External-stimulus-triggered conformational inversion of mechanically self-locked pseudo[1]catenate and gemini-catenanes based on A1/A2-alkyne–azide-difunctionalized pillar[5]arenes†

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Herein, we report a methodology for constructing mechanically self-locked molecules (MSMs) through the efficient intramolecular copper(i)-catalyzed alkyn–azide cycloaddition (CuAAC) of self-threaded A1/A2-azido-propargyl-difunctionalized pillar[5]arenes. The obtained monomeric “pseudo[1]catenate” and dimeric “gemini–catenate” were isolated and fully characterized using mass spectrometry, nuclear magnetic resonance (NMR) spectroscopy, and X-ray crystallography. Upon investigation by 1H NMR spectroscopy in chloroform, the observed motion for the threaded ring in the pseudo[1]catenate was reversibly controlled by the temperature, as demonstrated by variable-temperature 1H NMR studies. Two gemini–catenate stereoisomers were also isolated in which the two pillar[5]arene moieties threaded by two decyl chains were aligned in different topologies. Furthermore, the conformational inversion of pseudo[1]catenate and the gemini–catenanes triggered by solvents and guests was investigated and probed using 1H NMR spectroscopy, isothermal titration calorimetry, and single-crystal X-ray analysis.

Introduction

Mechanically interlocked molecules (MIMs) such as catenanes, rotaxanes, pseudo-rotaxanes, and molecular knots (knotanes) have been extensively synthesized and studied in recent decades, and they have found many applications in the design of molecular machines, chemical probes, molecular catalysts, and drug delivery systems. Macroyclic molecules such as crown ethers, cyclodextrin, cucurbituril, and calixarene are mainly used in the construction of MIM-based pseudo-rotaxanes, rotaxanes, and catenanes. In addition, pillar[n]arenes have recently attracted considerable interest due to their relative ease of formation, their facile functionalization, and their exceptional ability to selectively encapsulate different kinds of guest molecules. Taking advantage of their excellent host–guest properties, the pillar[5]arene-based [2]rotaxane was first produced through end-capping by the reaction between a diamine axle and a bulky aldehyde stopper; however, the product yield was low. Subsequently, many examples of pillar[5]arene-based [2]rotaxanes were reported based on the improved encapsulation of the axle and an optimized capping procedure. In addition, pillar[5]arene-based [1]rotaxanes in which the rotor and the axle are bound covalently to form a macrocyclic compound were synthesized by capping the self-inclusion axle of the pseudo[1]rotaxane. Moreover, a simple [2]catenate, in which two interlocked macrocycles were present, was prepared from a guest pyridinium derivative bearing alkene groups at both ends followed by a ring-closing metathesis reaction. Mechanically self-locked molecules (MSMs), where one of the covalently linked macrocycles is threaded into the other macrocycle, have been found to offer fascinating molecular architectures and topological features. Pseudo[1]catenanes or MSMs in which the guest alkyl cyclic chain is connected to one pillar[5]arene were initially produced from difunctionalized alkyl groups at the A1/A2 positions of the macrocycle and a 1,12-diazidododecane guest via a copper(i)-catalyzed alkyn–azide 1,3-dipolar cycloaddition “click” (CuAAC) reaction. Another example includes the preparation of a pseudo[1]catenate by a reaction between 1,4-dicyanobutane and 1,8-diaminoctane guests (i.e., bearing different lengths of diaminoalkane chains) with difunctionalized amino or carboxy groups present at the A1/A2 positions of the pillar[5]arene, respectively. More recently, pseudo[1]catenanes based on the pillar[5]thiacrown and pillar[5]azacrown structures, wherein planar chiral inversion is triggered by a metal cation or acid and is controlled by an anion or a base, have been reported. In addition, the chirality switching of planar chiral pseudo[1]catenanes has been reported to be regulated by guest molecules.

Since the early discovery of pillararenes, the CuAAC reaction has been employed in their functionalization to construct
a wide variety of molecular architectures in high yields. Importantly, this reaction exhibits an excellent functional group tolerance, in addition to being compatible with a wide range of substrates.\(^{24-31}\) Thus, we report the synthesis of a pseudo[1]catenane base of self-inclusion A1/A2-asymmetric difunctionalized pillar[5]arenes. In solution, stable pseudo[1]rotaxanes that are formed from the self-inclusion of the straight-chain bromodecyl group on the pillar[5]arene rim, enable the construction of pseudo[1]catenane and gemini-catenane structures via the conversion of bromine to an azide functional group followed by intramolecular CuAAC reaction. The role of external stimuli (i.e., a solvent or guest) in governing the conformational changes from self-included to dethreaded structures via host-guest interactions, which can consequently trigger conformational inversion, are probed by nuclear magnetic resonance (NMR) spectroscopy, isothermal titration calorimetry (ITC), and X-ray single-crystal diffraction. To the best our knowledge, this is the first report of intramolecular self-locked pseudo[1]catenane and 1 : 1 gemini-catenane structures based on A1/A2-asymmetric difunctionalized pillar[5]arenes and their conformational inversion.

### Results and discussion

#### Synthesis

Many pseudo[1]rotaxane based pillar[n]arenes have been reported in recent years due to their ability for self-inclusion when a long chain substituent is present on the macrocyclic rim. Recently, we reported the synthesis of a series of A1/A2-asymmetric-defunctionalized pillar[5]arenes and their concentration-dependent supramolecular self-assembly behaviors.\(^{32}\) Based on such systems, precursor compound 1-(10-bromodecyl)-4-propargyloxybenzene was synthesized via a two-step reaction starting from hydroquinone. An A1/A2-asymmetric difunctionalized pillar[5]arene bearing propargyl and bromo functional groups (Pillar-1) was then synthesized by the condensation of an asymmetric hydroquinone derivative and 1,4-dimethoxybenzene in a 1 : 4 ratio in the presence of paraformaldehyde and BF\(_3\)-OEt\(_2\), as shown in Scheme 1. The azide derivative, Pillar-2, was obtained following the reaction of bromo-derivative Pillar-1 with sodium azide (NaN\(_3\)) in DMF at room temperature (Scheme 1).

The \(^1\)H NMR spectrum of Pillar-1 (Fig. S6) shows a high upfield shift for the methylene proton resonances of the 10-bromodecylxoyl arm, thereby indicating the successful formation of the pseudo[1]rotaxane. Moreover, the self-inclusion of the long alkyl chain inside the pillar[5]arene cavity was not affected when the \(^1\)H NMR spectrum of Pillar-1 was recorded at a higher temperature of 313 K (Fig. S6). To investigate whether the inclusion behavior of the 10-bromodecylxoyl chain in the pillar[5]arene cavity involved the self-inclusion of a double-threaded dimer (i.e., an interpenetration structure) or an n-mer, \(^1\)H NMR spectroscopy was carried out at a range of Pillar-1 concentrations (1–64 mM) in chloroform-\(d\) at 298 K (Fig. S7). The insignificant changes observed in the chemical shift data clearly demonstrate that the behavior of Pillar-1 is concentration independent, suggesting that Pillar-1 exists predominantly in its single aggregate form (i.e., the pseudo[1]rotaxane). Further evidence was obtained from two-dimensional diffusion-ordered \(^1\)H NMR (DOSY) experiments. More specifically, the DOSY spectra of Pillar-1 at concentrations of 2 and 50 mM revealed a single set of signals, confirming the presence of a single aggregate form in solution. In the case where multiple aggregate sizes exist, a change in the diffusion coefficient (\(D\)) would be expected in the DOSY spectrum because larger aggregates possess larger hydrodynamic radii (\(R\)), and \(R\) is inversely proportional to \(D\) according to the Strokes–Einstein equation [\(D = \frac{k_BT}{6\pi\eta R}\)], where \(T\) denotes the temperature, \(k_B\) is the Boltzmann constant, and \(\eta\) is the dynamic viscosity of the solvent. As the concentration of Pillar-1 was increased from 2 to 50 mM, the weight-averaged diffusion coefficient (\(D\)) decreased from 6.72 \(\times\) 10\(^{-10}\) to 5.62 \(\times\) 10\(^{-10}\) m\(^2\) s\(^{-1}\), which was insufficient to suggest variation in the average aggregate dimensions at increasing concentrations (\(D_1/D_2 = 1.19\)). Similarly, the azide derivative Pillar-2 showed an upfield shift for the protons of the long alkyl chain, thereby further indicating that self-inclusion of the alkyl chain took place inside the pillar[5]arene cavity.

Subsequently, azide derivative Pillar-2 containing the long alkyl chain was subjected to the CuAAC reaction at room temperature as outlined in Scheme 1. Thin-layer chromatography confirmed the consumption of the starting material, and three distinct spots were separated by column chromatography using a dichloromethane/ethyl acetate mixture for elution (80 : 20, v/v). The first spot gave a high-resolution mass spectrometry (HRMS) signal at \(m/z\) 942.4905 [M + H]\(^+\), which is similar to the mass of Pillar-2 (i.e., \(m/z = 941.4823 \text{[M]}\)). However, the \(^1\)H NMR spectra of Pillar-2 and the unknown compound corresponding to the first spot differed significantly (Fig. S9) as did their melting points, i.e., 135–136 °C for Pillar-2, and 209–210 °C for the unknown. It should be noted here that the latter melting point corresponds to that of Pillar-3M. Thus,
the notable upfield chemical shift observed for the methylene protons of the alkyl chain along with higher splitting pattern that reflects their magnetically nonequivalent environments indicate the formation of a threaded self-locked pseudo[1]catenate, Pillar-3M, and precludes the formation of an endo-spirocyclic-like structure (Fig. 1a). Formation of the aromatic triazole moiety in this structure was confirmed by the downfield shift of the methine H12 proton from 2.16 to 5.65 ppm, in addition to the newly formed peaks observed at 124.5 and 140.6 ppm in the $^{13}$C NMR spectrum of Pillar-3M (Fig. S35†).

HRMS analysis of the isolated second (Pillar-3D1, vide infra) and third (Pillar-3D2, vide infra) spots showed similar m/z values of 1883.9242 [M + H]$^+$ and 1883.9063 [M + H]$^+$, respectively, which represent double the mass of Pillar-3M. It was therefore suggested that these dimeric products are either nonthreaded 1 : 1 dimer or self-locked gemini-catenanes.19 The presence of a partially reacted dimer was ruled out since the $^1$H NMR data indicated the absence of a resonance corresponding to a propargyl group. Moreover, the unusual chemical upfield shift of the decamethylene protons excluded the presence of a nonthreaded dimer (Fig. 1). Close inspection of the $^1$H NMR spectra shown in Fig. 1 indicates significant differences in the chemical shifts for both the aliphatic and aromatic regions of the spectrum that was assumed to correlate to Pillar-3D1 (Fig. 1b) when compared to the spectrum of Pillar-3M (Fig. 1a), whereas the spectrum that was considered to correlate to Pillar-3D2 (Fig. 1c) generally exhibited similar resonances to the $^1$H NMR spectrum of Pillar-3M. For example, the methylene H11 protons of Pillar-3D1 split into two sets of signals with noticeably higher upfield shifts (i.e., 4.74 and 4.85 ppm) compared to the same methylene signal in the Pillar-3M pseudo[1]catenate (5.49 and 5.58 ppm) and in the gemini-catenane-type structure Pillar-3D2 (5.52 and 5.59 ppm). Similarly, H8 split into two sets of signals with higher upfield shifts of −1.75 and −1.65 ppm, whereas the H8 protons of Pillar-3M and Pillar-3D2 appeared as single signals at lower upfield shifts of −1.02 and −1.03 ppm, respectively. These significant Fig. 2 Different views of the X-ray single-crystal structure of the Pillar-3D1 gemini-catenane, in (a) CDCl$_3$ and (b) CD$_2$Cl$_2$. Red, grey/green/light blue, and purple represent oxygen, carbon, and nitrogen, respectively. Hydrogen atoms are omitted for clarity.
oxygen, carbon, and nitrogen, respectively. Hydrogen atoms are omitted for clarity.

Differences in the chemical shifts observed for Pillar-3D1 suggest that the two pillar[5]arene rings are aligned in opposite directions (i.e., C2-symmetric, erythro), whereas Pillar-3D2 presents as the S2-symmetric isomer (achiral, threo). All our attempts to separate the stereoisomers of Pillar-3M and Pillar-3D using chiral HPLC were unsuccessful at this point. The opposite alignment of the pillararene rings in Pillar-3D1 was confirmed by single-crystal X-ray diffraction measurements following the growth of a suitable crystal from CHCl3 by the slow evaporation method (Fig. 2a). Unfortunately, all attempts to grow suitable crystals of Pillar-3M and Pillar-3D2 were unsuccessful. The melting points of the compounds isolated from these two spots were also different, i.e., 252–253 °C (second spot, Pillar-3D1) and 233–234 °C (third spot, Pillar-3D2).

The unsymmetrical nature of the threaded cyclic system in Pillar-3M enables the molecular motions to be monitored by simple 1H NMR spectroscopy. Interestingly, when the 1H NMR spectrum was recorded at 298 K in chloroform-d immediately after the preparation of Pillar-3M, the H12 methine hydrogen atom of the triazole moiety appeared at 6.25 ppm, whereas the H9 and H10 methylene protons of the octyl chain appeared as two sets of signals at −0.64 and −0.52 ppm and at 2.65 and 3.05 ppm, respectively (Fig. 3a). After allowing the NMR solution to stand for 24 h, the H9, H10, and H12 protons moved upfield, whereas the remainder of the aliphatic methylene protons shifted downfield (Fig. 3b). In addition, the H11 methylene protons shifted slightly downfield due to the effect of the deshielding region of the pillararene system. A similar movement of the proton signals was observed after 48 h (Fig. 3c), while beyond 48 h, the system was in equilibrium and no further shifts were detected. These results indicate that the triazole moiety moves inside the pillar[5]arene cavity and that the alky1 methylene chain moves out of the cavity due to aromatic donor-acceptor interactions between the triazole moiety and the aromatic groups in the pillararene ring. Upon drying and redissolving the sample in chloroform-d, the protons signals reset back to their original positions (Fig. 3a).

The observed molecular motion of the threaded cyclic ring in CDCl3 was further investigated by variable-temperature (VT) 1H NMR experiments (Fig. 4). Most notably, the chemical shift of the H12 methine proton of the triazole ring shifted gradually upfield from 6.49 to 5.15 ppm when the temperature was increased from −40 to 50 °C. In contrast, a downfield shift was observed for the H8 methylene protons, i.e., from −1.40 to −0.63 ppm. These results indicate that increasing the temperature led to movement of the triazole fragment inside the pillar[5]arene cavity, while at lower temperatures, the triazole ring was able to move outside of the pillararene cavity. The observed molecular motion of the threaded chain was therefore confirmed to be a reversible process induced by changes in temperature. No temperature-induced conformer inversion was observed during the VT-NMR study.

**Conformational inversion studies.** The chirality switching of chiral-planar pseudo[1]catenanes triggered by solvents,18 metal cations,21 acids,22 and guest molecules23 has been well documented in the literature. Such inversion occurs when one of the...
incorporated macrocycles in the bicyclic structure is dethreaded by aromatic ring tumbling. Thus, we screened a range of solvents (i.e., DMSO-$d_6$, pyridine-$d_5$, THF-$d_{10}$, DMF-$d_7$, and CD$_2$Cl$_2$) for their ability to trigger the inversion of the Pillar-3M_pseudo[1]catenane. The $^1$H NMR spectra recorded in DMSO-$d_6$, pyridine-$d_5$, and THF-$d_{10}$ showed no significant changes in chemical shifts for the proton signals of Pillar-3M, indicating that dethreading did not take place (Fig. S10†). In contrast, the proton signals of the decylene chain coalesced and shifted downfield when the $^1$H NMR spectra were recorded in DMF-$d_7$ and CD$_2$Cl$_2$ (Fig. S11†). For comparison, the stacked $^1$H NMR spectra of Pillar-3M in CDCl$_3$ and CD$_2$Cl$_2$ at 298 K are shown in

Fig. 4  Variable-temperature $^1$H NMR spectra (600 MHz, CDCl$_3$) of the Pillar-3M_pseudo[1]catenane.

Fig. 5  $^1$H NMR spectra (600 MHz, CDCl$_3$, 298 K) of (a) the Pillar-3M_pseudo[1]catenane at a concentration of 25 mM, and (b) and (c) Pillar-3M (25 mM) in the presence of the adiponitrile guest G at concentrations of (b) 7.5 mM and (c) 25 mM.
Fig. S12.† In the case of the CDCl₃ solvent system, the location of the methylene proton signals of the decylene chain in the far upfield region indicates that **Pillar-3M** adopted a self-included conformation (pseudo[1]catenane) as a result of the shielding effect of the pillar[5]arene cavity (Fig. S12a†). In contrast, the ¹H NMR spectrum of **Pillar-3M** in CD₂Cl₂ revealed the presence of a dethreaded conformer due to peak coalescence and the downfield chemical shift of the decylene chain proton signals (Fig. S12b†). On the other hand, solvent trigger conformational inversion of gemini-catenanes from self-included “in” to the de-threading “out” conformers involve simultaneous tumbling of the functionalized aromatic units. Stacked ¹H NMR spectra for gemini-catenane, **Pillar-3D1** in CDCl₃ and CD₂Cl₂ are shown in Fig. S13.†

Similarly, the threaded conformer **Pillar-3D1** in CDCl₃, show high upfield chemical shift for the methylene proton signals for the decylene chain caused by the shielding effect of pillar[5] arene cavity (Fig. S13a†), while in CD₂Cl₂, the decylene chain lactated outside the macrocyclic cavity as indicated by the downfield chemical shift and the coalesce of the methylene proton signals (Fig. S13b†). ¹H NMR recorder in CD₂Cl₂ for **Pillar-3D2** shows similar behavior to **Pillar-3D1** (Fig. S20†). The conformational assignment of the de-threaded conformer of **Pillar-3D1** was confirmed by single-crystal X-ray diffraction measurement when suitable crystal for analysis obtained from CH₂Cl₂/DMF solvent mixture (Fig. 2b).

Based on previous literature, it was considered that in CD₂Cl₂, the observed conformational change from self-included to dethreaded conformers was driven by host–guest complexation between the pillar[5]arene cavity and the CD₂Cl₂ solvent.²³ To further investigate the influence of host–guest complexation on the conformational change, adiponitrile was selected as a guest due to its ability to form highly stable 1:1 host–guest complexes with pillar[5]arenes, and because of its effectiveness in the conformational inversion of pseudo[1]catenane-based pillar[5]arenes.¹⁹,²³ Thus, Fig. 5 shows the ¹H NMR spectra recorded for the complexation of **Pillar-3M** with different concentrations of the adiponitrile guest G in CDCl₃. Upon the addition of 1 molar equivalent of G to **Pillar-3M**, significant downfield shifts were observed for the methylene proton signals of the decylene chain, and the methylene proton signals of G appeared as highly shielded signals (Fig. 5c) as a result of de-threading of the alkyl chain and guest encapsulation inside the pillar[5]arene cavity. At a lower guest concentration, signals

![Image 1](https://example.com/image1.png)

**Fig. 6** ¹H NMR spectra (600 MHz, CDCl₃, 298 K) of the **Pillar-3D1** gemini-catenane (10 mM) in the presence of different concentrations of the adiponitrile guest G.
corresponding to both the self-included and dethreaded conformers were observed in the $^1$H NMR spectrum (Fig. 5b).

The conformational inversion of Gemini-catenanes Pillar-3D1 and Pillar-3D2 promoted by the adiponitrile guest was then studied by $^1$H NMR spectroscopy. More specifically, inspection of $^1$H NMR spectra recorded in CDCl$_3$ upon the incremental addition of adiponitrile revealed that the inclusion of a single guest molecule in one pillar[5]arene cavity was sufficient to tumble the functionalized aromatic units of the Gemini-catenane and trigger chiral inversion. These results are supported by the crystal structure of Pillar-3D1 obtained after crystallization from CH$_2$Cl$_2$/DMF, which shows that only one pillar[5]arene cavity was occupied by a DMF molecule (Fig. S5†). The $^1$H NMR spectra of Pillar-3D1 obtained at different concentrations of adiponitrile are shown in Fig. 6. At a guest concentration of less than one equivalent, proton resonances corresponding to the threaded dimer were observed, and the addition of two equivalents of adiponitrile consolidated the experimentally-obtained binding molar ratio of 0.91 is close to unity, which indicates a 1 : 1 host-to-guest complexation ratio, wherein the association constant, $K_{11}$, was determined to be $4.93 \pm 0.24 \times 10^3$ M$^{-1}$. The negative enthalpy change ($\Delta H^\circ = -11.86$ kJ mol$^{-1}$) and positive entropy change ($\Delta S^\circ = 5.26$ kJ mol$^{-1}$) for this process indicate that the guest-promoted conformational inversion of Pillar-3M was driven by both enthalpically and entropically favorable changes, and thus, it is a spontaneous process (i.e., $\Delta G^\circ = -17.12$ kJ mol$^{-1}$). A similar trend was observed for the Pillar-3D1 and Pillar-3D2 Gemini-catenanes, with an increased contribution of favorable entropy changes being determined (Table 1). In both cases, the experimental binding molar ratio “n” was close to 2, which indicates a 1 : 2 host-to-guest complexation ratio with association constants, $K_{12}$, of $1.52 \pm 0.08 \times 10^5$ ($K_{11} = 1.43 \pm 0.11 \times 10^4$) and $1.44 \pm 0.14 \times 10^5$ ($K_{11} = 1.26 \pm 0.09 \times 10^4$) being determined for Pillar-3D1 and Pillar-3D2, respectively. For comparison, an analogous ITC host–guest complexation experiment was carried out using the permethylated DMP5 pillar[5]arene macrocycle at 10 mM in the presence of adiponitrile as the guest. The calculated thermodynamic parameters show that the molecular binding behavior is driven by van der Waals interactions, with a major contribution also being present from a particularly favorable enthalpy change ($\Delta H^\circ = -23.23$ kJ mol$^{-1}$; $T\Delta S^\circ = 0.25$ kJ mol$^{-1}$). The measured association constant for the complexation of DMP5 with adiponitrile ($K_{11} = 1.30 \pm 0.07 \times 10^4$ M$^{-1}$) was found to be approximately one order of magnitude higher than Pillar-3M due to the more readily accessible macrocyclic cavity that can easily accommodate the guest molecule.

### Table 1

| Host    | $\Delta H^\circ$ (kJ mol$^{-1}$) | $T\Delta S^\circ$ (kJ mol$^{-1}$ K$^{-1}$) | $K_4$ (M$^{-1}$) | Binding molar ratio (n) |
|---------|---------------------------------|----------------------------------------|----------------|------------------------|
| DMP5    | $-23.23$                        | $0.25$                                  | $1.30 \pm 0.07 \times 10^4$ | 0.85                    |
| Pillar-3M | $-11.86$                       | $5.26$                                  | $4.93 \pm 0.24 \times 10^3$ | 0.91                    |
| Pillar-3D1 | $-10.67$                      | $6.90$                                  | $1.52 \pm 0.08 \times 10^3$ | 1.94                    |
| Pillar-3D2 | $-9.55$                       | $8.48$                                  | $1.44 \pm 0.14 \times 10^3$ | 2.13                    |

* All titrations were carried out in chloroform at 25 °C with a fixed host concentration of 10 mM and varying guest concentrations. * Association constant $K_{12}$.

## Experimental

### Materials and methods

Nuclear magnetic resonance (NMR) spectroscopy was carried out on a Bruker Avance II 600 MHz spectrometer (Bruker, Germany). Electron impact ionization (EI) mass spectrometry was performed using a Thermo Scientific DFS High-Resolution GC/MS mass spectrometer (Thermo Scientific, USA). Electro-spray ionization in high-resolution mode was carried out using a Waters Xevo G2-S QToF LC MS/MS mass spectrometer (Waters, USA). Single-crystal data analysis was carried out using a Bruker X8 Prospector diffractometer (Bruker, Germany). Data were collected at $-123$ °C (Oxford Cryosystems, UK). Flash column chromatography was performed using silica gel (Silica gel 60, 40–60 mesh ASTM, EMD Millipore, Merck KGaA, Germany). The DMF, acetonitrile, and dichloroethane solvents were distilled prior to use. All other reagents and solvents were of reagent grade purity and were used without further purification. Permethylated-pillar [5]arene (DMP5) was synthesized according to the literature.17

### Preparation of single crystals for X-ray diffraction

Suitable single crystals of the synthesized inclusion complex Pillar-3D1 were grown by the slow solvent evaporation method from chloroform and a dichloromethane/DMF mixture. The data were collected on a Bruker X8 prospector diffractometer (Bruker, Germany) using Cu-K$_\alpha$ radiation at $-123$ °C. The reflection frames were then integrated with the Bruker SAINT Software package using a narrow-frame algorithm. Finally, the structure was solved using the Bruker SHELXTL Software Package and refined using SHELXL-2017/1. All non-hydrogen atoms were refined anisotropically and hydrogen atoms were refined using the riding model. CCDC 2049467 and 2081939.†

## ITC measurements

All ITC studies were carried out on an Affinity ITC system (TA Instruments, USA). The data were analyzed using NanoAnalyze, Version 3.10.0. For the ITC host–guest complexation
1-10-Bromodecyl)-4-propargylbenzene. 4-Propargyloxynphenol (2.20 g, 15 mmol) was dissolved in dry DMF (20 mL) at room temperature and potassium carbonate (2.80 g, 20 mmol) was added. The resulting solution was stirred for 30 min and then stirred further at 80 °C overnight after the addition of propargyl bromide (4.64 mL, 20 mmol). Then, the reaction mixture was poured into ice-cold water (250 mL) and the precipitate was filtered and washed with water (2 × 10 mL). The desired compound was then recrystallized from dichloromethane/methanol as a white solid (174 mg, 90%). Mp 135–136 °C. 1H NMR (600 MHz, CDCl3) δ: −0.15 (s, 2H), 0.05 (s, 2H), 0.22 (s, 4H), 0.72 (m, 2H), 1.04 (m, 2H), 1.23 (m, 2H), 1.43 (m, 2H), 1.75 (m, 2H), 2.07 (m, 3H), 3.64 (m, 2H), 3.69 (m, 12H), 3.84 (t, J = 6.6 and 6.0 Hz, 2H), 4.42 (t, J = 2.4 Hz, 2H), 6.70 (s, 1H), 6.73 (m, 3H), 6.79 (m, 4H), 7.48, 79.4, 113.7, 113.8, 113.8, 113.9, 114.1, 115.0, 115.1, 128.0, 128.3, 128.4, 128.4, 128.5, 128.6, 128.7, 148.9, 149.8, 150.6, 150.6, 150.7, 150.7, 150.8, 150.9. HRMS: (m/z) caleld for [M]+: 941.4821 (for C56H67O10N3); found 941.4823.

Copper(i)-catalyzed allyne-azide 1,3-dipolar cycloaddition reaction of 1-(10-bromodecyl)-4-propargylp[5]arene Pillar-3M and Pillar-3D(1–2).14,25 Pillar-2 (100 mg, 0.1 mmol) was dissolved in dry acetonitrile (30 mL) and degassed for 5 min. Thereafter, a degassed solution of tetrakis(acetonitrile)copper(i) hexafluorophosphate, Cu(CH3CN)2PF6 (18.4 mg, 0.048 mmol) and tris[[1-benzyl-1H-1,2,3-triazol-4-yl]methyl]amine (TBTA, 26.4 mg, 0.048 mmol) in an acetonitrile (1.5 mL) was added. The mixture was then stirred at room temperature under a nitrogen atmosphere for 24 h and concentrated under vacuum. The desired products were subsequently separated from the reaction mixture by silica gel column chromatography using a dichloromethane/ethyl acetate mixture (80:20, v/v).

Pillar-3M. White solid. Yield (42 mg, 42%). Mp: 209–210 °C. 1H NMR (600 MHz, CDCl3) δ: −1.39 (s, 2H), −1.20 (m, 2H), −0.65 (s, 1H), −0.52 (s, 1H), −0.27 (m, 2H), 0.77 (m, 2H), 1.32 (m, 1H), 1.39 (m, 1H), 1.45 (m, 1H), 1.59 (m, 1H), 1.73 (m, 1H), 1.84 (m, 1H), 2.52 (s, 2H), 2.65 (s, 1H), 3.80 (m, 3H), 3.97 (m, 1H), 4.19 (m, 1H), 5.51 (m, 2H), 6.25 (s, 1H), 6.48 (s, 1H), 6.77 (s, 1H), 6.82 (s, 1H), 6.85 (s, 1H), 6.93 (s, 3H), 6.97 (s, 1H), 7.08 (s, 1H). 13C NMR (150 MHz, CDCl3) δ: 22.5, 25.1, 26.1, 26.2, 26.5, 26.7, 27.0, 27.0, 28.0, 28.7, 28.8, 29.5, 30.1, 49.8, 55.3, 55.4, 55.7, 56.0, 56.3, 57.0, 57.1, 60.3, 67.0, 113.4, 113.5, 113.6, 113.8, 114.1, 114.2, 114.4, 114.6, 115.0, 124.6, 127.9, 128.1, 128.1, 128.4, 128.5, 128.9, 129.1, 129.4, 129.5, 140.7, 146.0, 145.0, 150.6, 150.6, 150.7, 150.7, 150.9, 151.0, 151.1. HRMS: (m/z) caleld for [M+H]+: 942.4905 (for C56H67O10N3); found 942.4905.

Pillar-3D1. White solid. Yield (15 mg, 15%). Mp: 252–253 °C. 1H NMR (600 MHz, CDCl3) δ: −1.70 (d, 2H), −0.10 (m, 4H), 0.19 (s, 2H), 0.91 (m, 2H), 1.24 (m, 1H), 1.41 (m, 1H), 1.68 (m, 1H), 1.76 (m, 1H), 1.95 (m, 1H), 2.35 (m, 2H), 3.50 (s, 4H), 3.77 (m, 3OH), 4.02 (m, 1H), 4.31 (s, 1H), 4.75 (m, 1H), 4.86 (s, 1H), 4.83 (s, 2H), 6.91 (m, 4H), 7.01 (m, 1H), 7.05 (s, 1H), 7.13

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Conflicts of interest

There are no conflicts to declare.

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