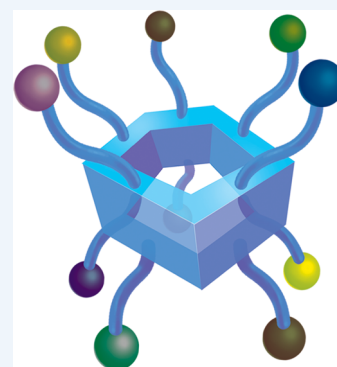


Functionalizing Pillar[*n*]arenes

Nathan L. Strutt, Huacheng Zhang, Severin T. Schneebeli, and J. Fraser Stoddart*

Department of Chemistry, Northwestern University, 2145 Sheridan Road, Evanston, Illinois 60201-3113, United States

CONSPECTUS: Macrocyclic chemistry has relied on the dominance of some key cavitands, including cyclodextrins, calixarenes, cyclophanes, and cucurbiturils, to advance the field of host–guest science. Very few of the many other cavitands introduced by chemists during these past few decades have been developed to near the extent of these four key players. A relatively new family of macrocycles that are becoming increasingly dominant in the field of macrocyclic chemistry are the pillar[*n*]arenes composed of *n* hydroquinone rings connected in their 2- and 5-positions by methylene bridges. This substitution pattern creates a cylindrical or pillar-like structure that has identical upper and lower rims. The preparation of pillar[*n*]arenes is facile, with pillar[5]- through pillar[7]arene being readily accessible and the larger macrocycles (*n* = 8–14) being accessible in diminishing yields. The rigid pillar[*n*]arene cavities are highly π -electron-rich on account of the *n* activated aromatic faces pointing toward their centers, allowing the cavities to interact strongly with a range of π -electron-deficient guests including pyridiniums, alkylammoniums, and imidazoliums. The substitution pattern of pillar[*n*]arenes bestows chirality onto the macrocycle in the form of *n* chiral planes.



The absolute configuration of the chiral planes in pillar[*n*]arenes can be either fixed or rapidly undergoing inversion.

The future of pillar[*n*]arenes is going to be dependent on their ability to fulfill specific applications. Chemical modification of the parent pillar[*n*]arenes lets us create functionalized hosts with anticipated chemical or physical properties. The featured potential applications of pillar[*n*]arenes to date are far reaching and include novel hosts with relevance to nanotechnology, materials science, and medicine. Pillar[*n*]arenes have an overwhelming advantage over other hosts since the number of ways available to incorporate handles into their structures are diverse and easy to implement. In this Account, we describe the routes to chemically modified pillar[*n*]arenes by discussing the chemistry of their functionalization: monofunctionalization, difunctionalization, rim differentiation, perfunctionalization, and phenylene substitution. We assess the synthetic complications of employing these functionalization procedures and survey the potential applications and novel properties that arise with these functionalized pillar[*n*]arenes. We also highlight the challenges and the synthetic approaches that have yet to be fully explored for the selective chemical modification of these hosts. Finally, we examine a related class of macrocycles and consider their future applications. We trust that this Account will stimulate the development of new methods for functionalizing these novel hosts to realize pillar[*n*]arene-containing compounds capable of finding applications.

■ INTRODUCTION

Host–guest chemistry¹ has been greatly influenced during the past four decades by the use of readily available cavitands such as cyclodextrins,² calixarenes,³ cyclophanes,⁴ and cucurbiturils.⁵ The introduction of new synthetic hosts allows chemists to explore novel supramolecular systems and investigate contemporary classes of materials. One of the recent classes of macrocycles to make their debut in host–guest chemistry are the pillar[*n*]arenes (Figure 1), which were first introduced by Ogoshi and co-workers⁶ in 2008. Closely related as they are to the calix[*n*]arenes, the pillar[*n*]arenes are composed of *n* hydroquinone units held together by methylene bridges linking the 2- and 5-positions of the *n*-hydroquinone units in cyclic arrays.

The reaction of 1,4-dimethoxybenzene with paraformaldehyde in the presence of $\text{BF}_3 \cdot \text{OEt}_2$ to form 1,4-dimethoxypillar[5]arene (DMpillar[5]arene), followed by the removal of the methoxyl protecting groups with BBr_3 constitutes⁶ the first ever synthesis (Scheme 1) of pillar[5]arene. Numerous investigations^{7–11} have been carried out to optimize this Friedel–Crafts alkylation to form good yields of pillar[5]arene^{7,8} or pillar[6]arene,⁹ coupled with moderate to low yields of pillar[7–14]arenes.^{10–12}

As a result of them being surrounded by preorganized hydroquinone rings, the cavities of the pillar[*n*]arenes are π -electron-rich and interact strongly with electron-poor species. Pillar[5]- and pillar[6]arene, the mostly widely investigated homologues to date, have cavity sizes of 5.5 and 7.5 Å, respectively,^{6,13} which are large enough to form 1:1 complexes with small electron-poor guests.¹⁴ The 1:1 complexes formed between pillar[*n*]arenes and derivatives of these guests have also been utilized in the production of mechanically interlocked molecules.^{15,16} The supramolecular properties of the pillar[8–14]arenes have become a focus of particular attention recently^{11,12} since these larger hosts are able to form ternary complexes with guests.

In order to exploit the properties of pillar[*n*]arenes for a range of different applications, they need to be functionalized with synthetic handles that can be further modified to select for novel physical or chemical characteristics or to incorporate them into a new material. In this Account, we examine the progress that has been made in the functionalization of pillar[*n*]arenes and

Received: April 30, 2014

Published: July 7, 2014

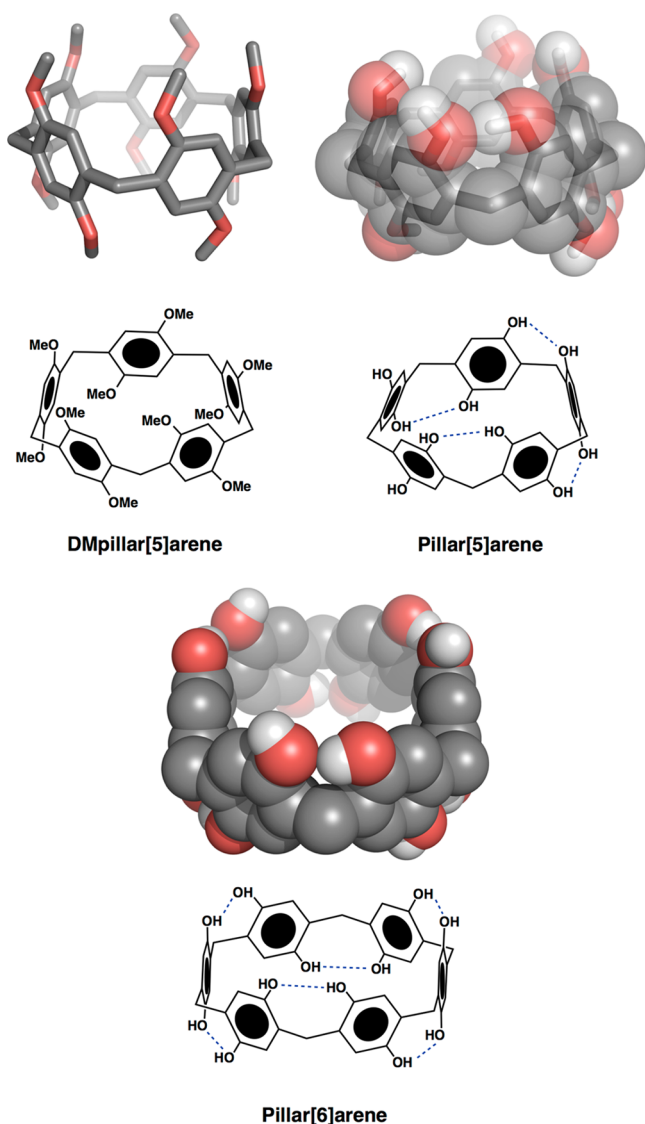
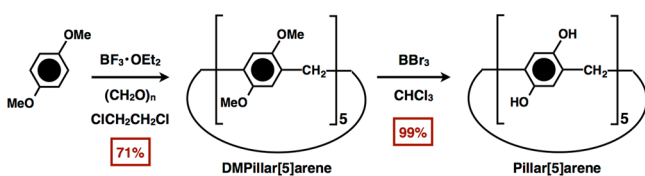


Figure 1. Pillar[*n*]arenes are receptors composed of *n* hydroquinone rings joined together at their 2- and 5-positions by methylene bridges. The X-ray crystal structures of 1,4-dimethoxypillar[5]arene⁶ (DMpillar[5]arene), pillar[5]arene,⁸ and pillar[6]arene¹³ are shown above their structural formulas, and the intramolecular hydrogen bonding between neighboring hydroxyl groups is indicated by blue dashed lines. In these solid-state structures, C atoms are gray, O atoms are red, and H atoms are white. Alkyl H atoms have been removed for visual clarity.

Scheme 1. Original Synthetic Pathway to Pillar[5]arene Reported by Ogoshi et al.,⁶ Which Was Later Optimized⁸ To Afford the Five-Membered Macrocycle in a 70% Overall Yield



highlight some of the challenges that remain to chemically modify these cavitands. The definition of a functionalized pillar[*n*]arene derivative in this Account encompasses pillar[*n*]arenes that have at least one functional group other than an alkyl group on their rims or

derivatives that contain reactive handles associated with either the hydroquinone units or the methylene groups. Since the perhydroxylated pillar[*n*]arenes have been reviewed^{14,17} recently, we will avoid discussing them in detail. We have divided our discussion into sections according to the substitution patterns (Figure 2) on the pillar[*n*]arenes that result from functionalization, that is, monofunctionalization, difunctionalization, rim-differentiation, perfunctionalization, and phenylene substitution. Each of these types of functionalization have their own accompanying challenges, and each produce pillar[*n*]arenes with novel potential applications.

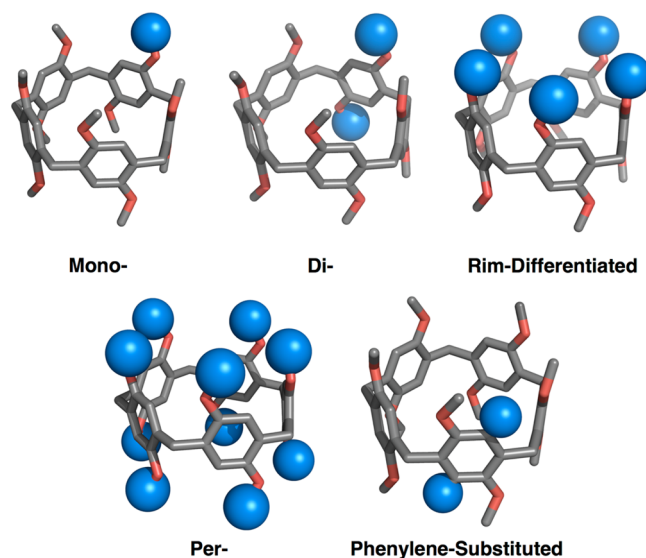
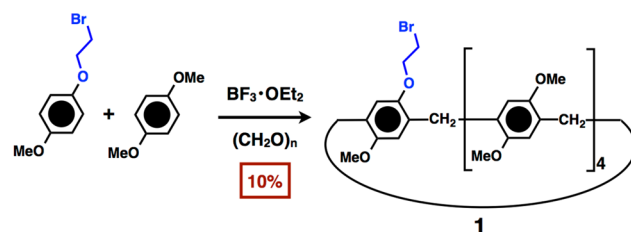


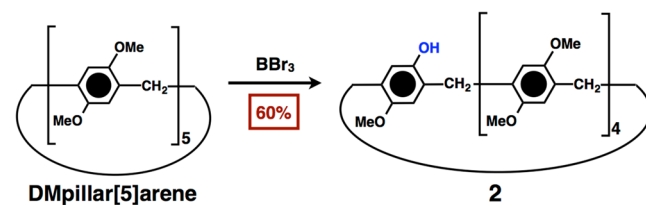
Figure 2. Five distinct patterns of pillar[*n*]arene functionalization reported thus far, wherein generic functional groups are represented by blue spheres.

Scheme 2. Monofunctionalized Pillar[5]arenes Have Been Synthesized Employing Two Distinct Approaches^a

Approach 1: Co-cyclization

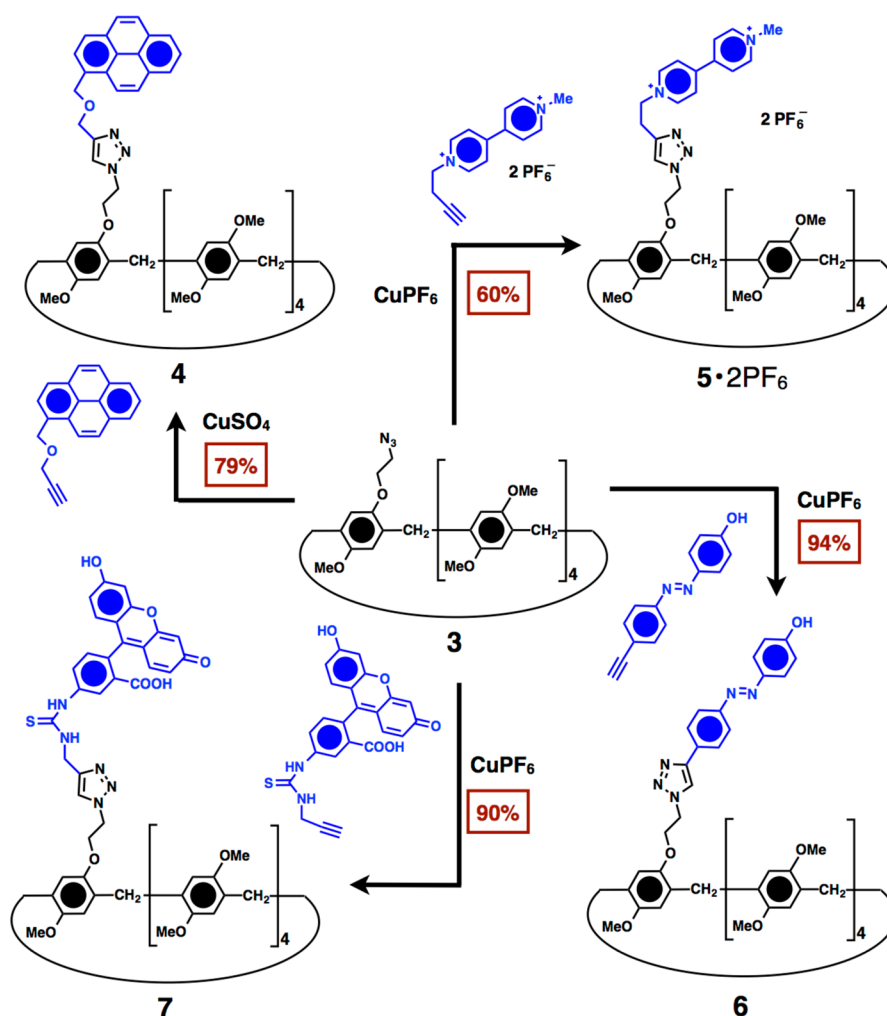


Approach 2: Deprotection



^aApproach 1 incorporates a bromoethoxyl handle onto the pillar[5]arene **1** by co-cyclizing¹⁵ 1,4-dimethoxybenzene and 1-(2-bromoethoxy)-4-methoxybenzene in the presence of paraformaldehyde and BF₃·OEt₂. Approach 2 introduced by Ogoshi¹⁸ involves the mono-deprotection of DMpillar[5]arene with BBr₃ to afford **2**. Cao and coworkers¹⁹ later optimized the synthesis of **2** to provide the monofunctionalized pillar[5]arene in a 60% yield.

Scheme 3. Azide-Containing Pillar[5]arene **3**, Which Can Undergo CuAAC with a Terminal Alkyne,¹⁵ Can Be Employed As a Common Starting Material in the Synthesis of Multiple Monofunctionalized Pillar[5]arenes, Including **4**, **5**·2PF₆⁻, **6**, and **7**^{21–23}



MONOFUNCTIONALIZED PILLAR[n]ARENES

Substitution at one reactive position on a cavitand allows for the addition of novel features without altering significantly its ability to recognize guests. Two approaches^{15,18,19} have been devised for the synthesis (Scheme 2) of the monofunctionalized pillar[5]arenes **1** and **2**. They rely on (i) co-cyclization of a mixed 1,4-dialkoxybenzene with a hydroquinone containing a Lewis acid-compatible functional group or (ii) deprotection of one alkoxy group of a fully alkylated pillar[5]arene. The first strategy was employed¹⁵ by us in 2011 to form a co-pillar[5]arene, **1**, in which one of the 10 hydroxyl groups is protected with a 2-bromoethoxyl and the remaining ones with methoxyl groups. The pillar[5]arene **3**, which is obtained (Scheme 3) when the bromine atom of **1** is substituted with an azide, is now capable of undergoing a copper-catalyzed azide–alkyne cycloaddition²⁰ (CuAAC). An alkyne-functionalized fluorophore has been reacted with **3** to afford **4**, which is capable of detecting the presence of alkanediamines bound in its cavity through fluorescence quenching.

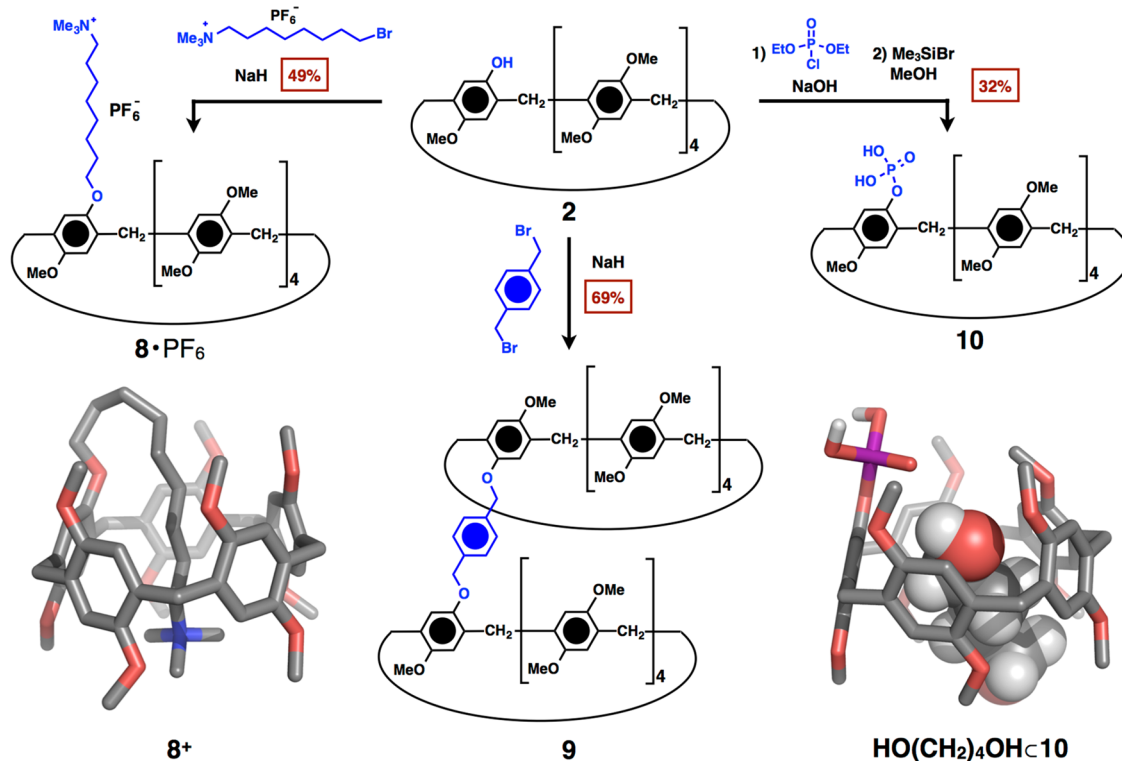
The monoazide pillar[5]arene **3** can serve as an easily accessible starting material for producing (Scheme 3) functionalized pillar[5]arene derivatives using CuAAC. In order to further an understanding of the noncovalent bonding interactions between the cavity of pillar[5]arenes and bipyridinium guests, we employed CuAAC to unite the host and guest into a

single molecule, that is, compound **5**·2PF₆⁻, which undergoes²¹ self-complexation in dilute solutions and forms supramolecular daisy-chain polymers that afford a gel at high concentrations.

Three-dimensional assemblies, including vesicles and micelles, of compounds produced (Scheme 3) from **3** have also been investigated.^{22,23} The azobenzene functionalized pillar[5]arene **6** forms hollow spherical vesicles in an aqueous environment.²² Exposing the sample to UV light causes an isomerization from *trans*- to *cis*-azobenzene, resulting in the transformation of the hollow spherical vesicles of **6** into solid particles. Fluorescein (FITC), which has been appended onto a pillar[5]arene **7** (Scheme 3) by CuAAC, allows the host to aggregate into vesicles that exhibit²³ thermoresponsive emissions at different temperatures.

The second synthetic strategy employed to produce monofunctionalized pillar[5]arenes was introduced by the Ogoshi group.¹⁸ In their approach (Scheme 2), the demethylation of DMpillar[5]arene was performed with less than one equivalent of BBr_3 leading to the isolation of the pillar[5]arenol **2**. This unmasked hydroxyl group can now be used to impart further functionality on the pillar[5]arene using a Williamson ether-type synthesis. In order to illustrate this strategy, a monofunctionalized pillar[5]arene, **8**·PF₆⁻ was produced (Scheme 4) with a single alkylammonium tether, allowing it to undergo self-complexation. Ogoshi²⁴ has utilized **2** to prepare (Scheme 4) a dimer **9** of pillar[5]arene connected through a *para*-xylenyl linker.

Scheme 4. Pillar[5]areneol **2** Can Serve¹⁸ as a Common Starting Material for the Synthesis of a Self-Complexing Species **8⁺**, a Dimer **9**, and a Monophosphoryl Pillar[5]arene **10**, Which Can Form 1:1 Complexes with Alkanediols^{19,24a}



^aIn the geometry-optimized models of **8⁺** and the 1:1 complex **HO(CH₂)₄OH⊂10**, the C atoms are gray, O atoms are red, N atoms are blue, P atoms are purple, and H atoms are white. Alkyl H atoms have been removed for visual clarity.

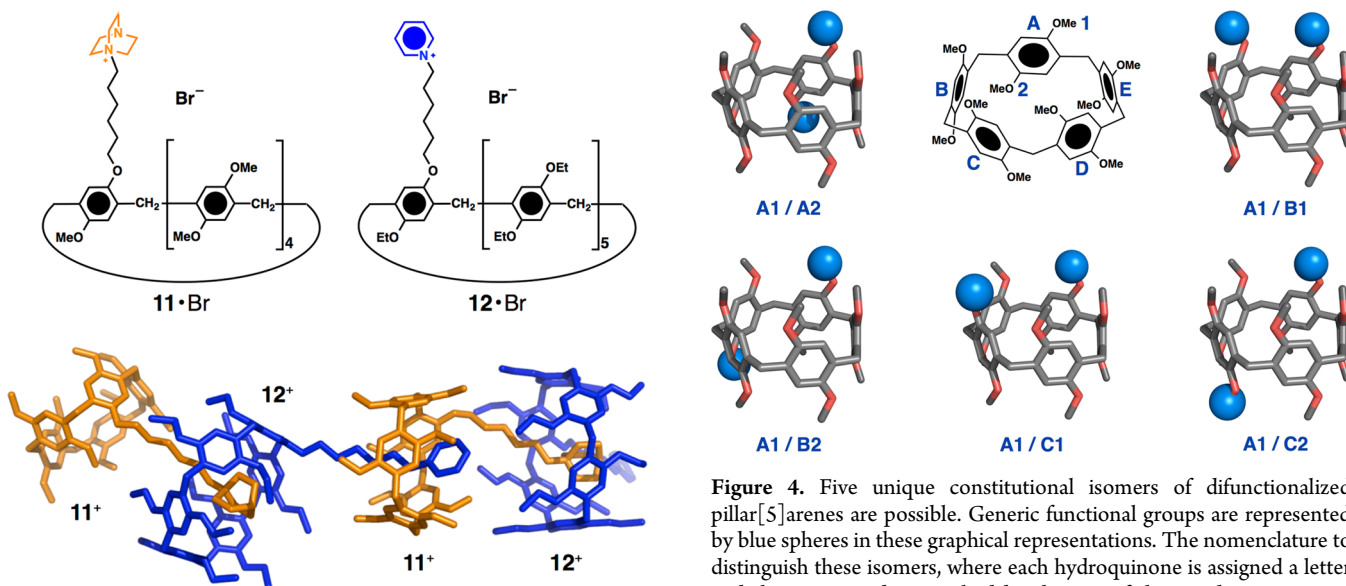


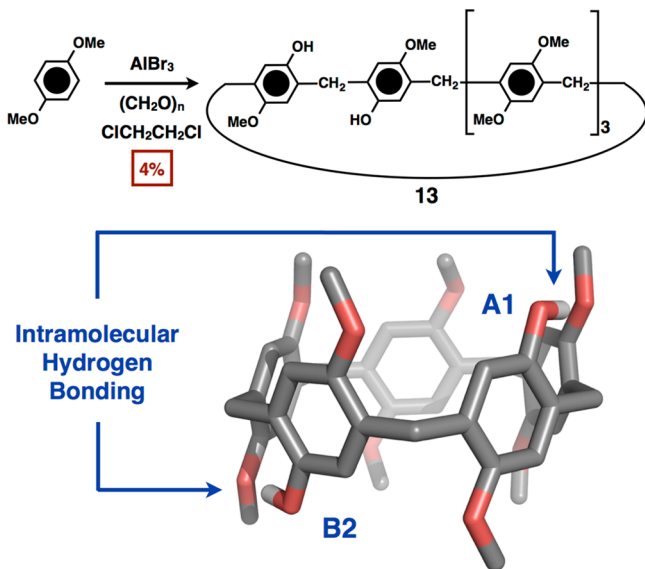
Figure 4. Five unique constitutional isomers of difunctionalized pillar[5]arene are possible. Generic functional groups are represented by blue spheres in these graphical representations. The nomenclature to distinguish these isomers, where each hydroquinone is assigned a letter and the rims are distinguished by the use of the numbers 1 or 2, is illustrated alongside the structural formula of DMPillar[5]arene.

Figure 3. Monofunctionalized pillar[5]arene **11**• Br and pillar[6]arene **12**• Br form an alternating supramolecular polymer²⁵ in solution in which the bulky ammonium ion of **11⁺** (orange) prefers to reside in the cavity of **12⁺** (blue), while the pyridinium of **12⁺** has a high affinity for the cavity of **11⁺**.

Cao and co-workers¹⁹ have employed (Scheme 4) the pillar[5]areneol **2** to produce a pillar[*n*]arene derivative **10** with a phosphoryl group, which can act as a hydrogen-bond acceptor for aliphatic alcohols residing in the host.

Pillar[6]areneol was synthesized by Ogoshi and co-workers²⁵ using a strategy similar to that¹⁸ employed to produce **2**. The five- and six-membered pillar[*n*]areneols were functionalized with a 1,4-diazabicyclo[2.2.2]octane (DABCO) cation and a pyridinium cation to afford (Figure 3) **11**• Br and **12**• Br , respectively. As a result of a mismatch between the host and guests in **11**• Br and **12**• Br , the DABCO cation is bound strongly inside the cavity of pillar[6]arene but is too large to be encompassed by pillar[5]arene,

Scheme 5. Ogoshi and Co-workers²⁶ Have Reported the A1/B2-Pillar[5]arenediol 13 Formed through the *in Situ* Cyclization and Deprotection of 1,4-Dimethoxybenzene^a



^aWhile other regioisomers of 13 are formed in this reaction, only the A1/B2 isomer is amenable to easy isolation. The X-ray crystal structure of 13 highlighting the intramolecular hydrogen bonding is shown at the bottom. C atoms are gray, O atoms are red, and H atoms are white. Alkyl H atoms have been removed for visual clarity.

while the pyridinium cation shows little affinity for the pillar[6]arene yet docks tightly within the cavity of pillar[5]arene. Mixtures of these two monofunctionalized pillar[*n*]arenes yield an alternating supramolecular polymer.

■ DIFUNCTIONALIZED PILLAR[*n*]ARENES

Following the establishment of multiple pathways to monofunctionalized pillar[*n*]arenes, the next logical challenge was to

uncover methods for their difunctionalization. In contrast with the monofunctionalization of pillar[5]arene, which results in only one constitutional isomer, difunctionalization of pillar[5]arene can produce²⁶ one of five constitutional isomers (Figure 4) with the substitution patterns A1/A2, A1/B1, A1/B2, A1/C1, or A1/C2. While the A1/A2 pattern²⁷ with the substitution at both ends of one hydroquinone unit is straightforward to attain, forming the other constitutional isomers regioselectively is currently an unsolved challenge.

The first isolation of an A1/B2-difunctionalized pillar[5]arene 13 was achieved (Scheme 5) by Ogoshi and co-workers²⁶ employing an *in situ* cyclization and deprotection reaction with the Lewis acid AlBr₃. Although the deprotection of the methyl groups in this reaction is uncontrollable, isomer 13 can be isolated easily as a consequence of its insolubility in MeOH. The A1/B2-pillar[5]arenediol 13 was utilized in the synthesis of a pillar[5]arene-containing oligomer in which the macrocyclic units are separated by *para*-xylenyl spacers.

The preparation of A1/A2-pillar[5]arenediol 14 requires the selective deprotection of one hydroquinone unit of DMpillar[5]arene. One approach^{28,29} to the synthesis of 14 involves (Scheme 6) the partial oxidation of DMpillar[5]arene to form the pillar[*n*]arene 15 containing four 1,4-dimethoxybenzene units and one benzoquinone ring, which can undergo a two-electron reduction to afford 14. An alternative synthesis of 14, introduced by us,³⁰ involves the formation of a co-pillar[5]arene 16 whose two 3-bromopropoxyl groups can be converted into allyl groups, yielding 17 which is deprotected readily to afford 14.

X-ray crystallography reveals^{28,30} that in its solid-state structure (Scheme 6), the hydroquinone unit in of A1/A2-pillar[5]arenediol 14 is flipped in the opposite direction from the remaining 1,4-dimethoxybenzene units to encompass the formation of two intramolecular hydrogen bonds. These hydrogen bonds exercise a significant influence on the rate of stereochemical inversion (Scheme 6) between the lowest energy enantiomeric conformations of 14, allowing the energy barrier (11.9 kcal·mol⁻¹) for inversion to be measured³¹ by dynamic ¹H NMR spectroscopy.

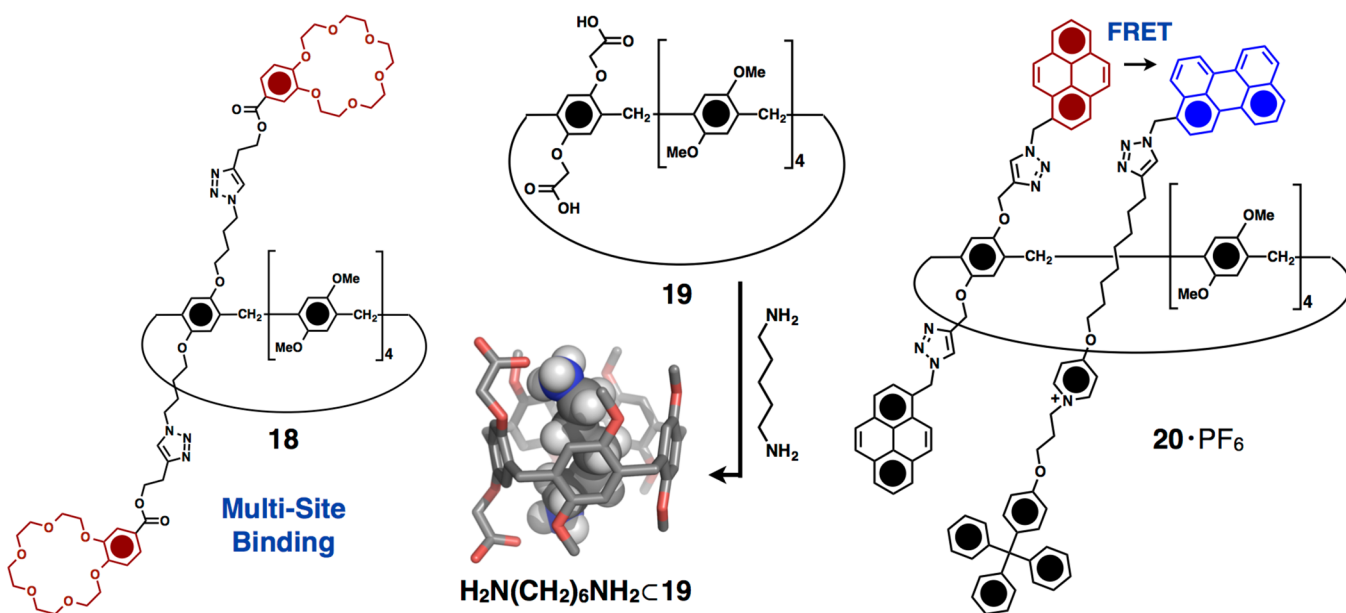
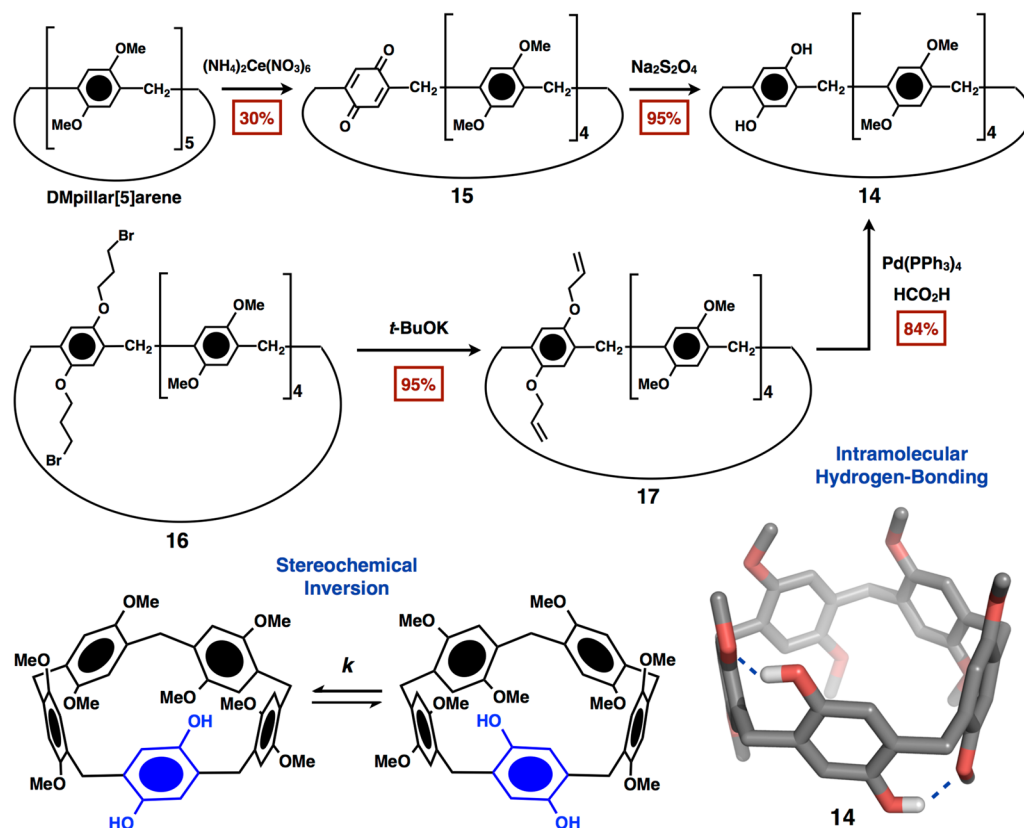


Figure 5. A1/A2-difunctionalization pattern for pillar[5]arenes has been employed^{32–34} to prepare a benzo-crown ether containing pillar[5]arene 18, a dicarboxylic acid 19, which can form a strong 1:1 complex with alkanediamines, and the [2]rotaxane 20 in which FRET occurs between the pyrene unit attached to the pillar[5]arene and the perylene stopper.

Scheme 6. A1/A2-Pillar[5]arene diol 14 Can Be Prepared through Two Separate Synthetic Pathways^a

^aThe first pathway^{28,29} includes the oxidation of one 1,4-dimethoxybenzene unit of DMpillar[5]arene to afford 15, which can undergo a two-electron reduction to produce 14. In an alternative approach,³⁰ a co-pillar[5]arene 16 includes bromoethoxy handles that are converted to allyl ether protecting groups to give 17 and deprotected, affording 14. The X-ray crystal structure of 14 illustrates flipping of the hydroquinone unit to form intramolecular hydrogen bonds. C atoms are gray, O atoms are red, and H atoms are white. Alkyl H atoms have been removed for visual clarity. The two low-energy conformational isomers of 14 can interconvert at a rate that is slow on the ¹H NMR time scale at room temperature.

With the aid of density functional theory (DFT) calculations, we were able to propose a mechanism for the inversion of 14, which involves a high-energy step, corresponding to the cleavage of one of the intramolecular hydrogen bonds.

A1/A2-Difunctionalization of pillar[*n*]arenes allows for chemical modifications at both ends of the receptor without altering significantly the properties of its cavity. Rim functionality can be employed to place an additional recognition site outside the cavity of the receptor. This strategy has been exemplified by Zhou and co-workers³² in their incorporation (Figure 5) of arenes terminated by benzo-18-crown-6 on the upper and lower rims of pillar[5]arene 18 following two CuAAC reactions. By control of the solution pH, the pillar[5]arene 18 can form a 1:1 complex reversibly with octane-1,8-diammonium dications where the aliphatic chain interacts with the cavity of pillar[5]arene while the ammonium cations bind strongly to the benzo-crown ethers. Yu et al.³³ have investigated similar superstructures (Figure 5) formed between the A1/A2-pillar[5]arene dicarboxylic acid 19 and alkanediamines. Proton transfer from the carboxyl groups in 19 to the alkanediamine creates a strong electrostatic interaction that increases the stability of the 1:1 complex.

Difunctionalized pillar[5]arenes have also been incorporated into mechanically interlocked molecules to examine their conformations in solution. Ogoshi et al.³⁴ have prepared (Figure 5) the [2]rotaxane 20-PF₆ with an A1/A2-dipyrene pillar[5]arene ring by a threading-followed-by-stoppering approach. Excitation at

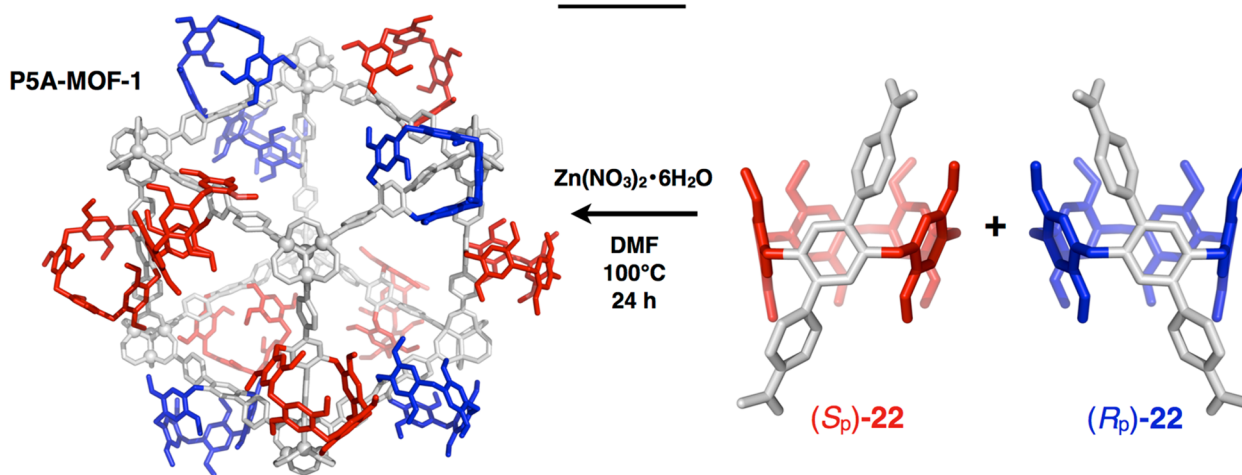
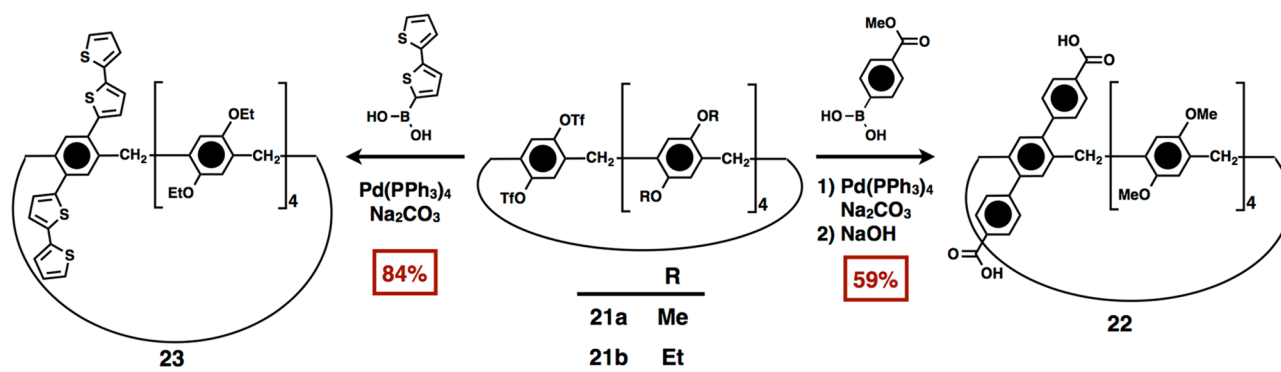
345 nm of the pyrene units of the [2]rotaxane results in a Förster resonance energy transfer (FRET) to the perylene stopper of the dumbbell. The FRET yield can be used to estimate an effective transfer distance of approximately 1.6 nm, providing information on the solution-state co-conformational freedom of 20-PF₆.

A1/A2-Difunctionalized pillar[5]arenes can be targeted for specific applications that require a rigid receptor. The ditriflate 21a (Scheme 7) was prepared by us³⁰ to produce a pillar[5]arene-containing organic strut 22, which was subsequently incorporated into a metal-organic framework (MOF), namely, PSA-MOF-1. The pillar[5]arene active domains of this MOF are able to sequester electron-poor pyridinium cations as well as *para*-dinitrobenzene from a Me₂CO solution. The direct incorporation of a rigid terphenyl strut into the pillar[5]arene scaffold inhibits the stereochemical inversion of 22, allowing the strut to exist as a racemic modification, namely, (*R_p*)- and (*S_p*)-22. Ogoshi et al.³⁵ employed the ditriflate 21b to give (Scheme 7) a rigid A1/A2-difunctionalized pillar[5]arene 23 incorporating a π -conjugated unit composed of thiophenes. Complexation of an achiral guest 1,4-dicyanobutane in the cavity of 23 was found to induce changes in the chiral host's circular dichroism (CD) spectrum.

■ RIM-DIFFERENTIATED PILLAR[*n*]ARENES

In contrast to the cyclodextrins² and calix[*n*]arenes,³ pillar[*n*]arenes have identical upper and lower rims. While this property is often a beneficial structural feature, some applications are

Scheme 7. Ditriflate Pillar[5]arene Derivatives 21a and 21b Can Be Employed^{30,35} To Prepare Rigidly A1/A2-Functionalized Pillar[5]arenes 22 and 23^a



^aThe rigid organic strut 22 is present as a mixture of two enantiomers, (*S_p*) and (*R_p*), which can be linked together with Zn_4O clusters to create P5A-MOF-1.

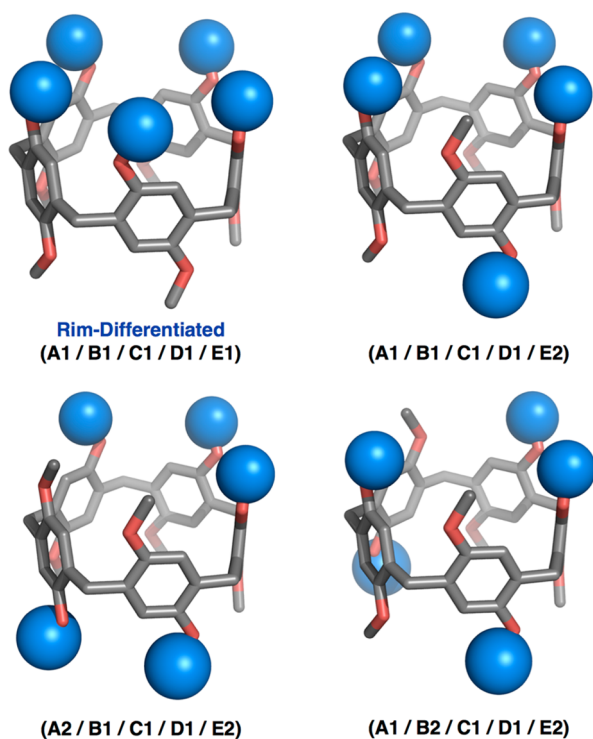


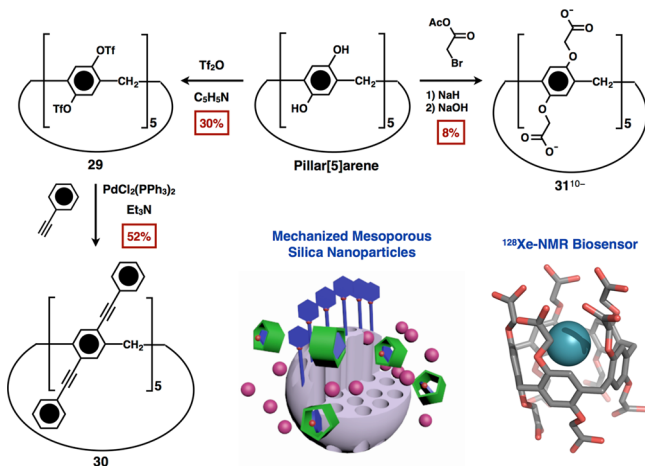
Figure 6. Four constitutional isomers are produced during the synthesis of a rim-differentiated pillar[5]arene. The lowest yielding constitutional isomer (A1/B1/C1/D1/E1) has functional handles, represented by blue spheres, along only one rim and is therefore rim-differentiated.

better suited for hosts that are unsymmetrical. Constitutional dissymmetry (Figure 6) can be achieved by producing pillar[*n*]arenes in which the (identical) substituents on the upper rim are different from those on the lower rim. The difficulty of producing rim-differentiated pillar[*n*]arenes stems from the regioisomers that can be formed when an unsymmetrical hydroquinone derivative is reacted under pillar[*n*]arene cyclization conditions. In separate reports, Meier et al.³⁶ and Huang et al.³⁷ demonstrated that four regioisomers are formed when 1-butoxy-4-methoxybenzene is used as the aromatic repeating unit of pillar[5]arene, with the C_5 -symmetric isomer being formed in the lowest yield (6%) of any isomer. The low yield of this isomer is the result of the statistical formation of the pillar[5]arene isomers, in which the other three regioisomers are formed in a combined yield that is 15 times higher than that of the rim-differentiated isomer. The high-yielding synthesis of a C_5 -symmetric rim-differentiated pillar[*n*]arene remains an unsolved challenge, which will most likely require a synthetic strategy that relies on templation.

Although rim-differentiated pillar[5]arene reactions are low yielding, numerous research groups have developed (Figure 7) them for specific reasons. A fluorescent rim-differentiated pillar[5]arene 24, which is able to bind fluoride anions selectively by forming five triazole C–H hydrogen bonds, has been reported³⁸ recently.

Rim-differentiated pillar[5]arenes are well-suited to act as amphiphiles in which one rim is substituted with hydrophilic groups and the other with hydrophobic groups. An amphiphilic pillar[5]arene 25 (Figure 7) forms³⁹ vesicles in water that

Scheme 8. Pillar[5]arene Can Be Perfunctionalized⁴³ with Triflates To Generate 29, a Receptor That Can Undergo 10 Pd-Catalyzed Sonogoshira Reactions To Give 30^a



^aA water-soluble pillar[5]arene 31¹⁰⁻ containing 10 carboxylates can also be prepared⁴⁴ and has found applications as a valve on the surface of the mechanized mesoporous silica nanoparticles⁴⁵ and as a ¹²⁸Xe-NMR biosensor.⁴⁶ C atoms are gray, O atoms are red, the Xe atom is green, and H atoms are white. Alkyl H atoms have been removed for visual clarity.

undergo conversion into micelles as a result of decreasing the pH of the solution. Interestingly, microtubes of 25 were found to form (Figure 7) after long incubation periods and were shown to adsorb trinitrotoluene on their surfaces. The amphiphilic

pillar[5]arenes 26, 27, and 28 have also been employed^{40–42} to create dimers, nanotubes, and micelles, respectively.

■ PERFUNCTIONALIZED PILLAR[*n*]ARENES

Pillar[*n*]arenes have 2*n* hydroxyl groups shared between their upper and lower rims, all of which can be reacted in the same way to create perfunctionalized pillar[*n*]arenes. Synthetic approaches to perfunctionalized pillar[*n*]arenes have either involved the (i) substitution of the parent pillar[*n*]arene or (ii) use of a functionalized hydroquinone monomer to create pillar[*n*]arene derivatives. The first synthetic protocol can be challenging since 2*n* reactions need to be effected on one platform to afford the desired symmetrical structure. The second approach is limited in scope since the desired functional group must not interfere with the Lewis acid-catalyzed Friedel–Crafts alkylation to form the pillar[*n*]arene. Numerous synthetic approaches to perfunctionalized pillar[*n*]arenes utilize both protocols, where a Lewis acid insensitive handle is incorporated into the protected hydroquinone so that the resulting pillar[*n*]arene can undergo further functionalization.

In 2009, Ogoshi and co-workers⁴³ reported (Scheme 8) the preparation of the perfunctionalized pillar[5]arene 29 in which all 10 hydroxyl groups are converted into triflates. Pertriflated pillar[5]arene 29 is a key starting material, which can potentially be used to create rigid perfunctionalized hosts. The decatriflate has been demonstrated (Scheme 8) to undergo 10 Sonogoshira Pd-catalyzed cross-couplings with ethynylbenzene to afford a highly conjugated pillar[5]arene 30, which exhibits through-space π -delocalization.

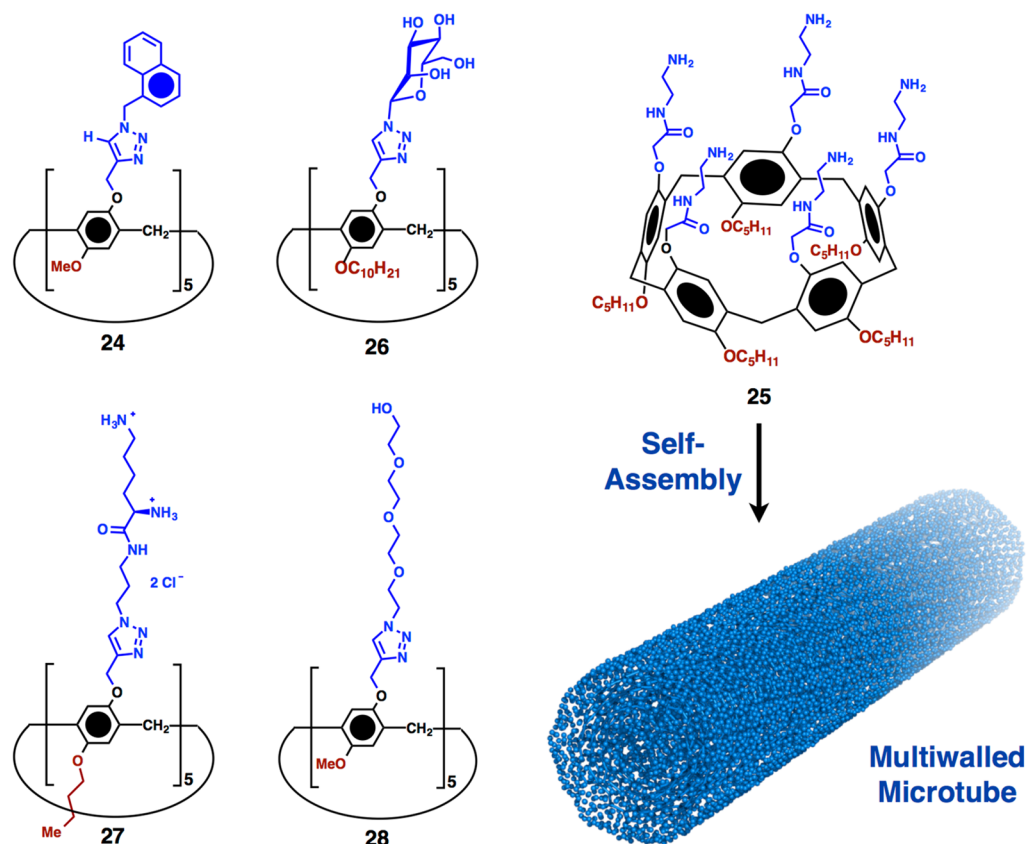
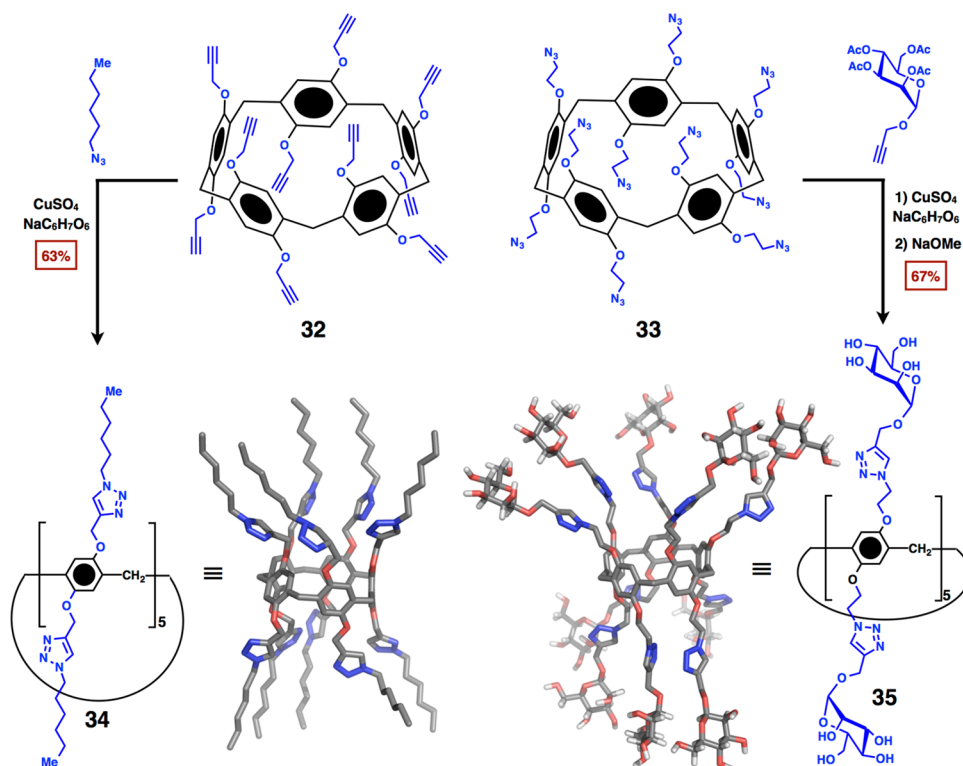


Figure 7. Examples of rim-differentiated pillar[5]arenes produced by CuAAC include 24, 26, 27, and 28.^{38–42} The amphiphilic rim-differentiated pillar[5]arene 25 self-assembles³⁹ to form vesicles in solution, which undergo slow conversion into multiwalled microtubes over the course of four months.

Scheme 9. Decaalkyne 32 or the Decaazide 33 Can Be Employed to Perfunctionalize Pillar[5]arene, Employing 10 CuAAC Reactions^a

^aOgoshi et al.⁴⁷ have reported that 32 can be reacted with 10 equiv of 1-azidohexane in the presence of a Cu(I) catalyst to afford 34. The pillar[5]arene glycocluster 35 results⁴⁹ from 10 CuAACs between an alkyne-substituted sugar and 33. In the geometry-optimized models of 34 and 35, the C atoms are gray, O atoms are red, N atoms are blue, and H atoms are white. Alkyl H atoms have been removed for visual clarity.

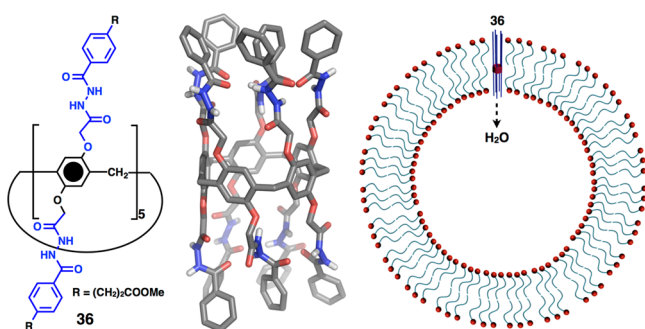


Figure 8. Hou and co-workers⁵¹ have reported the hydrazide- appended pillar[5]arene 36, which has a tubular structure and can act as an artificial transmembrane water channel when placed into the lipid membrane of a vesicle. The crystal structure of a pillar[5]arene with the same core components as 36 illustrates the intramolecular hydrogen bonding between hydrazide units which dictates the tubular structure. In this solid-state structure, C atoms are gray, O atoms are red, and H atoms are white. Alkyl H atoms have been omitted for the sake of clarity.

Perfunctionalization of pillar[*n*]arenes provides a convenient way to alter their solubility properties. The most targeted perfunctionalized pillar[*n*]arenes reported^{44–46} thus far are ones that allow the host to operate in water. Bringing the highly aromatic and relatively nonpolar pillar[*n*]arenes into an aqueous environment increases greatly their relevance with respect to biological and industrial applications. Ogoshi et al.⁴⁴ has described the synthesis (Scheme 8) of a water-soluble pillar[5]-arene 31¹⁰⁻ containing 10 carboxylates from pillar[5]arene. We have been able to incorporate⁴⁵ the water-soluble pillar[5]arene

31¹⁰⁻ into nanovalves (Scheme 8), which coat the surface of mechanized mesoporous silica nanoparticles (MSNPs). Lowering the pH of a solution of the MSNPs results in a decreased affinity between 31¹⁰⁻ and pyridinium stalks, leading to the release of cargo molecules from the pores of the nanoparticles. Cohen and co-workers⁴⁶ have also employed 31¹⁰⁻ to complex Xe in water, creating a system (Scheme 8) that can potentially act as a ¹²⁸Xe NMR-based biosensor.

Since it is high yielding and unlikely to produce byproducts, the CuAAC reaction is a useful method for the perfunctionalization of pillar[*n*]arenes. The decaalkyne 32 and decaazide 33 have both been used (Scheme 9) to attach 10 functional groups onto the pillar[5]arene ring through 10 CuAAC reactions.^{47–49} Ogoshi and co-workers⁴⁷ have demonstrated (Scheme 9) that the 10 CuAACs on 32 can produce 34 in a 63% yield, corresponding to a 95% conversion for each triazole ring formation. Nierengarten et al.⁴⁸ have employed (Scheme 9) the decaazide 33 and the analogous six-membered dodecaazide in their efforts to produce liquid-crystalline pillar[*n*]arenes, which have a broad enantiotopic mesophase as a result of their rigid chiral structures. The Strasbourg group⁴⁹ has also prepared (Scheme 9), starting from 33, a pillar[5]arene glycocluster 35 containing mannose, which shows promise as a disruptor of the adhesion of uropathogenic *Escherichia coli* to red blood cells. The decaalkyne 32 was also employed⁵⁰ in the synthesis of a polycationic dendrimer that is able to form nanoparticles with plasmid DNA and has been demonstrated to be useful in gene delivery applications.

The cylindrical shape of pillar[*n*]arenes can be extended through perfunctionalization to create artificial transmembrane channels. Thus, the pillar[5]arene 36 reported by Hou and

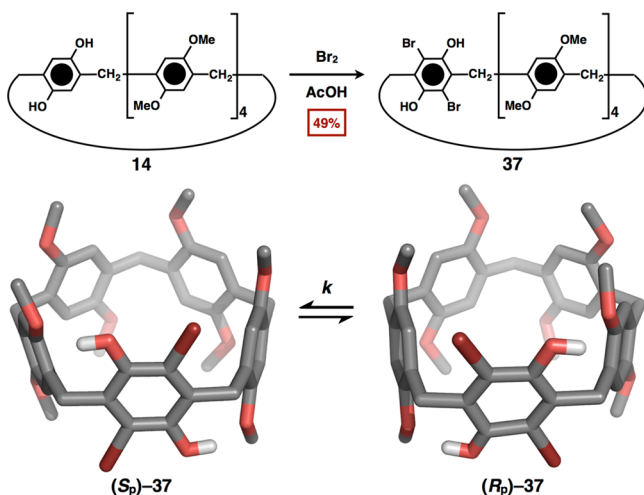
co-workers⁵¹ contains (Figure 8) hydrazide units, which form an intramolecular hydrogen-bonding network, allowing the molecule to adopt a tubular assembly. When inserted into a lipid bilayer, **36** acts as a single-molecule transmembrane channel for the transport of water.

■ PHENYLENE-SUBSTITUTED PILLAR[*n*]ARENES AND RELATED MACROCYCLES

The functionalization protocols discussed so far modify the hydroxyl groups on the pillar[*n*]arenes. Functionalization can also be extended to the hydroquinone positions, which are *ortho* to both the methylene bridges and oxygen substituents. This mode of functionalization leads to phenylene-substituted pillar[*n*]arenes. We have reported³¹ recently an early example (Scheme 10) of a phenylene-substituted pillar[5]arene, **37**, formed from the regiospecific bromination of A1/A2-pillar[5]arenediol **14**. The intramolecular hydrogen bonds between the hydroxyl groups and the oxygen atoms of the neighboring 1,4-dimethoxybenzenes of the dibrominated pillar[5]arene **37** are stronger than those in **14**, leading (Scheme 10) to a higher energy barrier for stereochemical inversion. The brominated pillar[5]arene **37** can serve as a starting material to create pillar[*n*]arene derivatives with increased functionality.

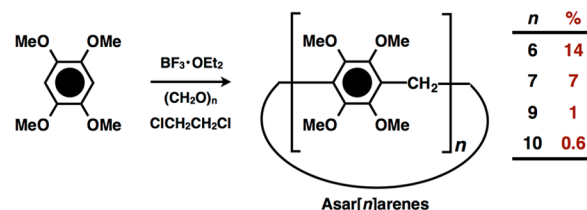
The asar[*n*]arenes introduced by us,⁵² which are assembled from 1,2,4,5-tetramethoxybenzene and so contain two additional methoxyl groups on each phenylene ring, are pillar[*n*]arenes that have been substituted at their *ortho*-positions. A range ($n = 6–15$) of asar[*n*]arenes has been synthesized and isolated (Scheme 11) in a single step by reacting 1,2,4,5-tetramethoxybenzene with paraformaldehyde in the presence of $\text{BF}_3 \cdot \text{OEt}_2$. In common with the pillar[*n*]arenes, the smallest member of the family, asar[6]arene, is favored as the thermodynamic product of the reaction since it minimizes both the ring strain in the methylene bridging units and the steric interactions between neighboring methoxyl groups. The solid-state structures (Figure 9) of the asar[*n*]arenes with 6–11 1,2,4,5-tetramethoxybenzene units

Scheme 10. A Phenylene-Substituted Pillar[5]arene **37** Results³¹ from the Electrophilic Bromination of A1/A2-Pillar[5]arenediol **14**^a



^aThe two lowest energy conformational isomers of **37** observed in the solid-state, (S_p) and (R_p), are enantiomers that can freely interconvert. C atoms are gray, O atoms are red, Br atoms are orange, and H atoms are white. Alkyl H atoms have been removed for visual clarity.

Scheme 11. Asar[*n*]arenes⁵² Are Formed from a Friedel–Crafts Alkylation between 1,2,4,5-Tetramethoxybenzene (Asarol Methyl Ether) and Paraformaldehyde^a



^aChanging the temperature and reaction time of this synthesis allows for the production of asar[6]- through asar[15]arene.

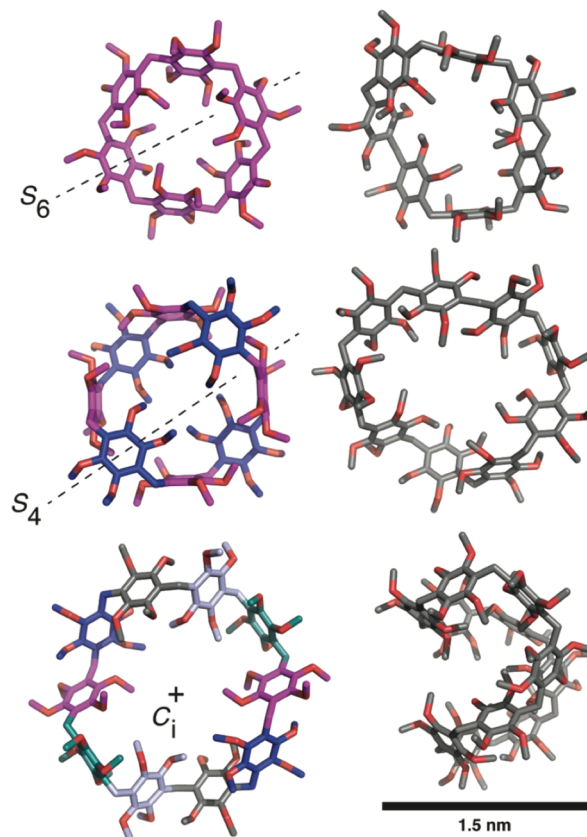


Figure 9. Solid-state structures⁵² of the asar[6]- through asar[11]arene. C atoms are shown in gray/blue/magenta/green/gray-blue and O atoms in red. H atoms have been omitted for the sake of clarity. Tetramethoxybenzene units, which can be transformed into one another using the highest symmetry operator present in each macrocycle, are illustrated with identical colors. Those symmetry operators, an S_6 axis for asar[6]arene, an S_4 -axis for asar[8]arene, and an inversion center for asar[10]arene, are also highlighted. This figure has been reproduced from ref 52 with permission. Copyright 2013 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

have been investigated by single-crystal X-ray crystallography. Asar[10]arene has the largest cavity (~ 1 nm) and forms infinite channels arranged in a checkerboard-like fashion in the solid-state.

■ CONCLUSIONS AND OUTLOOK

While pillar[*n*]arenes are a relatively new addition to the family of cavitands, their impact on the field of host–guest chemistry is increasing exponentially. The rise in their popularity among chemists can be attributed in part at least to the ease with which

they can be synthesized and functionalized. Since pillar[*n*]arenes have rather simple molecular structures, hydroquinones connected by methylene bridges, they can act as a platform for chemical modification, which leads to tailored macrocycles with targeted applications. The nature of their functionalization can be varied widely depending on the application, making the pillar[*n*]arene a truly versatile host. Although numerous methods of functionalization have been uncovered in different research laboratories, there are still challenges relating to the chemical modification of pillar[*n*]arenes that have yet to be tackled. They include (i) substitution at the methylene bridges, (ii) the selective synthesis of unsymmetrical difunctionalized pillar[*n*]arenes, and (iii) the high-yielding synthesis of rim-differentiated pillar[*n*]arenes. Although routes to phenylene-substituted pillar[*n*]arenes have been developed, applications relevant to this functionalization pattern have yet to be realized. Since we are still in the early days of pillar[*n*]arene research, we can be certain that their creative, simple, and efficient functionalizations are of crucial importance and will determine their future.

AUTHOR INFORMATION

Corresponding Author

*Professor J Fraser Stoddart. Tel: (+1)-847-491-3793. Fax: (+1)-847-491-1009. E-mail: stoddart@northwestern.edu.

Funding

This research is part (Project 32-949) of the Joint Center of Excellence in Integrated Nano-Systems (JCIN) at King Abdul-Aziz City for Science and Technology (KACST) and Northwestern University (NU). The authors thank both KACST and NU for their continued support of this research. N.L.S. thanks the National Science Foundation (NSF) for a Graduate Research Fellowship. S.T.S. thanks the International Institute for Nanotechnology (IIN) at NU for a postdoctoral fellowship.

Notes

The authors declare no competing financial interest.

Biographies

Nathan L. Strutt received his B.S. in chemistry from the University of Florida in 2009. During his undergraduate studies, he spent seven months in the laboratory of Professor Jean-Pierre Sauvage at the University of Strasbourg. Nathan joined the research group led by Professor Fraser Stoddart at Northwestern University (NU) in 2009, where he has investigated the functionalization and host-guest properties of pillar[*n*]arenes extensively.

Huacheng Zhang received his B.Sc. degree in Chemistry from Shandong Normal University, China, in 2005, and his Ph.D. degree in Organic Chemistry from Shandong University, China, in 2011 under the supervision of Professor Aiyu Hao. He was a visiting scholar in Professor Fraser Stoddart's group at Northwestern University (September 2010 to September 2011). After working as a Research Fellow in Professor Yanli Zhao's group in School of Physical and Mathematical Sciences at Nanyang Technological University, Singapore, he has returned to the group led by Fraser Stoddart as a postdoctoral scholar.

Severin T. Schneebeli received his B.A. in chemistry from the University of Zurich in 2006 and his Ph.D. in chemistry from Columbia University in New York under the direction of Professors Ronald Breslow and Richard Friesner. He is currently an International Institute of Nanotechnology (IIN) Postdoctoral Fellow in the laboratory of Professor Fraser Stoddart. In the fall of 2014, he will launch his independent academic career as an assistant professor of chemistry at the University of Vermont.

J. Fraser Stoddart received all (B.Sc., Ph.D., D.Sc.) of his degrees from the University of Edinburgh, U.K. Presently, he holds a Board of Trustees Professorship in the Department of Chemistry at NU. His research has opened up a new materials world of mechanically interlocked molecules and, in doing so, has produced a blueprint for the subsequent growth of functional molecular nanotechnology.

REFERENCES

- (1) Cram, D. J.; Cram, J. M. Host-Guest Chemistry. *Science* **1974**, *183*, 803–809.
- (2) D'Souza, V. T.; Lipkowitz, K. B. Cyclodextrins: Introduction. *Chem. Rev.* **1998**, *98*, 1741–1742.
- (3) Gutsche, C. D. *Calixarenes Revisited, Monographs in Supramolecular Chemistry*; Royal Society of Chemistry: Cambridge, U.K., 1998; Vol. 1.
- (4) Diederich, F. Supramolecular Cyclophane Chemistry. In *Supramolecular Chemistry*; Balzani, V., De Cola, L., Eds.; NATO ASI Series; Springer: Dordrecht, the Netherlands, 1992; Vol. 371; pp 119–136.
- (5) Freeman, W. A.; Mock, W. L.; Shih, N. Y. Cucurbituril. *J. Am. Chem. Soc.* **1981**, *103*, 7367–7368.
- (6) Ogoshi, T.; Kanai, S.; Fujinami, S.; Yamagishi, T.-a.; Nakamoto, Y. para-Bridged Symmetrical Pillar[5]arenes: Their Lewis Acid Catalyzed Synthesis and Host-Guest Property. *J. Am. Chem. Soc.* **2008**, *130*, 5022–5023.
- (7) Cao, D.; Kou, Y.; Liang, J.; Chen, Z.; Wang, L.; Meier, H. A Facile and Efficient Preparation of Pillararenes and a Pillarquinone. *Angew. Chem., Int. Ed.* **2009**, *48*, 9721–9723.
- (8) Ogoshi, T.; Aoki, T.; Kitajima, K.; Fujinami, S.; Yamagishi, T.-a.; Nakamoto, Y. Facile, Rapid, and High-Yield Synthesis of Pillar[5]arene from Commercially Available Reagents and Its X-Ray Crystal Structure. *J. Org. Chem.* **2011**, *76*, 328–331.
- (9) Ogoshi, T.; Ueshima, N.; Akutsu, T.; Yamafuji, D.; Furuta, T.; Sakakibara, F.; Yamagishi, T.-a. The Template Effect of Solvents for High Yield Synthesis, co-Cyclization of Pillar[6]arenes and Interconversion between Pillar[5]- and Pillar[6]arenes. *Chem. Commun.* **2014**, *50*, 5774–5777.
- (10) Chen, Y.; Tao, H. Q.; Kou, Y. H.; Meier, H.; Fu, J. L.; Cao, D. R. Synthesis of Pillar[7]arene. *Chin. Chem. Lett.* **2012**, *23*, 509–511.
- (11) Hu, X.-B.; Chen, Z.; Chen, L.; Zhang, L.; Hou, J.-L.; Li, Z.-T. Pillar[*n*]arenes (*n* = 8–10) with Two Cavities: Synthesis, Structures and Complexing Properties. *Chem. Commun.* **2012**, *48*, 10999–11001.
- (12) Ogoshi, T.; Ueshima, N.; Sakakibara, F.; Yamagishi, T.-a.; Haino, T. Conversion from Pillar[5]arene to Pillar[6–15]arenes by Ring Expansion and Encapsulation of C₆₀ by Pillar[*n*]arenes with Nanosize Cavities. *Org. Lett.* **2014**, *16*, 2896–2899.
- (13) Ma, Y.; Chi, X.; Yan, X.; Liu, J.; Yao, Y.; Chen, W.; Huang, F.; Hou, J.-L. Per-Hydroxylated Pillar[6]arene: Synthesis, X-ray Crystal Structure, and Host-Guest Complexation. *Org. Lett.* **2012**, *14*, 1532–1535.
- (14) Ogoshi, T. Synthesis of Novel Pillar-shaped Cavitands “Pillar[5]arenes” and Their Application for Supramolecular Materials. *J. Inclusion Phenom. Macrocyclic Chem.* **2012**, *72*, 247–262.
- (15) Strutt, N. L.; Forgan, R. S.; Spruell, J. M.; Botros, Y. Y.; Stoddart, J. F. Monofunctionalized Pillar[5]arene as a Host for Alkanediamines. *J. Am. Chem. Soc.* **2011**, *133*, 5668–5671.
- (16) Kitajima, K.; Ogoshi, T.; Yamagishi, T.-a. Diastereoselective Synthesis of a [2]catenane from a Pillar[5]arene and a Pyridinium Derivative. *Chem. Commun.* **2014**, *50*, 2925–2927.
- (17) Cragg, P. J.; Sharma, K. Pillar[5]arenes: Fascinating Cyclophanes with a Bright Future. *Chem. Soc. Rev.* **2012**, *41*, 597–607.
- (18) Ogoshi, T.; Demachi, K.; Kitajima, K.; Yamagishi, T.-a. Monofunctionalized Pillar[5]arenes: Synthesis and Supramolecular Structure. *Chem. Commun.* **2011**, *47*, 7164–7166.
- (19) Chen, Y.; He, M.; Li, B.; Wang, L.; Meier, H.; Cao, D. A Monophosphoryl Copillar[5]arene: Synthesis and Host-Guest Complexation with Alkanols. *RSC Adv.* **2013**, *3*, 21405–21408.
- (20) Meldal, M.; Tornøe, C. W. Cu-Catalyzed Azide-Alkyne Cycloaddition. *Chem. Rev.* **2008**, *108*, 2952–3015.

- (21) Strutt, N. L.; Zhang, H.; Giesener, M. A.; Lei, J.; Stoddart, J. F. A Self-Complexing and Self-Assembling Pillar[5]arene. *Chem. Commun.* **2012**, *48*, 1647–1649.
- (22) Zhang, H.; Strutt, N. L.; Stoll, R. S.; Li, H.; Zhu, Z.; Stoddart, J. F. Dynamic Clicked Surfaces Based on Functionalised Pillar[5]arene. *Chem. Commun.* **2011**, *47*, 11420–11422.
- (23) Zhang, H.; Ma, X.; Guo, J.; Nguyen, K. T.; Zhang, Q.; Wang, X.-J.; Yan, H.; Zhu, L.; Zhao, Y. Thermo-responsive Fluorescent Vesicles Assembled by Fluorescein-Functionalized Pillar[5]arene. *RSC Adv.* **2013**, *3*, 368–371.
- (24) Ogoshi, T.; Demachi, K.; Kitajima, K.; Yamagishi, T.-a. Selective Complexation of n-Alkanes with Pillar[5]arene Dimers in Organic Media. *Chem. Commun.* **2011**, *47*, 10290–10292.
- (25) Ogoshi, T.; Kayama, H.; Yamafuji, D.; Aoki, T.; Yamagishi, T.-a. Supramolecular Polymers with Alternating Pillar[5]arene and Pillar[6]-arene Units from a Highly Selective Multiple Host-guest Complexation System and Monofunctionalized Pillar[6]arene. *Chem. Sci.* **2012**, *3*, 3221–3226.
- (26) Ogoshi, T.; Kitajima, K.; Fujinami, S.; Yamagishi, T.-a. Synthesis and X-ray Crystal Structure of a Difunctionalized Pillar[5]arene at A1/B2 Positions by in situ Cyclization and Deprotection. *Chem. Commun.* **2011**, *47*, 10106–10108.
- (27) Zhang, Z.; Xia, B.; Han, C.; Yu, Y.; Huang, F. Syntheses of Copillar[5]arenes by Co-oligomerization of Different Monomers. *Org. Lett.* **2010**, *12*, 3285–3287.
- (28) Han, C.; Zhang, Z.; Yu, G.; Huang, F. Syntheses of a Pillar[4]arene[1]quinone and a Difunctionalized Pillar[5]arene by Partial Oxidation. *Chem. Commun.* **2012**, *48*, 9876–9878.
- (29) Ogoshi, T.; Yamafuji, D.; Kotera, D.; Aoki, T.; Fujinami, S.; Yamagishi, T.-a. Clickable Di- and Tetrafunctionalized Pillar[n]arenes ($n = 5, 6$) by Oxidation–Reduction of Pillar[n]arene Units. *J. Org. Chem.* **2012**, *77*, 11146–11152.
- (30) Strutt, N. L.; Fairen-Jimenez, D.; Iehl, J.; Lalonde, M. B.; Snurr, R. Q.; Farha, O. K.; Hupp, J. T.; Stoddart, J. F. Incorporation of an A1/A2-Difunctionalized Pillar[5]arene into a Metal–Organic Framework. *J. Am. Chem. Soc.* **2012**, *134*, 17436–17439.
- (31) Strutt, N. L.; Schneebeli, S. T.; Stoddart, J. F. Stereochemical Inversion in Difunctionalised Pillar[5]arenes. *Supramol. Chem.* **2013**, *25*, 596–608.
- (32) Yan, X.; Wei, P.; Li, Z.; Zheng, B.; Dong, S.; Huang, F.; Zhou, Q. A Dynamic [1]Catenane with pH-Responsiveness Formed via Threading-Followed-by-Complexation. *Chem. Commun.* **2013**, *49*, 2512–2514.
- (33) Yu, G.; Hua, B.; Han, C. Proton Transfer in Host–Guest Complexation between a Difunctional Pillar[5]arene and Alkylidiamines. *Org. Lett.* **2014**, *16*, 2486–2489.
- (34) Ogoshi, T.; Yamafuji, D.; Yamagishi, T.-a.; Brouwer, A. M. Forster Resonance Energy Transfer by Formation of a Mechanically Interlocked [2]Rotaxane. *Chem. Commun.* **2013**, *49*, 5468–5470.
- (35) Ogoshi, T.; Yamafuji, D.; Akutsu, T.; Naito, M.; Yamagishi, T.-a. Achiral Guest-Induced Chiroptical Changes of a Planar-Chiral Pillar[5]arene Containing One π -Conjugated Unit. *Chem. Commun.* **2013**, *49*, 8782–8784.
- (36) Kou, Y.; Tao, H.; Cao, D.; Fu, Z.; Schollmeyer, D.; Meier, H. Synthesis and Conformational Properties of Nonsymmetric Pillar[5]arenes and Their Acetonitrile Inclusion Compounds. *Eur. J. Org. Chem.* **2010**, 6464–6470.
- (37) Zhang, Z.; Luo, Y.; Xia, B.; Han, C.; Yu, Y.; Chen, X.; Huang, F. Four Constitutional Isomers of Bmpillar[5]arene: Synthesis, Crystal Structures and Complexation with n-Octyltrimethyl Ammonium Hexafluorophosphate. *Chem. Commun.* **2011**, *47*, 2417–2419.
- (38) Yu, G.; Zhang, Z.; Han, C.; Xue, M.; Zhou, Q.; Huang, F. A Nonsymmetric Pillar[5]arene-based Selective Anion Receptor for Fluoride. *Chem. Commun.* **2012**, *48*, 2958–2960.
- (39) Yao, Y.; Xue, M.; Chen, J.; Zhang, M.; Huang, F. An Amphiphilic Pillar[5]arene: Synthesis, Controllable Self-Assembly in Water, and Application in Calcein Release and TNT Adsorption. *J. Am. Chem. Soc.* **2012**, *134*, 15712–15715.
- (40) Nishimura, T.; Sanada, Y.; Matsuo, T.; Okobira, T.; Mylonas, E.; Yagi, N.; Sakurai, K. A Bimolecular Micelle Constructed from Amphiphilic Pillar[5]arene Molecules. *Chem. Commun.* **2013**, *49*, 3052–3054.
- (41) Yu, G.; Ma, Y.; Han, C.; Yao, Y.; Tang, G.; Mao, Z.; Gao, C.; Huang, F. A Sugar-Functionalized Amphiphilic Pillar[5]arene: Synthesis, Self-Assembly in Water, and Application in Bacterial Cell Agglutination. *J. Am. Chem. Soc.* **2013**, *135*, 10310–10313.
- (42) Zhang, H.; Ma, X.; Nguyen, K. T.; Zhao, Y. Biocompatible Pillararene-Assembly-Based Carriers for Dual Bioimaging. *ACS Nano* **2013**, *7*, 7853–7863.
- (43) Ogoshi, T.; Umeda, K.; Yamagishi, T.-a.; Nakamoto, Y. Through-Space π -Delocalized Pillar[5]arene. *Chem. Commun.* **2009**, *45*, 4874–4876.
- (44) Ogoshi, T.; Hashizume, M.; Yamagishi, T.-a.; Nakamoto, Y. Synthesis, Conformational and Host-Guest Properties of Water-Soluble Pillar[5]arene. *Chem. Commun.* **2010**, *46*, 3708–3710.
- (45) Sun, Y.-L.; Yang, Y.-W.; Chen, D.-X.; Wang, G.; Zhou, Y.; Wang, C.-Y.; Stoddart, J. F. Mechanized Silica Nanoparticles Based on Pillar[5]arenes for On-Command Cargo Release. *Small* **2013**, *9*, 3224–3229.
- (46) Adiri, T.; Marciano, D.; Cohen, Y. Potential ^{129}Xe -NMR Biosensors Based on Secondary and Tertiary Complexes of a Water-Soluble Pillar[5]arene Derivative. *Chem. Commun.* **2013**, *49*, 7082–7084.
- (47) Ogoshi, T.; Shiga, R.; Hashizume, M.; Yamagishi, T.-a. “Clickable” Pillar[5]arenes. *Chem. Commun.* **2011**, *47*, 6927–6929.
- (48) Nierengarten, I.; Guerra, S.; Holler, M.; Karmazin-Brelot, L.; Barberá, J.; Deschenaux, R.; Nierengarten, J.-F. Macrocyclic Effects in the Mesomorphic Properties of Liquid-Crystalline Pillar[5]- and Pillar[6]arenes. *Eur. J. Org. Chem.* **2013**, 3675–3684.
- (49) Nierengarten, I.; Buffet, K.; Holler, M.; Vincent, S. P.; Nierengarten, J.-F. A Mannosylated Pillar[5]arene Derivative: Chiral Information Transfer and Antiadhesive Properties Against Uropathogenic Bacteria. *Tetrahedron Lett.* **2013**, *54*, 2398–2402.
- (50) Nierengarten, I.; Nothisen, M.; Sigwalt, D.; Biellmann, T.; Holler, M.; Remy, J.-S.; Nierengarten, J.-F. Polycationic Pillar[5]arene Derivatives: Interaction with DNA and Biological Applications. *Chem.—Eur. J.* **2013**, *19*, 17552–17558.
- (51) Hu, X.-B.; Chen, Z.; Tang, G.; Hou, J.-L.; Li, Z.-T. Single-Molecular Artificial Transmembrane Water Channels. *J. Am. Chem. Soc.* **2012**, *134*, 8384–8387.
- (52) Schneebeli, S. T.; Cheng, C.; Hartlieb, K. J.; Strutt, N. L.; Sarjeant, A. A.; Stern, C. L.; Stoddart, J. F. Asararenes—A Family of Large Aromatic Macrocycles. *Chem.—Eur. J.* **2013**, *19*, 3860–3868.