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D_{3h}-Symmetrical Shape-Persistent Macrocycles Consisting of Pyridine–Acetylene–Phenol Conjugates as an Efficient Host Architecture for Saccharide Recognition

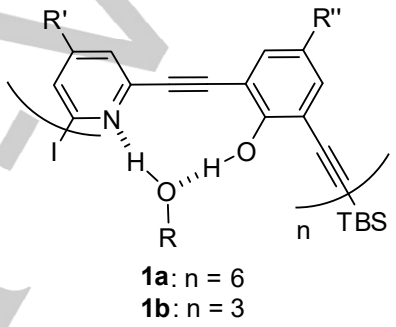
Hajime Abe,* Tetsuhiro Yoneda, Yuki Ohishi, and Masahiko Inouye*[a]

Abstract: Hexagonal shape-persistent macrocycles (SPMs) consisted of three pyridine and three phenol rings linked with acetylene bonds were developed as a preorganized host for saccharide recognition by push-pull-type hydrogen bonding. Three *tert*-butyl or 2,4,6-triisopropylphenyl substituents were introduced on the host to suppress self-aggregation by steric hindrance. In spite of the simple architecture, association constants K_a of the host with alkyl glycoside guests reached the order of 10^6 M^{-1} on the basis of UV-vis titration experiments. This glycoside recognition was much stronger than that in the cases of acyclic equivalent hosts because of the entropic advantage brought by pre-organization of the hydrogen-bonding sites. Solid-liquid extraction and liquid-liquid transport through a liquid membrane were demonstrated by using native saccharides, and much preference to mannose was observed.

Introduction

Shape-persistent macrocycles (SPMs) have attracted interests for their keen-edged structural, spectroscopic, and interactive properties originated from the well-defined rigid conformation.[1] Typically, self-aggregation of discotic SPMs has been studied to make columnar, fibril, and liquid crystalline nanostructures. From the viewpoint of host-guest chemistry, the center hole within a SPM framework seems to be attractive because the shape of the hole is also defined. Thus, if functional groups were located inside the framework, their positions must be highly predictable.[2–4] In some cases, such architecture would realize pre-organization of the functional groups to strongly recognize guest molecules fitted in the hole.[2h,3–6]

We have been developing host molecules consisting of hydrogen-bonding acceptor and donor units for interacting with the hydroxy groups of saccharides in a push-pull fashion. In this context, a pyridine–acetylene–(1*H*)-4-pyridone motif was selected and proved to be efficient for saccharide recognition.[4c,7,8] The acetylene spacer kept the distance between the acceptor and the donor to grip a hydroxy group, avoiding intramolecular interaction. On the other hand, the oligomers possessing the repeating units were also found to intermolecularly self-dimerize through pyridone-pyridinol tautomerization.[7] Very recently, we newly introduced a pyridine–acetylene–phenol unit as a hard to self-dimerize, hydrogen-bonding donor-acceptor alternative.[9] Taking advantage of the precise enthalpic gain arising from the push-pull hydrogen bonds, the oligomer **1a** strongly recognized various saccharides to form a chiral helical complex in an induced-fit manner (Figure 1). However, the work is not yet satisfactory because entropic loss remains to be minimized, particularly that resulted from the conformational freeze of the oligomers during the complexation.



1a: n = 6
1b: n = 3

Figure 1. *Pyridine–acetylene–phenol oligomers **1a,b** and an alcohol guest associated by push-pull hydrogen bonding. TBS = tert-butyldimethylsilyl.*

Now, we planned to study SPM hosts **2** and **3** consisted of the pyridine–acetylene–phenol conjugate as a highly efficient host architecture for saccharide recognition (Figure 2).[10,11] Their hexagonal framework has rigidity and D_{3h} symmetry reasonable for the mono-saccharide recognition in the hole with pre-organized hydrogen-bonding donors and acceptors. These structural aspects certainly guarantee entropic advantages during the recognition of saccharides, compared with the previous acyclic oligomers. Bulky groups were introduced in the peripherals of both the SPMs to avoid self-association. Actually a less bulky analogue **4** suffered from concentration dependence due to self-association (see below). The octyloxy groups were used for increasing the solubility. Herein we describe the preparation, properties, and saccharide recognition ability of the hosts, especially of **3** in detail. We also investigated not only usual binding experiments in a solution phase but also solid-liquid extraction and liquid-liquid hexose transport through a liquid membrane for **3**.

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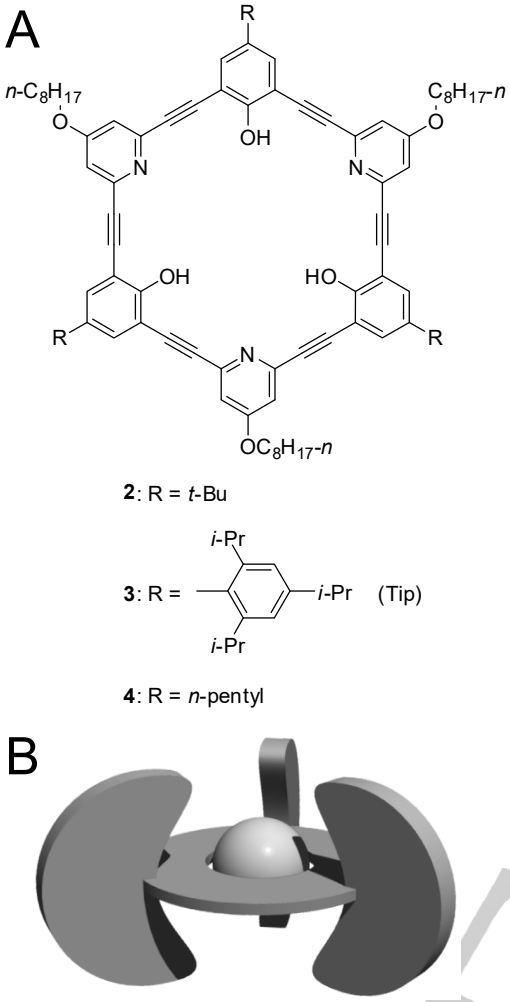


Figure 2. *(A) Pyridine–acetylene–phenol SPM hosts* ***2****,* ***3****, and* ***4****. Steric hindrance was introduced on* ***2*** *and* ***3****, and* ***4*** *is a less bulky preliminary analogue. (B) A conceptual illustration for structure of* ***3****. A ball, a ring, and three crescent-shaped plates represent a glycoside guest, a SPM center, and a steric hindrance, respectively.*

Results and Discussion

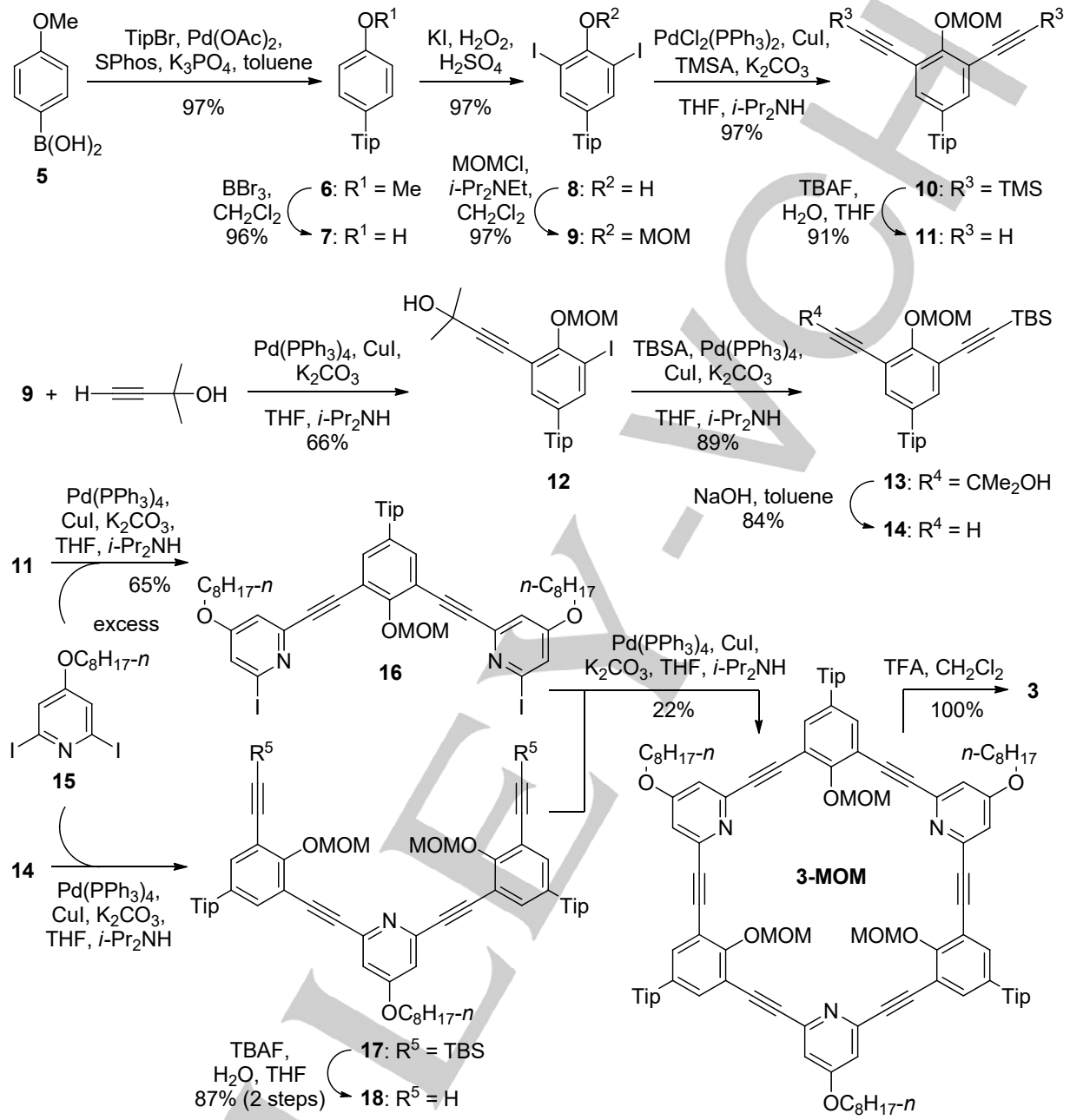
In a preliminary study, the less bulky SPM **4** was investigated as a prototype, prior to **2** and **3** possessing steric hindrance. The preparation and characteristics of **4** were described in the Supporting Information. The ^{1}H NMR chemical shifts for **4** were found to depend on the concentration, and the association constant assuming dimerization K_{dim} was estimated to be (2.1 ± 1.1) × 10^3 M^{-1} from the titration curve (Figures S1 and S2 in Supporting Information). The strong self-association would be due to π-stacking of the planar framework[4a,b] and would disturb the study of saccharide recognition. So we decided to introduce steric hindrance to avoid self-association in order to quantitatively evaluate the host ability of the pyridine–acetylene–phenol SPM framework.

The *tert*-butyl groups for **2** and 2,4,6-triisopropylphenyl (Tip) groups for **3** were expected to hinder the self-aggregation through stacking of the large π-plane. Starting from 4-*tert*-butylphenol, **2** was obtained by repeating Sonogashira reaction. The details of the synthetic procedure were described in Supporting Information. The concentration dependence of the ^{1}H NMR chemical shifts ([**2**] = 9.5 × 10^{-3} to 1.5 × 10^{-4} M) was observed, and the association constant (K_{dim} = (1.7 ± 0.6) × 10^1 M^{-1}) was found to be much small (Figures S3 and S4 in Supporting Information). In UV-vis measurements, no meaningful deviation from Beer's law was seen under the concentration of [**2**] ≤ 2.0 × 10^{-4} M (Figures S5 and S6 in Supporting Information), so that **2** certainly exists as a monomer below the concentration.

The SPM host **3** with bulkier substituents was prepared by the synthetic procedures shown in Scheme 1. Commercially available 2-bromo-1,3,5-triisopropylbenzene (TipBr) was coupled with 4-methoxybenzeneboronic acid (**5**) by Suzuki-Miyaura coupling to give diaryl **6**. After removal of the methyl group, phenol **7** was subjected to iodination followed by protection of the hydroxy group to afford **9**. The use of MOM groups was necessary to protect the phenolic hydroxy groups from the undesirable cyclization to benzofuran. Sonogashira coupling of **9** with (trimethylsilyl)acetylene (TMSA) and treatment with tetrabutylammonium fluoride (TBAF) gave **11**, one of phenol building blocks. On the other hand, **9** was coupled with 2-methyl-3-butyn-2-ol and (*tert*-butyldimethylsilyl)acetylene (TBSA) subsequently by two-step Sonogashira reactions to give hetero-diprotected diyne **13**. The liberation of acetone from **13** with base gave monoprotected diyne **14**, another phenol building block. Sonogashira reaction using **11** and an excess amount of 2,6-diiodo-4-(octyloxy)pyridine (**15**)[7] yielded diiodide trimer "I-pyridine-(MOM-phenol)-pyridine-I" **16**, while diyne trimer "ethynyl-(MOM-phenol)-pyridine-(MOM-phenyl)-ethynyl" **18** was obtained by Sonogashira reaction of **15** with two equivalents of **14**, followed by the treatment with TBAF. The trimer precursors **16** and **18** were subjected to final Sonogashira reaction to afford macrocyclized product **3-MOM**, and the MOM groups were removed by TFA to furnish **3** as a yellow solid.

The MOM protons of **3-MOM** were much deshielded after the macrocyclization, compared with the precursors **16** and **18**. The ^{1}H NMR signals of the methylene and methyl groups of **16** appeared at δ 5.51 and 3.76 ppm, respectively, and after the cyclization to **3-MOM**, they appeared at δ 5.73 and 4.05 ppm, respectively. This anisotropy would be due to a field effect from the oxygen atoms of the MOM groups stuffed into the hole. In the cases of **2-MOM** and **4-MOM**, similar anisotropy effects were observed.

The product **3** is well soluble to common organic solvents such as CH_2Cl_2, $CHCl_3$, and AcOEt. Owing to the steric hindrance, self-association could be completely suppressed, so that concentration dependence was not observed. Absorbance of **3** at 282 nm in CH_2Cl_2 was linearly dependent on the molar concentration [**3**] from 1.0 × 10^{-3} to 6.8 × 10^{-7} M (Figures S7 and S8 in Supporting Information). In addition, no meaningful change occurred for ^{1}H NMR chemical shifts in $CDCl_3$ even at a range of 1.4 × 10^{-2} to 2.1 × 10^{-4} M (Figure S9 in Supporting Information).



Scheme 1. Synthesis of SPM host **3**. Tip = 2,4,6-triisopropylphenyl, SPhos = 2-(dicyclohexylphosphino)-2',6'-dimethoxybiphenyl, TMSA = (trimethylsilyl)acetylene, TBAF = tetrabutylammonium fluoride, TBSA = (*tert*-butyldimethylsilyl)acetylene, TFA = trifluoroacetic acid.

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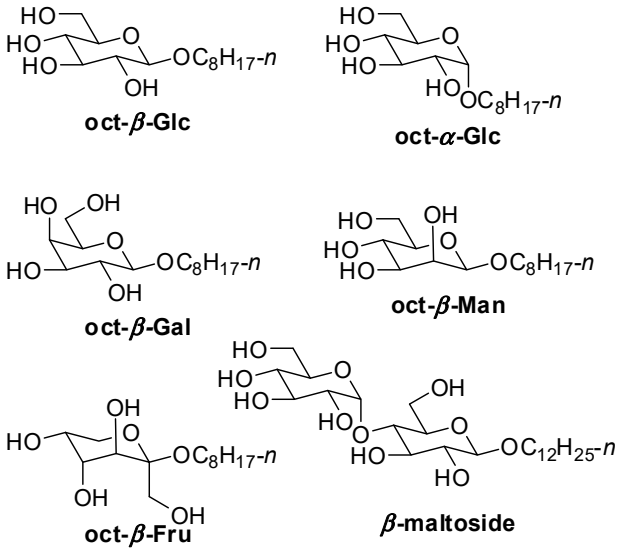

Figure 3. *Alkyl glycoside guests applied in this research.*

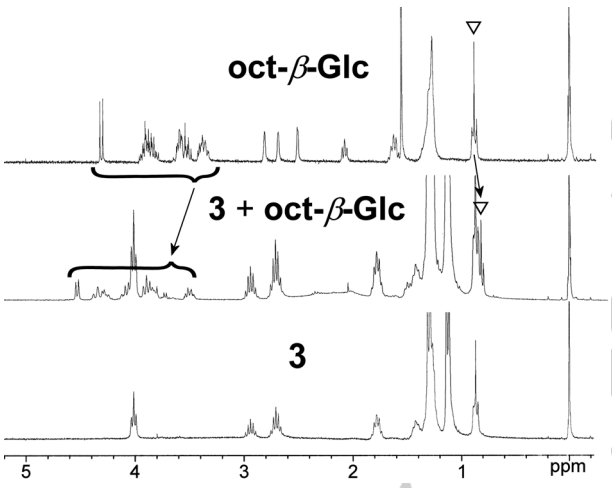

Figure 4. *^{1}H NMR spectra of (top)* ***oct-β-Glc****, (middle) a mixture of* ***3*** *and* ***oct-β-Glc****, and (bottom)* ***3****. Triangle indicate the terminal methyl protons of the octyl chains of* ***oct-β-Glc****. Conditions:* ***3*** *(3.0 × 10^{-3} M),* ***oct-β-Glc*** *(3.0 × 10^{-3} M), $CDCl_3$, 23 °C, 300 MHz.*

Association of **3** with octyl β-D-glucopyranoside (**oct-β-Glc**, Figure 3) was qualitatively studied on ^{1}H NMR experiments (Figure 4). When the spectrum of a mixed solution of **3** and **oct-β-Glc** ([**3**] = [**oct-β-Glc**] = 3.0 × 10^{-3} M) was compared to each ^{1}H NMR spectrum of **3** (3.0 × 10^{-3} M) and **oct-β-Glc** (3.0 × 10^{-3} M) in $CDCl_3$, it was found that the signals of C-*H* protons of the pyranoside moiety in **oct-β-Glc** moved downfield by association with **3**. The signals of the O-*H* protons could not be specified in the spectrum of the host-guest mixture because of overlapping with the C-*H* signals and significant broadening. Interestingly, even the signal of the terminal methyl protons of the octyl group of **oct-β-Glc** was found to move upfield, thus the influence of the host-guest interaction extended all along the complex.

To quantitatively study the saccharide recognition ability of **3**, titration experiments were carried out by the addition of several kinds of octyl glycosides (Figure 3) to a solution of **3** (3.0 × 10^{-6} M) in 1,2-dichloroethane (DCE) by UV-vis spectroscopy (Figure 5A). According to the addition of **oct-β-Glc**, red shift of the absorption band around 360 nm and hypochromism around 282 nm occurred in **3**. When absorbance at 375 nm was plotted against the molar concentration of the guest glycosides, the isotherms were well fitted with theoretical curves assuming 1:1 binding, and the association constants K_a was found to be (5.0 ± 2.2) × 10^6 M^{-1} (Figure 5B).

The additive effects of glycoside guests were also investigated by fluorescence spectroscopy. Figure 5C shows the changes of the fluorescence spectrum of a solution of **3** (3.0 × 10^{-6} M) in DCE by the addition of **oct-β-Glc**. The emissive band around 400 nm largely weakened during the titration (Figure 5D) possibly because the association yielded many vibratable hydrogen bonds that caused the increased nonradiative decay process.

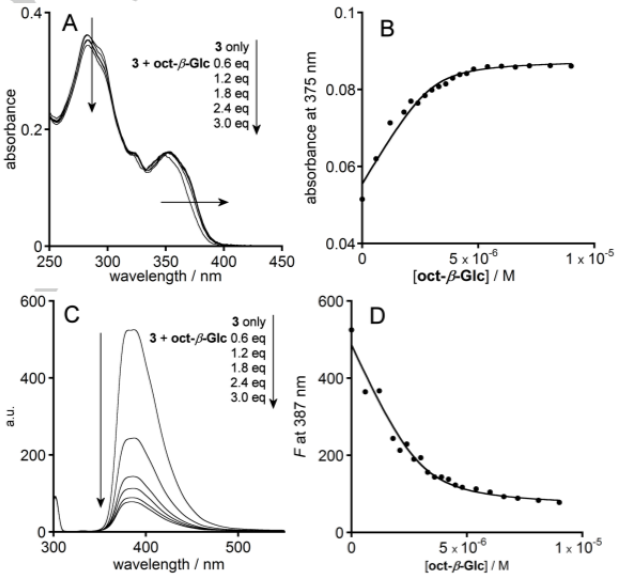

Figure 5. *Results of titration experiment of* ***3*** *with* ***oct-β-Glc****. (A) Changes of UV-vis spectrum of* ***3****. (B) Titration curve of absorbance at 375 nm. The line is fitted curve assuming 1:1 binding, K_a = 5.0 × 10^6 M^{-1}. (C) Changes of fluorescent spectrum. Conditions:* ***3*** *(3.0 × 10^{-6} M),* ***oct-β-Glc*** *(0 to 9.0 × 10^{-6} M), DCE, 25 °C, path length = 10 mm. (D) Titration curve of fluorescence at 387 nm. The line is fitted curve assuming 1:1 binding, K_a = 3.5 × 10^6 M^{-1}.*

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Table 1. Association Constants K_a of SPM Hosts **1a**,**b**, **2**, and **3** with Glycoside Guests[a]

Host	Guest	K_a[b] / M^{-1}	
		Procedure / UV-vis	Fluorescence
3	**oct-α-Glc**[c]	(4.6 ± 1.5) × 10^6	(3.8 ± 3.2) × 10^6
	oct-β-Glc	(5.0 ± 2.2) × 10^6	(3.5 ± 1.4) × 10^6
	oct-β-Gal	(1.7 ± 0.5) × 10^6	
	oct-β-Man[d]	(2.0 ± 1.3) × 10^6	(5.2 ± 1.1) × 10^6
	oct-β-Fru	(1.3 ± 0.3) × 10^6	(1.5 ± 0.6) × 10^6
	β-maltoside	(8.5 ± 2.3) × 10^5	(4.5 ± 2.2) × 10^5
2	**oct-β-Glc**	(1.7 ± 0.5) × 10^6	(1.4 ± 0.9) × 10^6
1a[e]	**oct-β-Glc**	(1.5 ± 0.4) × 10^7	(3.4 ± 0.4) × 10^7
1b[f]	**oct-β-Glc**	(5.3 ± 0.2) × 10^3	(7.0 ± 0.1) × 10^3

[a] Conditions: [**3**] = 3.0 × 10^{-6}, [guest] = 0 to 9.0 × 10^{-6} M, DCE, 25 °C, path length = 10 mm. The changes of spectra and titration curves were shown in Figure 5 and Figures S10−S14 and S17−18 in Supporting Information. [b] Association constants were obtained by curve-fitting analyses assuming 1:1 binding for the change of absorbance at λ_{max} and fluorescence intensity at F_{max}. [c] [**3**] = 5.0 × 10^{-6} M, [**oct-α-Glc**] = 0 to 1.5 × 10^{-5} M, CH_2Cl_2, 25 °C, path length = 10 mm. [d] [**3**] = 5.0 × 10^{-6}, [**oct-β-Man**] = 0 to 2.5 × 10^{-5} M, DCE, 25 °C, path length = 10 mm. [e] From reference 9a. [f] [**1b**] = 1.0 × 10^{-5}, [**oct-β-Glc**] = 0 to 3.8 × 10^{-3} M, DCE, 25 °C, path length = 10 mm.

The results using a series of glycosides (Figure 3) as a guest were summarized in Table 1. Various glycosides showed high K_a values with **3**. These K_a values exceed those for the corresponding acyclic hexameric analogue **1b** (K_a = 5.3 × 10^3 M^{-1} with **oct-β-Glc**), and compete with those for acyclic dodecameric **1a** (K_a = 1.5 × 10^7 M^{-1} with **oct-β-Glc**).[9a] This means that the recognition efficiency could be improved by the SPM framework. During these studies, no meaningful Cotton effect appeared at the absorptive wavelength of **3**. The structure of **3** would be so rigid that the glycoside guests did not induce chirality detectable by CD analyses. Therefore, above-mentioned spectral changes caused by the glycoside addition are most likely to be due to hydrogen bonding at the pyridine and phenol rings and not to distortion of the rigid macrocyclic π-framework.

The thermodynamic study was carried out about the recognition of **oct-β-Glc** by the cyclic hexamer **3** and the acyclic counterpart **1b** in order to evaluate the advantage of the pre-organization in **3**. The association constants K_a of these cyclic and acyclic hosts with **oct-β-Glc** were collected at 15, 20, 25, and 30 °C in DCE, and the thermodynamic parameters were calculated from the van't Hoff plots (Table 2, and Figures S15 and S16 in Supporting Information). Association of **3** and **oct-β-Glc** gave rise to the free-energy change of −37 ~ −38 $kJmol^{-1}$, meaning that the one pair of the pyridine−phenol conjugate played a role in the stabilization of more than 10 $kJmol^{-1}$ on the average. Moreover, the entropic loss was much smaller in the case of **3** compared with **1b**, while the enthalpic gain is similar between them. This suggests that the strong host ability of **3** is secured by rigidity of the framework and pre-organization of the hydrogen-bonding sites.

Table 2. Thermodynamic parameters of association of hosts **3** and **1b** with **oct-β-Glc**.

Host	Guest	ΔG[c] / $kJmol^{-1}$	ΔH / $kJmol^{-1}$	ΔS / $JK^{-1}mol^{-1}$	$T\Delta S$[c] / $kJmol^{-1}$
3[a]	**oct-β-Glc**	−38	−46	−27	−8
1b[b]	**oct-β-Glc**	−21	−50	−97	−29

[a] Conditions: [**3**] = 3.0 × 10^{-6} M, [**oct-β-Glc**] = 0 to 9.0 × 10^{-6} M, DCE, 15, 20, 25, and 30 °C, path length = 10 mm. [b] Conditions: [**1b**] = 1.0 × 10^{-5} M, [**oct-β-Glc**] = 0 to 3.8 × 10^{-3} M, DCE, 15, 20, 25, and 30 °C, path length = 10 mm. The titration curves and van't Hoff plots were shown in Figures S15 and S16 in Supporting Information. [c] T = 298 K.

Association constant between *tert*-butyl groups-substituted **2** and **oct-β-Glc** could be obtained as K_a = 1.7 × 10^6 M^{-1} by UV-vis titration (Figure S18 in Supporting Information). This value was a little smaller than the K_a between **3** and **oct-β-Glc**, possibly because of the positive interaction between the octyl group of **oct-β-Glc** and the triisopropylphenyl groups of **3** as suggested in the above ^{1}H NMR analyses (Figure 4). The less bulky host **4** also showed affinity with **oct-β-Glc** qualitatively in ^{1}H NMR measurements (Figure S19 in Supporting Information), however, the strong self-association of **4** prevented quantitative measurements.

Solid-liquid extraction experiments were performed by using native hexose insoluble in apolar organic solvents. A solution of **3** (5.0 × 10^{-4} M, 1.5 × 10^{-6} mol) in $CDCl_3$ (3.0 mL) was shaken with powdery D-glucose for 10 h at room temperature, and the mixture was filtered through a membrane filter to remove insoluble residue. The ^{1}H NMR spectrum of the filtrate showed broad signals at a range of 3~6 ppm, which was supposed to be those of glucose (Figure S20A in Supporting Information). The amount of the extracted glucose was determined by back-extraction with D_2O followed by the addition of sodium 3-(trimethylsilyl)propane-1-sulfonate (DSS) as an internal reference (Figure S20B in Supporting Information). The molar concentration of glucose extracted in the filtrate was reckoned at 1.9 × 10^{-6} mol, 1.3 equiv to the applied host **3**. When absorption spectrum of the filtrate after the extraction was compared to that of a solution of **3** in DCE, hypochromism was observed in ε values at the bands around 282 and 348 nm (Figure S21 in Supporting Information). When the filtrate was subjected to a dilution experiment to [**3**] = 9.8 × 10^{-7} M, the plot of absorbance

at 282 nm against [**3**] did not deviate from linearity probably because the association of **3** with native glucose was too strong to dissociate in DCE (Figure S22 in Supporting Information).

D-Mannose was also extracted (6.5×10^{-4} M, 1.3 equiv to **3**) from a solid phase to a solution of **3** (5.0×10^{-4} M) in $CDCl_3$, while D-maltose could not. The difference probably resulted from the size of the saccharides: the hole of **3** was not enough large to accommodate disaccharide. Interestingly, when a mixture of D-glucose and D-mannose (1:1) was applied to the solid-liquid extraction experiment, D-mannose was selectively extracted. Figure 6 showed the ^{1}H NMR spectrum of the D_2O layer after back-extraction from the $CDCl_3$ filtrate of the mixture. Observed were the signals of anomeric protons of α- and β-mannose, and were not those of α- and β-glucose. On the other hand, in homogeneous conditions, host **3** bound with **oct-β-Glc** to **oct-β-Man** comparably as shown in Table 1. This difference of selectivity would be caused by the substituent at 1-position of the guests, which might affect on the binding manner, and/or caused by the stablity of solid glucose. In general glucose is less soluble to polar media than mannose.[12]

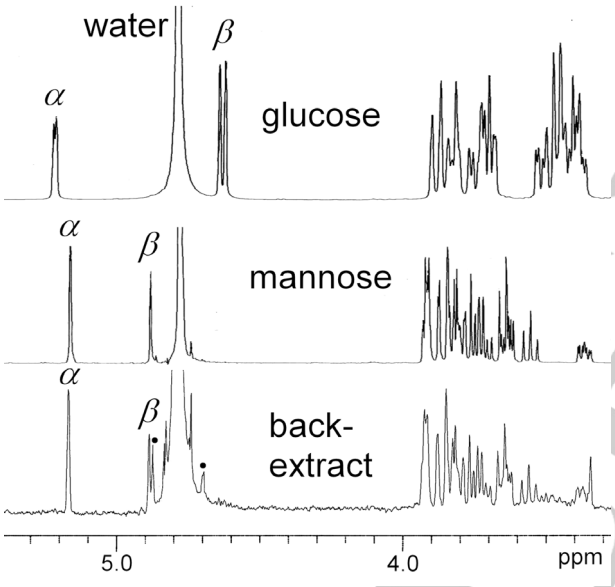

Figure 6. *^{1}H NMR spectra of (top) D-glucose in D_2O, (middle) D-mannose in D_2O, and (bottom) a D_2O layer back-extracted from the filtrate after solid-liquid extraction experiment for a mixture of D-glucose and D-mannose. Extraction procedure: a mixture of **3** (5.0×10^{-4} M), D-glucose (10 mg), and D-mannose (10 mg) in $CDCl_3$ (2.0 mL) was stirred for 10 h at room temperature and filtered through a membrane filter. The filtrate was subjected to back-extraction with a D_2O (2.0 mL) layer, which was brought to ^{1}H NMR measurement. Conditions for NMR measurements: 24 °C, 400 MHz. Letters α and β indicate anomeric C-H protons and dots indicate spinning side bands..*

Transport experiment of hexoses through a liquid membrane was executed with a U-tube apparatus. For a typical procedure, a source D_2O (2.0 mL) phase with a mixture of D-glucose and D-mannose (each of 4.0×10^{-3} mol) and a receiving D_2O (2.0 mL) phase were laid on a liquid membrane $CDCl_3$ (5.0 mL) phase with **3** (5.0×10^{-4} M) as shown in Figure 7. A stirring bar was set at the bottom of the $CDCl_3$ phase, and gently stirred for seven days at room temperature. The amounts of transported hexoses were determined by ^{1}H NMR measurement of the resulting receiving D_2O phase with DSS as an internal reference. In one experiment, 1.8×10^{-5} mol of D-glucose and 5.8×10^{-5} mol of D-mannose were transported. The membrane liquid phase can be recycled with replacing source and receiving D_2O phases (Table 3). In each cycle, D-mannose was transported more than D-glucose, and the selectivity for D-glucose:D-mannose was approximately 1:4. The control experiments in the absence of **3** showed no hexose transport. D-Maltose could not be transported by **3** as well as the case of solid-liquid extraction because of the size mismatch..

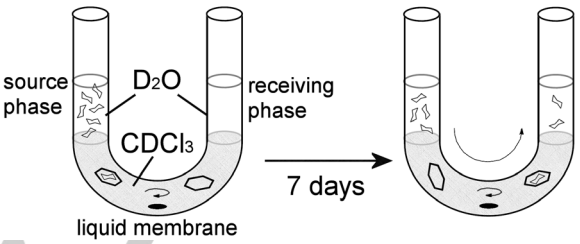

Figure 7. *An apparatus for hexose transport through a membrane filter.*

Table 3. Results of transport experiments by recycling a liquid membrane phase.[a]

Cycle	Hexose transported[d]		Ratio
	D-Glucose / 10^{-5} mol	D-Mannose / 10^{-5} mol	
1	1.8	5.8	24:76
2[b]	4.4	20	18:82
3[c]	4.0	13	24:76

[a] The apparatus and the procedure of the experiment were described in Figure 7 and the text. [b] After cycle 1, the D_2O phases were removed and the liquid membrane phase was washed with D_2O and brought to the cycle 2. [c] After cycle 2, the D_2O phases were removed and the liquid membrane phase was brought to the cycle 3 without washing. [d] Evaluated with ^{1}H NMR spectra using DSS as an internal reference.

Conclusions

In summary, we developed hexagonal SPM hosts consisted of three pyridine and three phenol rings linked with acetylene bonds. To inhibit self-aggregation of the host, bulky 2,4,6-triisopropylphenyl groups were introduced on the phenol rings as steric hindrance. The macrocyclic hosts efficiently recognized alkyl hexosides such as glucoside and mannoside. The

thermodynamic study revealed that the main advantage of the macrocyclic host is an entropic factor in comparison with the host of acyclic analogue. Native glucose and mannose could be recognized by the macrocyclic host in heterogeneous conditions. Solid-liquid extraction and liquid membrane experiments showed the preference for mannose to glucose. Maltose and maltoside were not or only weakly recognized by the macrocyclic host because of the size-mismatch of the host with the disaccharide. We confirmed the advantages of SPM structure for designing host molecules and the thermodynamic differences between macrocyclic and helical host structures. The investigation of size-sensitive molecular recognition using other classes of compounds than saccharides are underway.

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were collected on Varian GEMINI300 and JEOL ECX400 spectrometers by using tetramethylsilane (TMS) as an internal reference. ESI-HRMS analyses were carried out on a JEOL JMS-T100LC mass spectrometer by using MeOH solutions of the analytes. IR, UV-vis, and fluorescence spectra were measured by JASCO spectrometers FT/IR-460 plus, V-560, and FP-6500, respectively. Melting points were measured on a Yanaco MP-500D apparatus and not corrected. All reactions were carried out under an argon atmosphere. THF was freshly distilled from sodium benzophenone ketyl before use. Intermediate 4-octyloxy-2,6-diiodopyridine (**15**) was prepared by the procedure we previously reported.[7]

2,4,6-Triisopropyl-4'-methoxydiphenyl (6)

To a mixture of $Pd(OAc)_2$ (90 mg, 0.40 mmol) and SPhos (330 mg, 0.80 mmol) in toluene (200 mL) were added K_3PO_4 (13 g, 80 mmol), 4-methoxyphenylboronic acid (**5**, 9.1 g, 60 mmol), and 2-bromo-1,3,5-triisopropylbenzene (11 g, 40 mmol). The mixture was stirred under reflux for 13 h, allowed to room temperature, and filtered through a Florisil bed. The filtrate was concentrated with a rotary evaporator and subjected to silica gel column chromatography (eluent: $CHCl_3$/hexane = 1:10 to 1:5) to give **6** (12 g, 97%) as a colorless solid. M.p. 105−107 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.09 (d, J = 8.4 Hz, 2 H), 7.04 (s, 2 H), 6.93 (d, J = 8.8 Hz, 2 H), 3.86 (s, 3 H), 2.94 (septet, J = 7.0 Hz, 1 H), 2.64 (septet, J = 7.0 Hz, 2 H), 1.30 (d, J = 6.8 Hz, 6 H), 1.08 (d, J = 7.2 Hz, 12 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.1, 147.7, 146.9, 136.7, 132.9, 130.7, 120.5, 113.3, 55.2, 34.2, 30.2, 24.2, 24.1; IR (KBr): ν 2956, 2867, 2831, 1515, 1467 cm^{-1}; HRMS (ESI-TOF): m/z calcd for $C_{22}H_{31}O$ [M + H^+]: 311.2375; found: 311.2378.

4-Hydroxy-2',4',6'-triisopropyldiphenyl (7)

BBr_3 (19 g, 77 mmol) was added to a solution of **6** (12 g, 39 mmol) in CH_2Cl_2 (75 mL) at −80 °C. This solution was allowed to room temperature with stirring for 5 h and quenched by the addition of saturated aq $NaHCO_3$ (50 mL). The organic layer was washed with brine, dried over Na_2SO_4, and concentrated with a rotary evaporator to give **7** (11 g, 96%) as a colorless solid. This product was found to be highly pure by ^{1}H NMR and brought to the next step without further purification. For analyses, it could be purified by silica gel column chromatography (eluent: hexane/AcOEt = 10:1). M.p. 173−175 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.04 (s, 2 H), 7.04 (d, J = 8.4 Hz, 2 H), 6.86 (d, J = 8.8 Hz, 2 H), 4.74 (s, 1 H), 2.93 (septet, J = 7.0 Hz, 1 H), 2.64 (septet, J = 6.9 Hz, 2 H), 1.30 (d, J = 7.2 Hz, 6 H), 1.07 (d, J = 6.8 Hz, 12 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 154.0, 147.7, 146.9, 136.6, 133.2, 130.9, 120.5, 114.8, 34.2, 30.2, 24.2, 24.1; IR (KBr): ν 3266 (br), 2965, 2930, 2868, 1515, 1459, 1436 cm^{-1}; HRMS (ESI-TOF): m/z calcd for $C_{21}H_{28}NaO$ [M + Na^+]: 319.2038; found: 319.2047.

4-Hydroxy-3,5-diiodo-2',4',6'-triisopropyldiphenyl (8)

To a solution of **7** (11 g, 37 mmol) in MeOH (300 mL) were added subsequently H_2SO_4 (11 g, 110 mmol), KI (18 g, 110 mmol), and H_2O_2 (30% aqueous solution, 12 mL, 150 mmol) at 0 °C. The mixture was stirred for 40 h at room temperature, treated with aq $NaHSO_3$ (0.2 M, 300 mL), and extracted with $CHCl_3$ (150 mL). The organic layer was washed with H_2O (100 mL), dried over Na_2SO_4, and concentrated with a rotary evaporator to give **8** (20 g, 97%) as a colorless solid. This product was found to be highly pure by ^{1}H NMR and brought to the next step without further purification. For analyses, it could be purified by silica gel column chromatography (eluent: hexane/AcOEt = 10:1). M.p. 209−211 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.52 (s, 2 H), 7.02 (s, 2 H), 5.75 (s, 1 H), 2.91 (septet, J = 6.7 Hz, 1 H), 2.59 (septet, J = 6.9 Hz, 2 H), 1.28 (d, J = 6.8 Hz, 6 H), 1.09 (d, J = 6.8 Hz, 12 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 152.1, 148.7, 146.8, 140.2, 137.0, 133.6, 120.7, 81.8, 34.3, 30.3, 24.13, 24.06; IR (KBr): ν 3459, 2957, 2925, 2865, 1459, 1445 cm^{-1}; HRMS (ESI-TOF): m/z calcd for $C_{21}H_{27}I_2O$ [M + H^+]: 549.0151; found: 549.0176.

3,5-Diiodo-4-(methoxymethoxy)-2',4',6'-triisopropyldiphenyl (9)

To a solution of **8** (20 g, 36 mmol) and MOMCl (15 g, 180 mmol) in CH_2Cl_2 (200 mL) was added i-Pr_2NEt (19 g, 140 mmol) at 0 °C. The mixture was stirred for 30 min at that temperature and allowed to room temperature. The resulting reaction mixture was neutralized with saturated aq $NaHCO_3$ (100 mL) and washed with brine. The organic layer was dried over Na_2SO_4 and concentrated with a rotary evaporator to give **9** (21 g, 97%) as a colorless solid. This product was found to be highly pure by ^{1}H NMR and brought to the next step without further purification. For analyses, it could be purified by silica gel column chromatography (eluent: CH_2Cl_2). M.p. 229−232 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.64 (s, 2 H), 7.02 (s, 2 H), 5.23 (s, 2 H), 3.80 (s, 3 H), 2.91 (septet, J = 6.9 Hz, 1 H), 2.55 (septet, J = 6.9 Hz, 2 H), 1.28 (d, J = 7.2 Hz, 6 H), 1.09 (d, J = 6.8 Hz, 12 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 155.0, 148.8, 146.5, 141.1, 140.9, 133.4, 120.7, 100.2, 90.8, 58.9, 34.3, 30.3, 24.2, 24.0; IR (KBr): ν 2958, 2923, 2865, 1462, 1432 cm^{-1}; HRMS (ESI-TOF): m/z calcd for $C_{23}H_{30}I_2NaO$ [M + H^+]: 615.0233; found: 615.0246.

4-(Methoxymethoxy)-3,5-bis(trimethylsilylethynyl)-2',4',6'-triisopropyldiphenyl (10)

A mixture of THF (200 mL) and i-Pr_2NH (200 mL) was bubbled with argon for 30 min, and to this mixture were added K_2CO_3 (4.7 g, 34 mmol), $PdCl_2(PPh_3)_2$ (0.59 g, 0.84 mmol), **9** (5.0 g, 8.4 mmol), (trimethylsilyl)acetylene (TMSA, 5.0 g, 51 mmol), and CuI (32 mg, 0.17 mmol) at room temperature. The reaction mixture was stirred for 30 min at room temperature and additionally stirred for 16 h under reflux. The resulting mixture was filtered through a Florisil bed, concentrated with a rotary evaporator, and subjected to silica gel column chromatography (eluent: hexane/$CHCl_3$ = 20:1 to 5:1) to give **10** (4.4 g, 97%) as a yellow solid. M.p. 163−165 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.23 (s, 2 H), 7.02 (s, 2 H), 5.43 (s, 2 H), 3.75 (s, 3 H), 2.91 (septet, J = 6.9 Hz, 1 H), 2.59 (septet, J = 6.9 Hz, 2 H), 1.28 (d, J = 6.8 Hz, 6 H), 1.09 (d, J = 6.8 Hz, 12 H), 0.23 (s, 18 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.6, 148.4, 146.7, 136.4, 135.5, 134.6, 120.6, 117.3, 101.1, 99.2, 99.0, 57.7, 34.3, 30.2, 24.3, 24.1, −0.18; IR (KBr): ν 2959, 2927, 2868, 2156, 1456, 1436 cm^{-1}; HRMS (ESI-TOF): m/z calcd for $C_{33}H_{49}O_2Si_2$ [M + H^+]: 533.3271; found: 533.3257.

3,5-Diethynyl-4-(methoxymethoxy)-2',4',6'-triisopropyldiphenyl (11)

To a mixture of **10** (1.5 g, 2.8 mmol), THF (72 mL), and H_2O (1.0 mL) was added Bu_4NF (TBAF, 1.0 M in THF, 8.4 mL, 8.4 mmol) at 0 °C, and this mixture was allowed to room temperature with stirring for 50 min. The resulting mixture was washed with brine, dried over Na_2SO_4, concentrated with a rotary evaporator, and subjected to silica gel column chromatography to give **11** (1.0 g, 91%) as a colorless solid. M.p. 199−202 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.29 (s, 2 H), 7.03 (s, 2 H), 5.44 (s, 2 H), 3.73 (s, 3 H), 3.28 (s, 2 H), 2.92 (septet, J = 6.9 Hz, 1 H), 2.57 (septet, J = 6.9 Hz, 2 H), 1.29 (d, J = 6.8 Hz, 6 H), 1.09 (d, J = 6.4 Hz, 12 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.7, 148.5, 146.7, 139.1, 136.6, 136.0, 134.4, 120.7, 116.5, 99.4, 81.8, 79.8, 64.6, 57.8, 34.3, 30.2, 24.2, 24.1; IR (KBr): ν 3268, 2961, 2926, 2869, 1464, 1436 cm^{-1}; HRMS (ESI-TOF): m/z calcd for $C_{27}H_{32}NaO_2$ [M + Na$^+$]: 411.2300; found: 411.2317.

3-(3-Hydroxy-3-methyl-1-butynyl)-5-iodo-4-(methoxymethoxy)-2',4',6'-triisopropyldiphenyl (12)

A mixture of THF (300 mL) and i-Pr_2NH (300 mL) was bubbled with argon for 30 min, and to this mixture were added **9** (15 g, 25 mmol), K_2CO_3 (14 g, 100 mmol), $Pd(PPh_3)_4$ (2.9 g, 2.5 mmol), CuI (96 mg, 0.51 mmol), and 3-methyl-3-butyn-2-ol (1.5 g, 18 mmol). The reaction mixture was stirred for 30 min at room temperature and then additionally stirred for 14 h under reflux. The resulting mixture was filtered through a Florisil bed, concentrated with a rotary evaporator, and subjected to silica gel column chromatography (eluent: hexane/$CHCl_3$ = 2:1 to $CHCl_3$) to give **12** (6.4 g, 66%) as a reddish brown solid. M.p. 45−47 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.60 (d, J = 1.6 Hz, 1 H), 7.20 (d, J = 2.0 Hz, 1 H), 7.03 (s, 2 H), 5.36 (s, 2 H), 3.77 (s, 3 H), 2.92 (septet, J = 6.9 Hz, 1 H), 2.57 (septet, J = 6.8 Hz, 2 H), 2.43 (s, 1 H), 1.28 (d, J = 6.8 Hz, 6 H), 1.11−1.08 (m, 12 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.4, 148.6, 146.5, 140.8, 138.3, 135.0, 134.1, 120.6, 116.2, 99.5, 99.0, 91.7, 78.2, 65.6, 58.5, 34.3, 31.2, 30.2, 24.19, 24.16, 24.0; IR (KBr): ν 3420 (br), 2960, 2925, 2867, 1457, 1436 cm^{-1}; HRMS (ESI-TOF): m/z calcd for $C_{28}H_{37}INaO_3$ [M + Na$^+$]: 571.1685; found: 571.1709.

3-((*tert*-Butyldimethylsilyl)ethynyl)-5-(3-hydroxy-3-methyl-1-butynyl)-4-(methoxymethoxy)-2',4',6'-triisopropyldiphenyl (13)

A mixture of THF (50 mL) and i-Pr_2NH (60 mL) was bubbled with argon for 30 min, and to this mixture were added subsequently K_2CO_3 (3.6 g, 26 mmol), $Pd(PPh_3)_4$ (0.37 g, 0.32 mmol), a solution of **12** (3.5 g, 6.4 mmol) in THF (10 mL), CuI (25 mg, 0.13 mmol), and (*tert*-butyldimethylsilyl)acetylene (TBSA, 3.6 g, 26 mmol). The reaction mixture was stirred for 30 min at room temperature and additionally stirred for 13 h under reflux. The resulting mixture was filtered through a Florisil bed, concentrated with a rotary evaporator, and subjected to silica gel column chromatography (eluent: hexane/$CHCl_3$ = 1:1) to give **13** (3.2 g, 89%) as a yellow solid. M.p. 62-65 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.23 (d, J = 2.4 Hz, 1 H), 7.18 (d, J = 2.4 Hz, 1 H), 7.03 (s, 2 H), 5.43 (s, 2 H), 3.75 (s, 3 H), 2.92 (septet, J = 6.9 Hz, 1 H), 2.59 (septet, J = 6.7 Hz, 2 H), 1.28 (d, J = 7.2 Hz, 6 H), 1.09 (d, J = 7.2 Hz, 12 H), 0.98 (s, 9 H), 0.17 (s, 6 H) (A small amount of impurity was observed); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.8, 148.4, 146.7, 146.4, 136.4, 135.5, 135.1, 134.7, 120.6, 117.3, 116.8, 101.7, 99.1, 98.2, 97.6, 78.5, 65.7, 57.8, 34.3, 31.3, 30.22, 30.19, 26.1, 24.3, 24.24, 24.21, 24.19, 24.1, 16.7, −4.68; IR (KBr): ν 3446 (br), 2959, 2930, 2859, 2155, 2115, 1456, 1436 cm^{-1}; HRMS (ESI-TOF): m/z calcd for $C_{36}H_{52}NaO_3Si$ [M + Na$^+$]: 583.3583; found: 583.3606.

3-((*tert*-Butyldimethylsilyl)ethynyl)-5-ethynyl-4-(methoxymethoxy)-2',4',6'-triisopropyldiphenyl (14)

A solution of **13** (1.7 g, 3.0 mmol) in toluene (200 mL) was heated to 120 °C using a Dean-Stark apparatus. Keeping that temperature, ground NaOH (0.18 g, 4.4 mmol) was added to this solution, which was stirred for 1 h, and ground NaOH (0.088 g, 2.2 mmol) was added again to the solution. The reaction mixture was additionally stirred for 30 min at 120 °C and filtered after cooling to room temperature. The filtrate was concentrated with a rotary evaporator and subjected to silica gel column chromatography (eluent: hexane/AcOEt = 70:1) to give **14** (1.2 g, 84%) as a yellow solid. M.p. 102−106 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.28−7.26 (m, 2 H), 7.04 (s, 2 H), 5.45 (s, 2 H), 3.73 (s, 3 H), 3.25 (s, 1 H), 2.92 (septet, J = 6.8 Hz, 1 H), 2.66−2.55 (m, 2 H), 1.29 (d, J = 7.2 Hz, 6 H), 1.11−1.08 (m, 12 H), 0.98 (s, 9 H), 0.17 (s, 6 H) (A small amount of impurity was observed); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 160.7, 150.6, 148.8, 138.2, 137.6, 122.8, 122.7, 119.4, 118.6, 103.6, 101.3, 100.0, 83.6, 59.9, 36.4, 32.3, 28.2, 26.4, 26.35, 26.28, 26.2, 18.8, −2.6 (A small amount of impurity was observed); IR (KBr): ν 3270, 2960, 2928, 2866, 2153, 1464, 1435 cm^{-1}; HRMS (ESI-TOF): m/z calcd for $C_{30}H_{38}NaO_3$ [M + Na$^+$]: 525.3165; found: 525.3164.

I-pyridine-(MOM-phenol)-pyridine-I Trimer 16

A mixture of THF (37 mL) and i-Pr_2NH (37 mL) was bubbled with argon for 30 min, and to this mixture were added 2,6-diiodo-4-(octyloxy)pyridine[7] (**15**, 2.5 g, 5.3 mmol), $Pd(PPh_3)_4$ (0.52 g, 0.45 mmol), K_2CO_3 (0.49 g, 3.6 mmol), and **11** (0.35 g, 0.89 mmol). The reaction mixture was stirred for 16 h under reflux and filtered through a Florisil bed The filtrate was concentrated with a rotary evaporator and subjected to silica gel column chromatography (eluent: hexane/AcOEt = 40:1 to 5:1) to give recovered **15** and product **16** (0.61 g, 65%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37 (s, 2 H), 7.21 (d, J = 2.0 Hz, 2 H), 7.04 (s, 2 H), 6.99 (d, J = 2.4 Hz, 2 H), 5.51 (s, 2 H), 3.98 (t, J = 6.6 Hz, 4 H), 3.76 (s, 3 H), 2.93 (septet, J = 7.0 Hz, 1 H), 2.58 (septet, J = 6.8 Hz, 2 H), 1.82−1.75 (m, 4 H), 1.45−1.29 (m, 26 H), 1.09 (d, J = 6.8 Hz, 12 H), 0.89 (t, J = 6.6 Hz, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.0, 158.6, 148.5, 146.6, 144.2, 136.9, 136.0, 134.2, 120.61, 120.59, 117.9, 116.5, 114.1, 99.7, 91.8, 86.1, 68.7, 58.0, 34.3, 31.7, 30.3, 29.2, 29.1, 28.7, 25.8, 24.2, 24.0, 22.6, 14.1; IR (KBr): ν 2958, 2926, 2854, 2219, 1576, 1533 cm^{-1}; HRMS (ESI-TOF): m/z calcd for $C_{53}H_{69}I_2N_2O_4$ [M + H$^+$]: 1051.3347; found: 1051.3321.

TBSA-(MOM-phenol)-pyridine-(MOM-phenol)-TBSA Trimer 17

A mixture of THF (100 mL) and i-Pr_2NH (100 mL) was bubbled with argon for 30 min, and to this mixture were added **15** (0.31 g, 0.68 mmol), $Pd(PPh_3)_4$ (79 mg, 0.068 mmol), K_2CO_3 (0.38 g, 2.7 mmol), CuI (2.6 mg, 0.014 mmol), and **14** (1.4 g, 2.7 mmol). The reaction mixture was stirred for 30 min at room temperature and additionally stirred for 13 h under reflux. The resulting mixture was filtered through a Florisil bed, concentrated with a rotary evaporator, and subjected to silica gel column chromatography (eluent: hexane/AcOEt = 50:1 to 20:1) to give **17** (0.81 g 87%) as a colorless solid. M.p. 88−90 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.33 (d, J = 1.6 Hz, 2 H), 7.28 (d, J = 2.4 Hz, 2 H), 7.03 (s, 4 H), 6.99 (s, 2 H), 5.50 (s, 4 H), 4.01 (t, J = 6.4 Hz, 2 H), 3.75 (s, 6 H), 2.92 (septet, J = 6.9 Hz, 2 H), 2.60 (septet, J = 6.8 Hz, 4 H), 1.82−1.78 (m, 2 H), 1.46−1.41 (m, 2 H), 1.37−1.26 (m, 20 H), 1.10−1.07 (m, 24 H), 0.98 (s, 18 H), 0.89 (t, J = 6.2 Hz, 3 H), 0.17 (s, 6 H) (A small amount of impurity was observed); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.4, 146.7, 144.7, 136.5, 136.4, 135.3, 134.5, 130.9, 120.6, 117.3, 116.6, 113.3, 101.5, 99.3, 97.9, 92.4, 85.4, 57.9, 34.3, 31.8, 30.2, 29.2, 26.1, 26.0, 25.9, 24.3, 24.2, 24.1, 22.6, 16.7, 14.1, −4.7; IR (KBr): ν 2958, 2928, 2858, 2218, 2156, 1581,

1550, 1456 cm^{-1}; HRMS (ESI-TOF): *m*/*z* calcd for $C_{79}H_{110}NO_5Si_2$ [M + H^+]: 1208.7923; found: 1208.7955.

Ethynyl-(MOM-phenol)-pyridine-(MOM-phenol)-ethynyl Trimer 18

To a mixture of **17** (0.70 g, 0.58 mmol), THF (80 mL), and H_2O (1.0 mL) was added TBAF (1.0 M in THF, 1.2 mL, 1.2 mmol) at 0 °C, and this mixture was stirred for 30 min at 0 °C, allowed to room temperature, and additionally stirred for 2.5 h at room temperature. The resulting mixture was quenched with brine and extracted with AcOEt (50 mL × 2). The combined AcOEt layer was dried over Na_2SO_4, concentrated with a rotary evaporator, and subjected to silica gel column chromatography (eluent: hexane/AcOEt = 20:1) to give **18** (0.57 g, 100%) as a pale yellow solid. M.p. 77−80 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36 (d, *J* = 2.0 Hz, 2 H), 7.30 (d, *J* = 2.4 Hz, 2 H), 7.03 (s, 4 H), 6.99 (s, 2 H), 5.49 (s, 4 H), 4.02 (t, *J* = 6.6 Hz, 2 H), 3.75 (s, 6 H), 3.28 (s, 2 H), 2.92 (septet, *J* = 7.0 Hz, 2 H), 2.58 (septet, *J* = 6.9 Hz, 4 H), 1.82−1.78 (m, 2 H), 1.48−1.41 (m, 2 H), 1.38−1.27 (m, 20 H), 1.09−1.07 (m, 24 H), 0.89 (t, *J* = 7.0 Hz, 3 H) (A small amount of *t*-$BuMe_2SiOH$ was observed); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.3, 158.7, 148.5, 146.6, 144.6, 136.7, 136.3, 135.7, 134.3, 120.6, 116.6, 113.4, 99.5, 92.6, 85.2, 81.8, 79.8, 57.9, 34.3, 31.8, 30.2, 29.23, 29.18, 28.8, 25.9, 24.24, 24.19, 24.0, 22.6, 14.1 (A small amount of *t*-$BuMe_2SiOH$ was observed); IR (KBr): ν 3275, 2960, 2926, 2869, 2220, 1581, 1550, 1458 cm^{-1}; HRMS (ESI-TOF): *m*/*z* calcd for $C_{67}H_{82}NO_5$ [M + H^+]: 980.6193; found: 980.6144.

3-MOM

A mixture of THF (270 mL) and *i*-Pr_2NH (310 mL) was bubbled with argon for 30 min. To this mixture were added K_2CO_3 (56 mg, 0.41 mmol), $Pd(PPh_3)_4$ (12 mg, 0.010 mmol), and **16** (0.11 mg, 0.10 mmol), and the mixture was stirred for 10 h at room temperature. After the addition of CuI (0.38 mg, 0.0020 mmol), a solution of **18** (0.10 g, 0.10 mmol) in THF (40 mL) was added to the mixture dropwise during 1.5 h. The reaction mixture was stirred for 14 h under reflux, filtered through a Florisil bed, concentrated with a rotary evaporator, and subjected to silica gel column chromatography (eluent: hexane/$CHCl_3$ = 2:1) and gel permeation chromatography (Shodex K-2001 and Shimadzu Shim-pack K-2002, eluent: $CHCl_3$) to give **3-MOM** (40 mg, 22%) as a yellow solid. M.p. 148−150 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37 (s, 6 H), 7.06 (s, 6 H), 6.94 (s, 6 H), 5.73 (s, 6 H), 4.05 (s, 9 H), 4.00 (t, *J* = 6.6 Hz, 6 H), 2.94 (septet, *J* = 6.9 Hz, 3 H), 2.67 (septet, *J* = 7.0 Hz, 6 H), 1.80−1.74 (m, 6 H), 1.44−1.40 (m, 6 H), 1.40−1.25 (m, 42 H), 1.13 (d, *J* = 6.4 Hz, 36 H), 0.87 (t, *J* = 6.8 Hz, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.0, 160.0, 148.5, 146.8, 144.7, 135.5, 134.6, 120.6, 117.0, 112.9, 100.2, 93.2, 84.8, 68.4, 58.6, 34.3, 31.8, 30.3, 29.21, 29.18, 28.8, 25.8, 24.3, 24.10, 24.07, 22.6, 14.1; IR (KBr): ν 2958, 2925, 2866, 2220, 1582, 1550, 1457 cm^{-1}; HRMS (ESI-TOF): *m*/z calcd for $C_{120}H_{147}N_3O_9$ [M + H^+]: 1776.1275; found: 1776.1249.

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To a solution of **3-MOM** (0.18 mg, 0.10 mmol) in CH_2Cl_2 (70 mL) was added trifluoroacetic acid (TFA, 3.5 mL) at 0 °C. The mixture was stirred for 2 h at that temperature, then neutralized with saturated aq $NaHCO_3$, washed with brine, and dried over Na_2SO_4. The organic layer was concentrated with a rotary evaporator and subjected to silica gel column chromatography (eluent: hexane/$CHCl_3$ = 1:2) to afford **3** (165 mg, 100%) as a yellow solid. M.p. 230 °C (dec); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.31 (s, 6 H), 7.06 (s, 6 H), 6.95 (s, 6 H), 4.02 (t, *J* = 6.4 Hz, 6 H), 2.94 (septet, *J* = 6.8 Hz, 3 H), 2.72 (septet, *J* = 6.9 Hz, 6 H), 1.83−1.74 (m, 6 H), 1.45−1.26 (m, 48 H), 1.13 (d, *J* = 6.8 Hz, 36 H), 0.87 (t, *J* = 6.6 Hz, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.4, 148.3, 147.0, 144.2, 135.4, 135.0, 120.5, 112.7, 109.5, 93.3, 68.5, 34.3, 31.7, 30.3, 29.7, 29.24, 29.19, 29.16, 28.7, 25.8, 24.4, 24.2, 24.1, 22.6, 14.1; IR (KBr): ν 3446 (br), 2959, 2926, 2867, 2217, 1583, 1550, 1464 cm^{-1}; HRMS (ESI-TOF): *m*/z calcd for $C_{114}H_{135}N_3O_6$ [M + H^+]: 1644.0435; found: 1644.0462.

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Keywords: Host-guest systems • Macrocycles • Glycosides • Hydrogen bonds •Shape-persistent macrocycles

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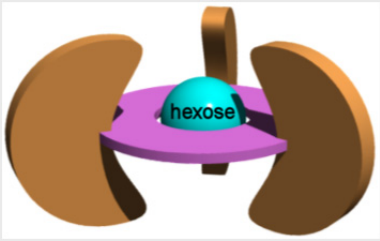
Grasp Hexose: D_{3h}-Symmetrical shape-persistent macrocycles (SPMs) were developed as a synthetic host for saccharide recognition. They consisted of phenol–acetylene–pyridine structure, and steric hindrance was introduced on them to prevent self-aggregation. Strong affinity for alkyl hexosides such as glucoside and mannoside was shown in organic solvent. In addition, solid-liquid extraction and liquid-liquid transport of native hexoses could be performed.



Hajime Abe, Tetsuhiro Yoneda, Yuki Ohishi, and Masahiko Inouye**

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D_{3h}-Symmetrical Shape-Persistent Macrocycles Consisting of Pyridine–Acetylene–Phenol Conjugates as an Efficient Host Architecture for Saccharide Recognition