecular ion peak at 1890.07 corresponding to [(+)-**10**@**1**(NH_2, NH_2)+K]$^+$ (Figure 3b). The detection of the ion peak of the 1:1 host−guest complex (+)-**10**@**1**(NH_2, NH_2) on the MALDI-TOF MS indicated that the host−guest complex is stable. The association constant was determined to be 608 M^{-1} at 300 K by dilution experiments (see the SI, Section 5 for details).[16] **1**(OH, NH_2) also included (+)-**10** with a similar association constant (K = 641 M^{-1}); on the other hand, the complexation of **1**(OH, OH) with (+)-**10** was not observed at all by ^{1}H NMR analysis. The complexation of **1**(NH_2, NH_2) and 1,1′-binaphtyl was also not observed by ^{1}H NMR analysis. From these observations, this inclusion behavior is thought to mainly derive from the interaction between one NH_2 group of the host and the P(O)OH group of the guest (acid−base pair formation), not from electrostatic interactions between polar functional groups or CH−π interactions between host and guest. This result clearly demonstrated that *endo*-functionalized cyclic oligophenylenes

https://doi.org/10.1021/acsomega.2c05926
ACS Omega 2022, 7, 45347−45352

1 with a well-defined cavity associate with a 1 nm sized guest molecule through direct interaction with the functional group of the guest molecule.

CONCLUSIONS

In summary, we have successfully synthesized the four *endo*-functionalized novel cyclic oligophenylenes **1**(OH), **1**(OH, NH_2), **1**(OH, OH), and **1**(NH_2, NH_2). It is noteworthy that the annulation precursors **2** and **3** were systematically synthesized by using biphenyl derivative **4** in reasonable yields. This **4** enables facile access to the various unexplored *endo*-functionalized cyclic oligophenylenes **1**. The application of other *endo*-functionalized cyclic oligophenylenes **1** to host molecules is now in progress in our group. Construction of nanochannels with a functionalized inner wall by using *endo*-functionalized cyclic oligophenylenes **1** and their application to porous materials are also under investigation.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.2c05926.

Instrumentation details, synthesis details, copies of NMR spectra, X-ray crystallography data, and experimental details of complexation study and temperature dependent NMR study (PDF)

X-ray data for **1**(OMe) (CIF)

AUTHOR INFORMATION

Corresponding Author

Kosuke Ono − *Department of Chemistry, Faculty of Science, Tokyo University of Science, Shinjuku-ku, Tokyo 162-8601, Japan;* Present Address: Department of Chemistry, School of Science, Tokyo Institute of Technology, O-okayama, Meguro-ku, Tokyo 152-8551, Japan; orcid.org/0000-0002-6349-9617; Email: k.ono@chem.titech.ac.jp

Authors

Yusei Tanaka − *Department of Chemistry, Faculty of Science, Tokyo University of Science, Shinjuku-ku, Tokyo 162-8601, Japan*

Kana Sugimoto − *Department of Chemistry, Faculty of Science, Tokyo University of Science, Shinjuku-ku, Tokyo 162-8601, Japan*

Shigemi Kinubari − *Department of Chemistry, Faculty of Science, Tokyo University of Science, Shinjuku-ku, Tokyo 162-8601, Japan*

Hidetoshi Kawai − *Department of Chemistry, Faculty of Science, Tokyo University of Science, Shinjuku-ku, Tokyo 162-8601, Japan;* orcid.org/0000-0002-3367-0153

Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.2c05926

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by JSPS KAKENHI Grant Number 18K05093 (K.O.), and Kondokinen-zaidan Grant Number 2018-2 (K.O.). The authors thank Prof. K. Goto for constructive discussion and Mr. H. Baba, Mr. T. Ishikawa, Mr. T. Kawamura, and Mr. F. Sasamori for optimization of the synthetic procedures.

REFERENCES

(1) (a) Kirby, A. J. Enzyme Mechanisms, Models, and Mimics. *Angew. Chem., Int. Ed.* **1996**, *35*, 706−724. (b) Cleland, W. W.; Frey, P. A.; Gerlt, J. A. The Low Barrier Hydrogen Bond in Enzymatic Catalysis. *J. Biol. Chem.* **1998**, *273*, 25529−25532. (c) Ringe, D.; Petsko, G. A. How Enzymes Work. *Science* **2008**, *320*, 1428−1429.

(2) (a) Harris, K.; Fujita, D.; Fujita, M. Giant hollow M_nL_{2n} spherical complexes: structure, functionalisation and applications. *Chem. Commun.* **2013**, *49*, 6703−6712. (b) Popov, A. A.; Yang, S.; Dunsch, L. Endohedral Fullerenes. *Chem. Rev.* **2013**, *113*, 5989−6113. (c) Yang, J.; Chatelet, B.; Dufaund, V.; Herault, D.; Michaund-Chevallier, S.; Robert, V.; Dutasta, J.-P.; Martinez, A. Endohedral Functionalized Cage as a Tool to Create Frustrate Lewis Pairs. *Angew. Chem., Int. Ed.* **2018**, *57*, 14212−14215. (d) Holloway, L. R.; Bogie, P. M.; Lyon, Y.; Ngai, C.; Miller, T. F.; Julian, R. R.; Hooley, R. J. Tandem Reactivity of a Self-Assembled Cage Catalyst with Endohedral Acid Groups. *J. Am. Chem. Soc.* **2018**, *140*, 8078−8081.

(3) Cram, D. J.; Lein, G. M. Host-Guest Complexation. 36. Spherand and Lithium and Sodium Ion Complexation Rates and Equilibria. *J. Am. Chem. Soc.* **1985**, *107*, 3657−3668.

(4) (a) Hensel, V.; Lutzow, K.; Schluter, A.-D.; Jacob, J.; Gessler, K.; Saenger, W. Repetitive Construction of Macrocyclic Oligophenylenes. *Angew. Chem., Int. Ed.* **1997**, *36*, 2654−2656. (b) Hensel, V.; Schlüter, A.-D. Building Blocks for the Construction of Large Chloro-Functionalized, Hexagonal Oligophenylene Cycles. *Eur. J. Org. Chem.* **1999**, *1999*, 451−458. (c) Hensel, V.; Schlüter, A. D. A Cyclotetraicosaphenylene. *Chem.—Eur. J.* **1999**, *5*, 421−429.

(5) (a) Iyoda, M.; Yamakawa, J.; Rahman, M. J. Conjugated Macrocycles: Concepts and Applications. *Angew. Chem., Int. Ed.* **2011**, *50*, 10522−10553. (b) Grave, C.; Schlüter, A. D. Shape-Persistent, Nano-Sized Macrocycles. *Eur. J. Org. Chem.* **2002**, *2002*, 3075−3098. (c) Van Raden, J. M.; White, B. M.; Zakharov, L. N.; Jasti, R. Nanohoop Rotaxanes from Active Metal Template Syntheses and Their Potential in Sensing Applications. *Angew. Chem., Int. Ed.* **2019**, *58*, 7341−7345.

(6) (a) Yamago, S.; Kayahara, E.; Iwamoto, T. Organoplatium-Mediated Synthesis of Cyclic π-Conjugated Molecules: Towards a New Era of Three-Dimensional Aromatic Compounds. *Chem. Rec.* **2014**, *14*, 84−100. (b) Golder, M. R.; Jasti, R. Syntheses of the Smallest Carbon Nanohoops and the Emergence of Unique Physical Phenomena. *Acc. Chem. Res.* **2015**, *48*, 557−566. (c) Lewis, S. E. Cycloparaphenylenes and related nanohoops. *Chem. Soc. Rev.* **2015**, *44*, 2221−2304. (d) Segawa, Y.; Yagi, A.; Matsui, K.; Itami, K. Design and Synthesis of Carbon Nanotube Segments. *Angew. Chem., Int. Ed.* **2016**, *55*, 5136−5158. (e) Hammer, B. A. G.; Müllen, K. Dimensional Evolution of Polyphenylenes: Expanding in All Directions. *Chem. Rev.* **2016**, *116*, 2103−2140. (f) Xu, Y.; von Delius, M. The Supramolecular Chemistry of Strained Carbon Nanohoops. *Angew. Chem., Int. Ed.* **2020**, *59*, 559−573. (g) Hermann, M.; Wassy, D.; Esser, B. Conjugate Nanohoops Incorporating Donor, Acceptor, Hetero- or Polycyclic Aromatics. *Angew. Chem., Int. Ed.* **2021**, *60*, 15743−15766.

(7) (a) Della Sala, P.; Talotta, C.; Caruso, T.; De Rosa, M.; Soriente, A.; Neri, P.; Gaeta, C. Tuning Cycloparaphenylene Host Properties by Chemical Modification. *J. Org. Chem.* **2017**, *82*, 9885−9889. (b) Lu, D.; Zhuang, G.; Jia, H.; Wang, J.; Huang, Q.; Cui, S.; Du, P. A novel symmetrically multifunctionalized dodecamethoxy-cycloparaphenylene: synthesis, photophysical, and supramolecular properties. *Org. Chem. Front.* **2018**, *5*, 1446−1451. (c) Cui, S.; Zhuang, G.; Wang, J.; Huang, Q.; Wang, S.; Du, P. Multifunctionalized octamethoxy[8]cycloparaphenylene: facile synthesis and analysis of novel photophysical and photoinduced electron transfer properties. *Org. Chem. Front.* **2019**, *6*, 1885−1890.

(8) (a) Höger, S.; Meckenstock, A.-D. Template-Directed Synthesis of Shape-Persistent Macrocyclic Amphiphiles with Convergently Arranged Functionalites. *Chem.—Eur. J.* **1999**, *5*, 1686−1691. (b) Vliegenthart, A. B.; Welling, F. A. L.; Roemelt, M.; Gebbink, R.

https://doi.org/10.1021/acsomega.2c05926
ACS Omega 2022, 7, 45347−45352

J. M. K.; Otte, M. Synthesis and Characterzation of a Brønsted Pair Functionalized Shape-Persistent Macrocycle. *Org. Lett.* **2015**, *17*, 4172−4175. (c) Abe, H.; Yoneda, T.; Ohishi, Y.; Inouye, M. D_{3h}-Symmetrical Shape-Persistent Macrocycles Consisting of Pyridine-Acetylene-Phenol Conjugates as an Efficient Host Architecture for Saccharide Recognition. *Chem.—Eur. J.* **2016**, *22*, 18944−18952.

(9) For the construction of boroxine cages, *o*-methylated benzene boronic acid units were used to create a well-defined cavity. (a) Ono, K.; Johmoto, K.; Yasuda, N.; Uekusa, H.; Fujii, S.; Kiguchi, M.; Iwasawa, N. Self-Assembly of Nanometer-Sized Boroxine Cages from Diboronic Acids. *J. Am. Chem. Soc.* **2015**, *137*, 7015−7018. (b) Ono, K.; Shimo, S.; Takahashi, K.; Yasuda, N.; Uekusa, H. Dynamic interconversion between boroxine cages based on pyridine ligation. *Angew. Chem., Int. Ed.* **2018**, *57*, 3113−3117. (c) Ono, K.; Iwasawa, N. Dynamic behavior of covalent organic cages. *Chem.—Eur. J.* **2018**, *24*, 17856−17868. (d) Ono, K.; Iwasawa, N. Oligoboroxine-based architectures. *J. Incl. Phenom. Macrocycl. Chem.* **2021**, *101*, 19−29.

(10) (a) Mukherjee, A.; Dixit, K.; Sarma, S. P.; Desiraju, G. R. Aniline-phenol recognition: from solution through supramolecular synthons to cocrystals. *IUCrJ.* **2014**, *1*, 228−239. (b) Sood, A.; Desiraju, G. R. Looking at aniline-phenol recognition in molecular crystals: an evergreen endeavour. *Struct. Chem.* **2017**, *28*, 173−199.

(11) Noguchi, H.; Hojo, K.; Suginome, M. Boron-Masking Strategy for the Selective Synthesis of Oligoarenes via Iterative Suzuki-Miyaura Coupling. *J. Am. Chem. Soc.* **2007**, *129*, 758−759.

(12) Sinclair, D. J.; Sherburn, M. S. Single and Double Suzuki-Miyaura Couplings with Symmetric Dihalobenzenes. *J. Org. Chem.* **2005**, *70*, 3730−3733.

(13) Other combinations of Pd source (10 mol %) and phosphine ligand (20 mol %) were examined, such as $Pd_2(dba)_3$ and P(*tert*-butyl)$_3$, $Pd_2(dba)_3$ and P(*cyclo*-hexyl)$_3$, or $Pd_2(dba)_3$ and SPhos. These conditions were not reproducible.

(14) (a) Akiyama, T.; Itoh, J.; Yokota, K.; Fuchibe, K. Enantioselective Mannich-Type Reaction Catalyzed by a Chiral Brønsted Acid. *Angew. Chem., Int. Ed.* **2004**, *43*, 1566−1568. (b) Uraguchi, D.; Terada, M. Chiral Brønsted Acid-Catalyzed Direct Mannich Reactions via Electrophilic Activation. *J. Am. Chem. Soc.* **2004**, *126*, 5356−5357.

(15) The inclusion of catalyst is one of the interesting topics in supramolecular chemistry, and it has been reported that included transition-metal catalysts in coordination cages can exhibit unique reactivities and selectivities; see: (a) Leung, D. H.; Bergman, R. G.; Raymond, K. N. Highly Selective Supramolecular Catalyzed Allylic Alcohol Isomerization. *J. Am. Chem. Soc.* **2007**, *129*, 2746−2747. (b) Jongkind, L. J.; Caumes, X.; Hartendorp, A. P. T.; Reek, J. N. H. Ligand Template Strategies for Catalyst Encapsulation. *Acc. Chem. Res.* **2018**, *51*, 2115−2128.

(16) The titration method could not be applied due to the low solubility of both host and guest in $CDCl_3$; see: Bisson, A. P.; Carver, F. J.; Eggleston, D. S.; Haltiwanger, R. C.; Hunter, C. A.; Livingstone, D. L.; McCabe, J. F.; Rotger, C.; Rowan, A. E. Synthesis and Recognition Properties of Aromatic Amide Oligomers: Molecular Zippers. *J. Am. Chem. Soc.* **2000**, *122*, 8856−8868.

https://doi.org/10.1021/acsomega.2c05926
ACS Omega 2022, 7, 45347−45352