Pillar-Shaped Ma
Pillar[n]arenes:
From Simple Receptors to

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What are pillar[n]arenes?

Macrocyclic host molecules have an angstrom-level space because of their cyclic structures. Guest molecules that fit the space can be selectively bound by physical interactions such as hydrogen bonding, ionic, and aromatic interactions. This cavity-size-dependent guest binding is a lock-and-key relationship. Such selective guest binding enables their use in medical and material applications. The production of macrocyclic host molecules with new structures and properties has opened up new fields of chemistry with global participation. The history of macrocyclic host molecules is long and started in the 1880s.[1] Figure 1 shows some widely used macrocyclic host molecules.

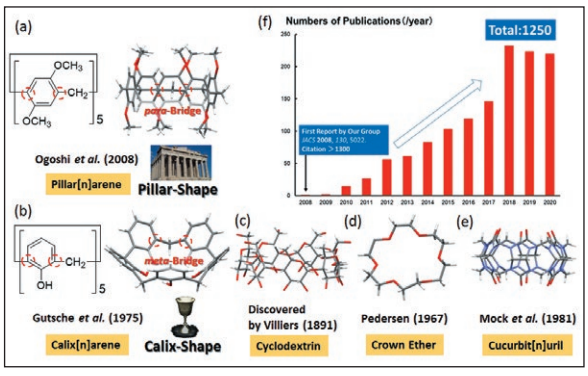

Figure 1 Structures of macrocyclic hosts of (a) pillar[n]arene, (b) calix[n]arene, (c) cyclodextrin, (d) crown ether, (e) cucurbit[n]uril and (f) number of reports concerning pillar[n]arenes from 2008 to 2020.

During their long history, the development of macrocyclic host molecules, which are now used by many chemists, was limited until recently. To enable their widespread use, macrocyclic host molecules must be easy-to-synthesize or commercially available, have unique host–guest properties, highly symmetric structures, and versatile functionalities, and endow the host–guest products with original properties that come from the structures and chemical compositions of the macrocyclic hosts. Cyclodextrins (Figure 1c), which are composed of sugar units, are typically obtained from natural products and have the longest history among macrocyclic host molecules. Their structures were first discovered by Villiers in 1891.[2] Despite their long history, cyclodextrins have been mainly used by chemists until now. Crown ethers were first synthesized by Pedersen in 1967 (Figure 1d).[3] They were the first macrocyclic compounds to be synthesized by chemists, therefore synthetic macrocyclic chemistry began with Pedersen's work. To honor the greatness of his achievement, Pedersen received the Novel Prize for Chemistry at 1987. In the 1980s, calix[n]arenes were popularized by Gutsche (Figure 1b). In these compounds, phenol units are connected by a methylene bridge at the meta-position, therefore they have calix-shaped structures, and this is the origin of their name.[4] Other calix-shaped meta-bridged phenolic macrocyclic compounds, namely calix[n]resorcinarenes, have also been developed.[5] Bowl-shaped macrocyclic hosts, which are formed from ortho-methylene-bridged phenolic units, i.e., cyclotriveratrylenes, have also been produced.[6] Cucurbit[n]urils are unique pumpkin-shaped macrocyclic host molecules (Figure 1e).[7-9] In 1981, Mock and coworkers identified a hexamer, i.e., cucurbit[6]uril, by X-ray crystallographic analysis.[7] However, the chemistry of cucurbit[6]uril was not expanded after this first discovery because of its low solubilities in common solvents. In 2000, 19 years after this first

crocyclic Hosts

Supramolecular Assemblies

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report, Kim and coworkers discovered other cucurbit[n]uril homologs, i.e., cucurbit[5-8]urils.[8] These were obtained by tuning the reaction conditions. Their development triggered the expansion of cucurbit[n]uril chemistry because, apart from cucurbit[6]uril, cucurbit[n]uril homologs have relatively high solubilities in common solvents. However, these host molecules were reported until 2000, which suggests that the discovery of new classes of macrocyclic hosts that can be used widely by chemists is challenging.

In 2008, we unexpectedly discovered new type of pillar-shaped macrocyclic host molecules, i.e., pillar[n]arenes (Figure 1a).[10,11] Figure 1f lists a number of publications that report pillar[n]arenes. Until 2011, only a limited number of researchers, including ourselves, worked in this field. However, from 2012, global interest in pillar[n]arenes began to grow, and this triggered further expansion of pillar[n]arene chemistry. Since 2018, which is the tenth anniversary of pillar[n]arene chemistry, the number of publications per year has exceeded 200. This shows that pillar[n]arene chemistry is expanding. The success of pillar[n]arene chemistry has been recognized by chemists as a new route to novel fields of chemistry and this has instigated the development of new macrocyclic host molecules. Pillar[n]arenes are therefore recognized as game-changing molecules in supramolecular chemistry in the early 21st century.

How were pillar[n]arenes discovered?

The discovery of pillar[n]arenes was accidental as were the discoveries of other famous macrocyclic hosts. Pillar[n]arenes were first obtained as an unexpected product when we synthesized phenolic polymers. When I started my academic career as an assistant professor at Kanazawa University, one of the projects in the laboratory was the synthesis of new types of phenolic polymers. I started my research on the synthesis of new phenolic polymers by designing phenolic monomers with my students. We tried to synthesize new phenolic polymers by reacting 1,4-dimethoxybenzene with paraformaldehylde in the presence of a Lewis acid. We screened the polymerization conditions and obtained phenolic polymers with high molecular weights by changing the reaction conditions such as the types of Lewis acids and solvents. Unexpectedly, when 1,2-dichloroethane was used as the solvent, the product was not a polymer but a particular oligomer (Figure 2a).

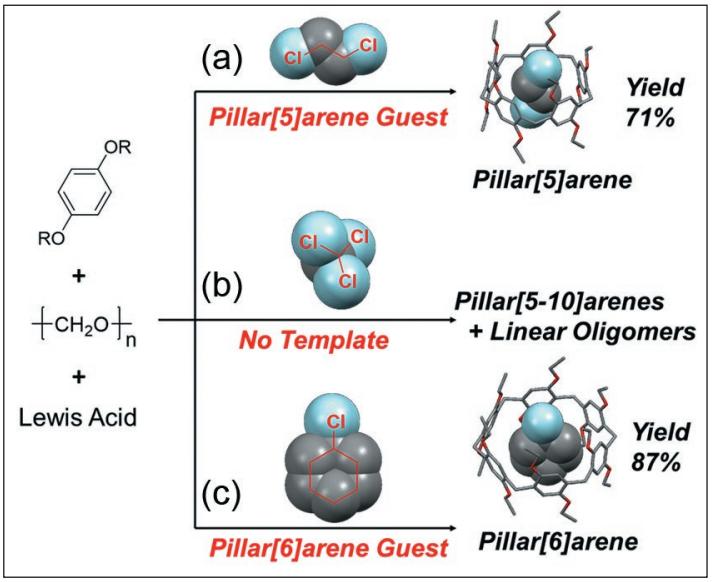

Figure 2 Solvent effect on macrocyclic formation. (a) 1,2-dichloethane and (c) chlorocylohexane acted as templates for pillar[5]arenes and pillar[6]arenes synthesis, respectively. (b) Chloroform did not act as a template for the particular pillar[n] arene formation.

X-ray crystallographic analysis showed that the obtained product was a cyclic pentamer composed of five 1,4-dimethoxybenzene units connected by methylene bridges at the 2,5-position (Figure 1a,

para-position). Because of the para-bridge linkage, the macrocycle had a highly symmetric pillar-shaped architecture, which was quite different from that of calix[n]arenes. Typical calix[n]arenes have vase-shaped structures because of the meta-bridge linkage (Figure 1b). We called this new type of macrocycle as pillar[5]arene because of its shape.[10]

What is the key to pillar[n]arene formation?

The difficult part of macrocycle synthesis is formation of cyclic structures. The synthesis of macrocyclic structures requires connection of the ends of linear compounds. We obtained pillar[5]arene in high yield in one simple step under reaction conditions similar to those used for phenolic resin synthesis. The question is: why can we prepare pillar[5]arene in such a high yield? Generally, a template works well for macrocyclic compound synthesis in high yields. Macrocyclic compounds are formed by complexation with a template (guest). A single macrocyclic compound that reflects the template size can therefore be obtained in high yield in the presence of the template. In other words, the obtained macrocyclic compounds are thermodynamically stable products in the presence of the template. Without the template, a mixture of macrocyclic compounds with various cavity sizes is produced. The macrocyclic formation efficiency depends on the strain energies of the macrocyclic compounds. In the absence of a template, macrocyclic compounds formed in a kinetically controlled system. Careful tuning of the reaction temperature and time is therefore necessary to obtain macrocyclic compounds. In the synthesis of pillar[5]arene, we selectively obtained the product in high yield without careful reaction condition tuning, which indicates that some reagents work as a template for pillar[5]arene formation. We therefore investigated various reaction conditions to identify the template for selective production of pillar[5]arene. We realized that solvents for the cyclization acted as the templates for the selective formation of pillar[5]arene. When we used 1,2-dichloroethane, a cyclic pentamer, i.e., pillar[5]arene, was selectively obtained in high yield (>70%, Figure 2a).[12] In contrast, with chloroform as the solvent, the obtained products were a mixture of linear oligomers and pillar[5–10]arenes (Figure 2b).[13] These results are related to the host–guest properties of pillar[5]arenes. The cavity size of a pillar[5]arene is ca. 4.7 Å, which fits linear molecules. 1,2-Dichloroethane is a linear molecule, and therefore acts as a template for selective pillar[5]arene synthesis. In contrast, chloroform is a branched molecule, and therefore does not act as a template for a pillar[n]arene with a particular size. In chloroform, the reaction proceeds under kinetic control. Precise tuning of the reaction time therefore resulted in the synthesis of larger pillar[n]arene homologs (n= 6, 7, 8, 9 and 10), but their yields were low because of the kinetic control system.[13] Based on these results, we tried to synthesize pillar[6]arene by using the template method. When we used chlorocyclohexane as a solvent, pillar[6]arene was obtained in 87% yield (Figure 2c). Chlorocyclohexane is a suitable size for the pillar[6]arene cavity, and therefore acts as a template for selective pillar[6]arene synthesis.[14]

How can pillar[n]arenes be functionalized?

Simple pillar[n]arenes have alkoxy groups on both rims. The alkoxy groups can be converted to phenolic groups by deprotection. Pillar[n]arenes with phenolic groups are useful key compounds for producing functionalized pillar[n]arenes because phenolic groups show high functionality. The easiest way to functionalize pillar[n]arenes by using the reactivity of the phenolic groups is etherification between the phenolic groups and compounds with a halogen group.[15-17] The introduction of triflate groups enables the use of cross-coupling reactions such as the Suzuki, Sonogashira coupling to directly connect aryl groups. Pillar[n]arenes with phenolic groups are therefore useful key compounds for preparing various functionalized pillar[n]arenes.

Pillar[n]arenes with 2n phenolic groups can be produced by deprotection of alkoxy groups with BBr_3 (Figure 3a).[10]

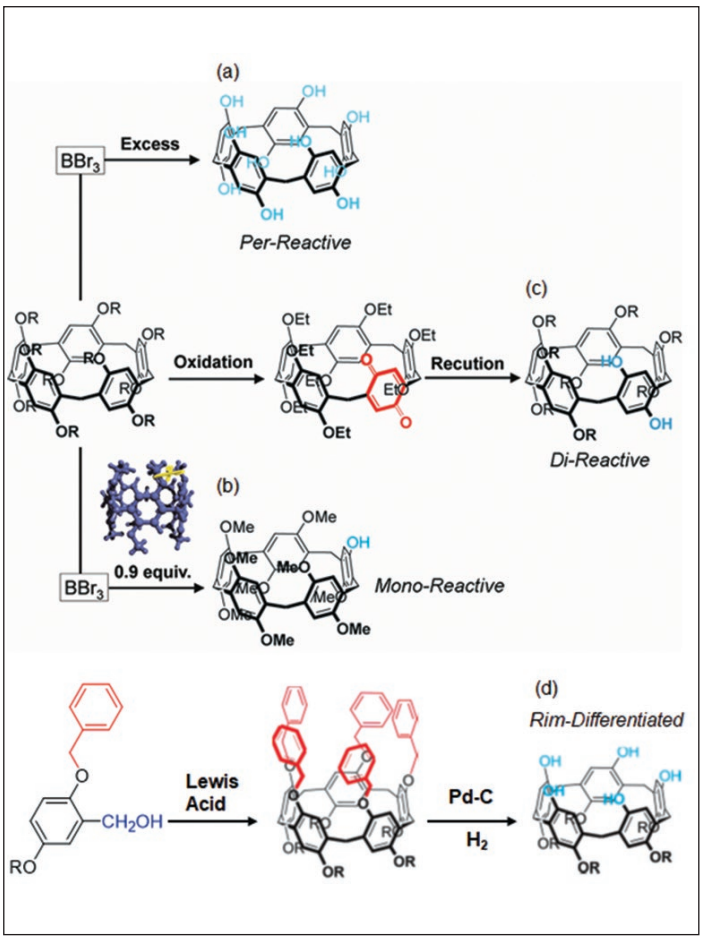

Figure 3 Procedures for (a) per-, (b) mono-, and (c) di-functional pillar[5]arenes, and (d) rim-differentiated pillar[5]arenes.

By tuning the deprotection conditions (Figure 3b), we prepared pillar[n]arenes with one phenolic group in moderate yields.[15] In the case of pillar[n]arenes with two or more phenolic groups, a major problem is that these pillar[n]arenes have isomers. For example, difunctionalized pillar[5]arenes and pillar[6]arenes have five and seven possible isomers, respectively. These phenolic pillar[5,6]arenes cannot be obtained by direct deprotection of alkoxy groups because many constitutional isomers are generated by direct deprotection. We reported a new route for synthesizing pillar[5]arenes and pillar[6]arenes with two or more phenolic groups via oxidation–reduction of the pillar[n]arene units (Figure 3c). Pillar[5]arenes with one and two benzoquinone units, and pillar[6]arenes with one, two, three, and four benzoquinone units were obtained by direct oxidation of the units.[16,17] Subsequent reduction of the benzoquinone units, gave pillar[5,6]arenes with phenolic groups at the same units. Rim-differentiated pillar[5]arenes, which have the same five substituents on one rim, can be produced by a "pre-orientation" strategy, which was developed by Ma et al., and Zuilhof and Sue et al in 2018.[18-20] In this strategy, hydroxymethyl groups were first installed into monomers (Figure 3d). The pre-orientation enabled successful synthesis of rim-differentiated pillar[5]arenes in moderate yields (ca. 15%–20%). A pillar[5]arene with five phenolic groups on one rim was obtained by using an oriented monomer with a benzyl group because deprotection of the benzyl group affords phenolic groups.[20]

What are good guests for pillar[n]arenes?

Pillar[n]arenes are composed of electron-donating 1,4-dialkoxybezene units, therefore the interior cavity is an electron-rich space (Figure 4a).[21-27]

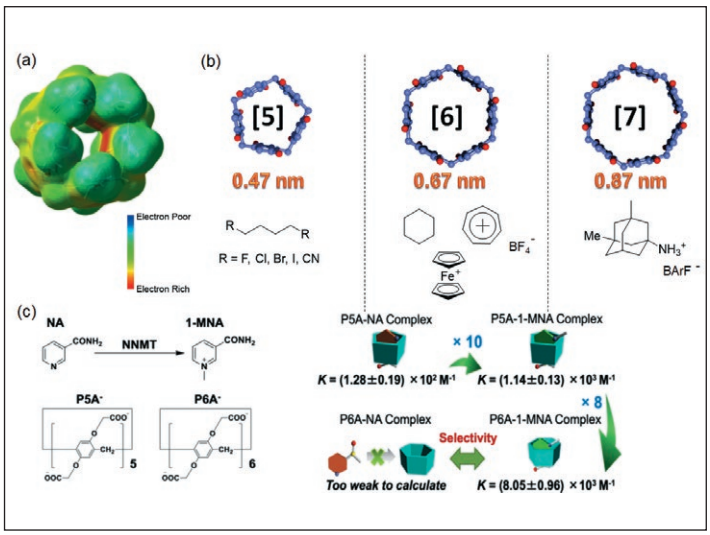

Figure 4 (a) Electrostatic potential profile of permethylated pillar[5]arene. (b) Guest molecules for pillar[5–7]arenes. (c) Chemical structures of anionic pillar[5,6]arenes and guests, and summary of the association constants for each host–guest complex. Reproduced with permission from reference.[27]

Pillar[n]arenes capture electron acceptors that fit the pillar[n]arene cavity size. Pillar[n]arenes also form host–guest complexes with neutral guest molecules. Pillar[5]arenes can capture linear hydrocarbons such as *n*-hexane because of multiple efficient CH-π interactions between the C-H groups of hydrocarbons and electron-rich benzene groups in the 1,4-dialkoxybenzene units (Figure 4b).[21] Linear molecules fit the pillar[5]arene cavity (ca. 4.7 Å). However, the host–guest interactions are less strong for *n*-alkanes (association constants: K = ca. 20–50 M^{-1}). Linear alkanes with electron-withdrawing groups such as cyano, triazole, and halogens at both ends are better guest molecules than non-substituted linear alkanes. In particular, *n*-butylenes with these terminal substituents are good guest molecules ($K > 10^3$ M^{-1}) because the pillar[5]arene height is suitable for the length of *n*-butylenes, and because of the high acidity of the C-H groups neighboring the electron-withdrawing groups.

In pillar[6]arenes, the cavity size is ca. 6.7 Å, which is a suitable size for branched and cyclic compounds such as cyclohexane, ferrocenium and tropylium cations.[22,23] An adamantane derivative is good guest molecules for pillar[7]arenes because the pillar[7]arene cavity size (ca. 8.7 Å) is suitable for the derivative.[24]

Substituents on the rims of pillar[n]arenes are important not only for enhancing the stability of the host–guest complex but also for changing the pillar[n]arene solubility. Normally, simple pillar[n]arenes with alkoxy groups are soluble in organic solvents such as halogenated and aromatic solvents. Host–guest complexation events are therefore mainly investigated in these organic solvents when simple pillar[n]arenes are used as the hosts. However, the solubilities of pillar[n]arenes depend on the types of the substituents. Cationic, anionic, and nonionic pillar[n]arenes are soluble in water, therefore water can be used as the host–guest complexation medium. In water, in addition to CH-π and charge-transfer interactions, hydrophobic–hydrophilic interactions stabilize host–guest complexes. In the case of cationic pillar[n]arenes, cationic–anionic interactions between the pillar[n]arenes and anionic guests also stabilize complexation.[25] In the converse combination, anionic pillar[n]arenes can capture cationic guests by cationic–anionic interactions.[26]

Our group discovered that one application of the host–guest properties of pillar[n]arenes is the use of pillar[6]arene with carboxylic anions as a biosensor for the vitamin metabolite 1-methylnicotinamide (1-MNA, Figure 4c).[27] 1-MNA is produced from nicotinamide by the enzymatic reaction of cancer-associated nicotinamide N-methyltransferase (NNMT). In aggressive cancer cells, high levels of 1-MNA are observed because NNMT activity increases in cancer cells. In the detection of the cancer-related molecule, 1-MNA is therefore an important research target. 1-MNA is cationic and water-soluble, therefore we hypothesized that a pillar[n]arene with carboxylate anions could be used as a biosensor for 1-MNA in aqueous media. An anionic pillar[5]arene formed a 1:1 complex with 1-MNA in water. The association constant (K) of the host–guest complex was $1.14 \pm 0.13 \times 10^3$ M^{-1}. The size of 1-MNA (ca. 0.58 nm × 0.68 nm) is larger than that of the pillar[5]arene cavity (ca. 0.47 nm), therefore the K value is not so high. Another weak point is that the anionic pillar[5]arene also formed relatively stable host–guest complex with nicotinamide ($K = 1.28 \pm 0.19 \times 10^2$ M^{-1}), which is metabolized to 1-MNA by NNMT and in present in normal cells. To overcome the problem, our next choice for increasing the association constant was use of an anionic pillar[6]arene. The association constant (K) of the pillar[6]arene–1-MNA complex is $8.05 \pm 0.96 \times 10^3$ M^{-1}, which is eight times higher than that of the complex with pillar[5]arene. The cavity size of pillar[6]arene is ca. 0.67 nm, which should be suitable size for 1-MNA. Furthermore, the anionic pillar[6]arene hardly formed a host–guest complex with nicotinamide. The anionic pillar[6]arene therefore acted as a biosensor for 1-MNA.

How can planar chiral pillar[n]arenes be separated?

Simple pillar[n]arenes do not have stereogenic carbons, but show planar chirality because of the position of the alkoxy substituents (Figure 5a).[28-31]

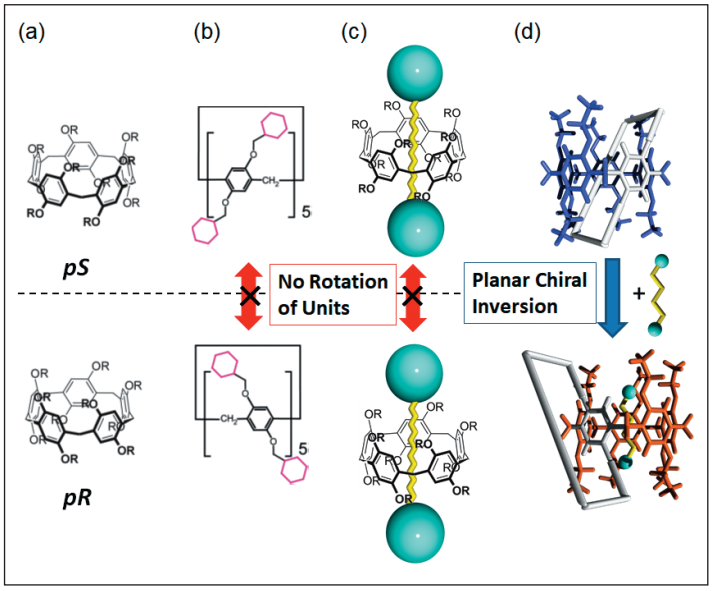

Figure 5 (a) Planar chirality of pillar[5]arene. Separation of enantiomers by (b) introducing bulky substituents and (c) formation of [2]rotaxane. (d) A schematic representation of the planar chiral inversion triggered by achiral guest. Reproduced with permission from reference.[31]

In their single crystal structures, we found enantiomers in pS and pR forms in a 1:1 ratio. However, in most cases, we could not separate the enantiomers by chiral column chromatography because racemization occurred via rotation of the units. This means that separation of the enantiomers is possible if we can stop the unit rotation. One useful way to stop the unit rotation is introduction of bulky substituents on the rim because the steric hindrance inhibits the unit rotation (Figure 5b).[29] When we installed cyclohexylmethyl groups on the rims, the unit rotation was inhibited, and the enantiomers were successfully separated by chiral column chromatography. This is the first example of the separation of pillar[n]arene enantiomers. Another method for enantiomer separation is formation of rotaxane structures in which a cyclic molecule is threaded onto an axle molecule and end-capped with bulky groups at the terminal of the axle molecule. Formation of a rotaxane structure also inhibits the unit rotation because of the presence of the axle in the cavity (Figure 5c).[30]

In contrast to point chirality, one of the interesting aspects of planar chirality is the dynamic chirality changes caused by the unit rotation. By controlling the unit rotation, the pS and pR forms can be switched. To control the chirality, we designed a new catenane-like structure (Figure 5d).[31] Catenanes are compounds in which two or more macrocycles are mechanically interlocked. In this molecule, the guest is an alkyl chain connected to one pillar[5]arene unit. Rotation of the unit connecting the alkyl chain therefore switches inclusion and dethreading of the alkyl chain. In the inclusion form, the structure is similar to that of [2]catenane. In the dethreaded form, two rings are connected covalently, but are not interlocked with each other. The molecule can therefore be described as a pseudo[1]catenane. The pS and pR enantiomers of the inclusion form were successfully separated by chiral column chromatography because of inhibition of the unit rotation in the inclusion form. On addition of a competitive guest, the planar chirality was converted from pS to pR or pR to pS because the unit rotation occurred via structural changes from the inclusion form to the dethreading form.

How can pillar[n]arenes be assembled?

Formation of one-dimensional (1D) tubes: Pillar[n]arenes are highly symmetric polygonal structures. The pillar-shaped structures differ from those of other macrocyclic hosts and should be suitable for the construction of 1D tubes. The versatile functionality of pillar[n]arenes enables 1D tube formation from inter-molecular assemblies of pillar[n]arenes. Pillar[n]arenes have two faces of the same size, and this introduces sites for interactions such as hydrogen-bonding and ionic interactions on both rims, which leads to the formation of continuous 1D tubes. For example, pillar[5]arene with 10 hydroxy groups can form 1D tubes via inter-molecular hydrogen bonds, and this assembly can form bundle structures eventually (Figure 6a).[32]

The formation of 1D tubular structures has also been induced by host–guest complexation of pillar[5]arene crystals with long, linear *n*-alkane guests (Figure 6b).[33] A pillar[5]arene with 10 ethoxy groups formed herringbone assemblies by complexation with short *n*-alkane guests such as *n*-hexane C6 (Cn, C_nH_{2n+2}), and C7 because C6 and C7 are shorter than the height of pillar[5]arene. The formation of 1D channels was achieved by complexation with long *n*-alkanes with chains containing more than eight carbon atoms (>C8). This is because the pillar[5]arene height is less than the length of C8. The C8 molecule is not completely covered by a single molecule of pillar[5]arene, therefore a neighboring pillar[5]arene needs to cooperatively cover the protruding part of C8, which results in 1D channel formation. The length of the *n*-alkane guest determines the supramolecular assembly of pillar[5]arenes in the crystalline state.

Complexation with a linear polymer also triggers 1D channel formation because polymer chains are much longer than the height of pillar[5]arene.[34] Poly(ethylene oxide) (PEO) has been used as the linear polymeric chain. The melting point of PEO is approximately 60°C, therefore PEO is in the molten state at 80°C. Immersion of pillar[5]arene crystals in molten PEO affords 1D channel structures via complexation of PEO with pillar[5]arene. Pillar[5]arene crystals selectively took up high-molecular-weight PEO from a mixture of PEOs of various molecular weights (Figure 6c). This high mass fractionation resulted from the increasing number of attractive CH-π interactions between PEO C-H groups and the π-electron-rich 1D channel of pillar[5]arene with increasing PEO chain length. This was determined by molecular mechanics simulations.

Length-controlled 1D tubes can be produced by layer-by-layer assembly of cationic and anionic pillar[5]arenes (Figure 7).[35]

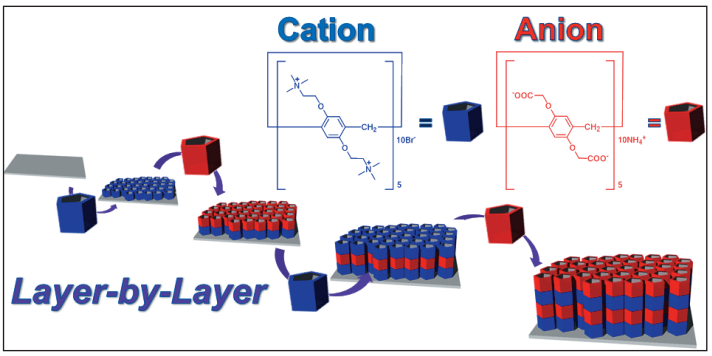

Figure 7 Layer-by-layer assembly by consecutive adsorption of cationic and anionic pillar[5]arenes. Reproduced with permission from reference.[35]

Normally, cationic and anionic polymers are used for layer-by-layer assembly because there are multiple cationic–anionic interactions between cationic and anionic polymeric chains. Pillar[n]arenes have two faces, and the two faces have multiple interaction sites. The formation of 1D channels on the surface via layer-by-layer assembly is therefore possible. Immersion of an inorganic substrate with anionic charges on the surface in a cationic pillar[5]arene solution leads to cationic pillar[5]arene assembly on the surface. An important point regarding this system is that pillar[5]arene has two cationic rims; one cationic rim is used

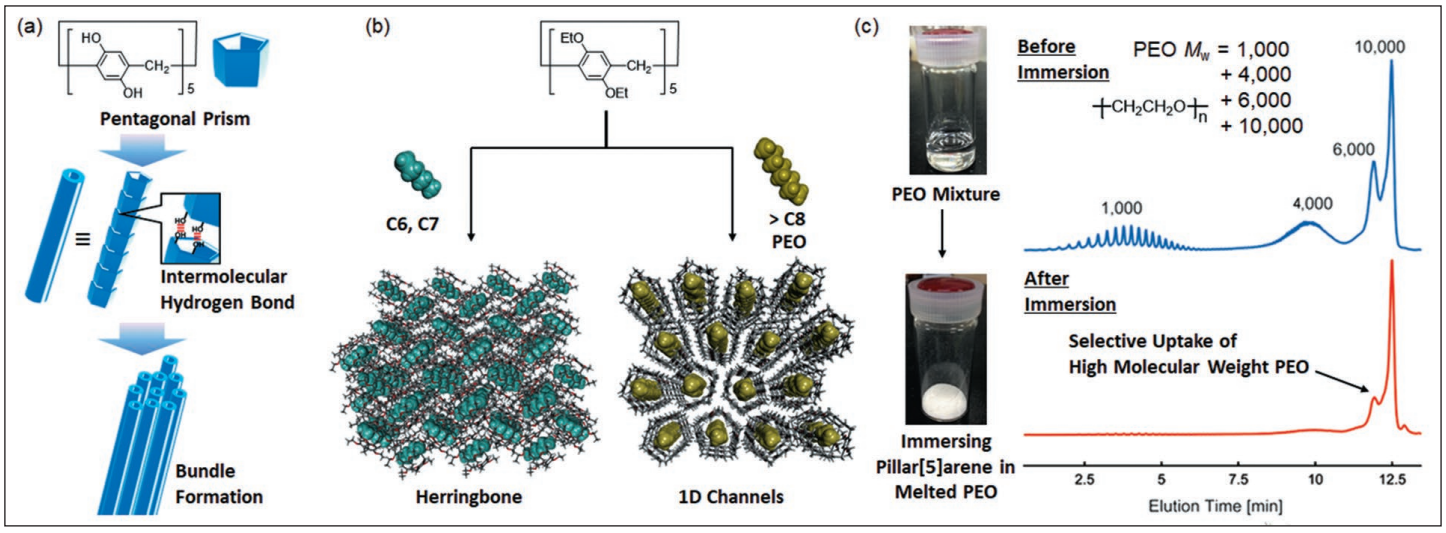

Figure 6 (a) 1D tube formation by inter-molecular hydrogen bonding between pillar[5]arenes with 10 hydroxy groups. (b) Guest length selective supramolecular assemblies of crystalline pillar[5]arenes. (c) High mass fractionation by 1D pillar[5]arene channels. Liquid chromatography traces of an equal-weight mixture of PEOs (upper) and host–guest complex crystals after the immersion in the mixture (lower). Reproduced with permission from reference.[34]

for adsorption on the inorganic surface by cationic–anionic interactions, but the other rim still has positive charges. Dimeric tubular structures can therefore be formed on the surface by immersing the cationic pillar[5]arene film in an anionic pillar[5]arene solution. At this stage, the surface is anionic, therefore immersing the resulting film into a cationic pillar[5]arene solution results in formation of trimeric tubular structures. Eventually, by alternating immersions of the film, length-controlled 1D tubes can be obtained.

Pillar[n]arenes have two interaction faces, and therefore form continuous 1D channel structures. Pillar[n]arenes with one interactive face and one face with no interaction sites can be used as the ends of 1D tubes to obtain length-controlled discrete 1D tubes (Figure 8a).[36]

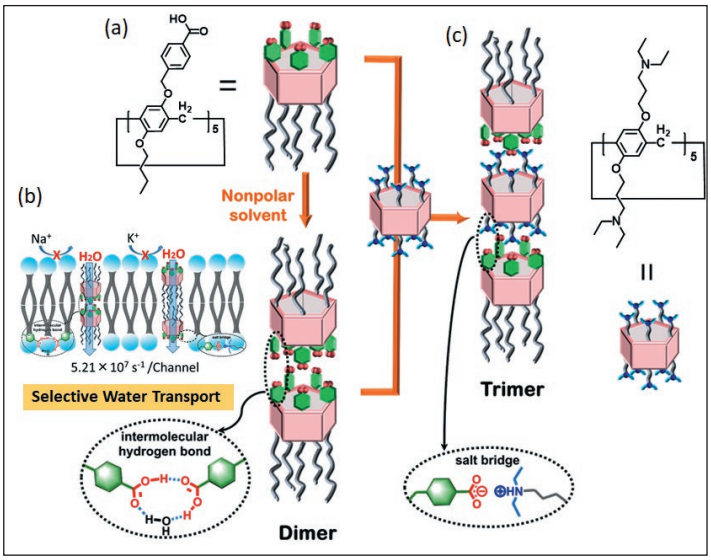

Figure 8 Rational design of discrete tubes by dimerization and trimerization of pillar[5]arenes. Reproduced with permission from reference.[36]

Use of an improved procedure for synthesizing rim-differentiated pillar[5]arenes, enabled the synthesis of new rim-differentiated pillar[5]arenes bearing benzoic acid groups on one rim and alkyl chains on the other rim. Benzoic acids form dimeric structures at high concentrations, therefore the rim-differentiated pillar[5]arenes form dimeric structure at high concentrations. The formation of dimeric structures was confirmed by single-crystal analysis of the rim-differentiated pillar[5]arene. Two molecules of the rim-differentiated pillar[5]arene interact with each other head-to-head via hydrogen bonds, which results in a dimeric tubular structure.

Discrete dimers can act as transportation channels for water molecules, but not for larger cations such as sodium or potassium cations (Figure 8b).[37] The normal pillar[5]arene cavity size is ca. 4.7 Å, but a discrete dimer has a narrow cavity on the benzoic acid group rim. The inter-molecular hydrogen bonds between the benzoic acid groups on the rim narrow the cavity size to ca. 2.8 Å; this can act as a water channel but blocks the passage of sodium or potassium cations. Another interesting feature is a rapid water transportation ability. These dimers can transport ca. 10^7 water molecules s^{-1}/channel, which is only one order of magnitude lower than the value for the natural membrane protein aquaporin (ca. 10^{8-9} water molecules s^{-1}/channel).

The dimer can be converted to a discrete trimer (Figure 8c).[36] Mixing a rim-differentiated pillar[5]arene and peralkylamino-substituted pillar[5]arene in a 2:1 feed ratio resulted in formation of a discrete tubular trimer via multiple ionic interactions.

Formation of two-dimensional (2D) sheets: Pillar[5]arenes and pillar[6]arenes are regular pentagonal and hexagonal molecules, respectively. Hexagonal molecules are good building blocks for obtaining well-defined 2D supramolecular assemblies because the structures are more highly symmetric than pentagonal molecules, this is known as molecular tiling. We therefore decided to use hexagonal pillar[6]arene as a building block for 2D sheet synthesis (Figure 9).[38]

As the driving force for assembling pillar[6]arenes, we used formation of the intermolecular supramolecular charge-transfer complex between hydroquinone and benzoquinone, which is generated by oxidation of hydroquinone. Chemical or electrochemical oxidation of pillar[6]arene resulted in formation of 2D hexagonal sheets. The 2D hexagonal sheets have pores (4.04 Å) that arise from the pillar[6]arene assembly (4.10 Å).

We speculated that the 2D porous sheets could potentially be used as a source for synthesizing carbon materials by carbonization at 900°C because they have many phenolic groups similarly to good carbon sources such as phenolic resins. Carbonization of the 2D sheet gave carbon material in relatively high yield (54%). The carbon material had pores of size 4.09 Å, which was similar to those of the 2D sheet (4.04 Å) and the pillar[6]arene assembly (4.10 Å). A porous carbon material with pores of the same size as those of the organic building block can therefore be produced by the assembly and subsequent carbonization. Angstrom-level pore control of carbon materials has been investigated by using porous coordination polymers or metal–organic frameworks and covalent organic frameworks. However, their original porous structures were destroyed during the carbonization process in most cases. Porous material synthesis from the pillar[6]arene assembly is therefore a new strategy for creating carbon materials with pores controlled at the angstrom level from organic building blocks.

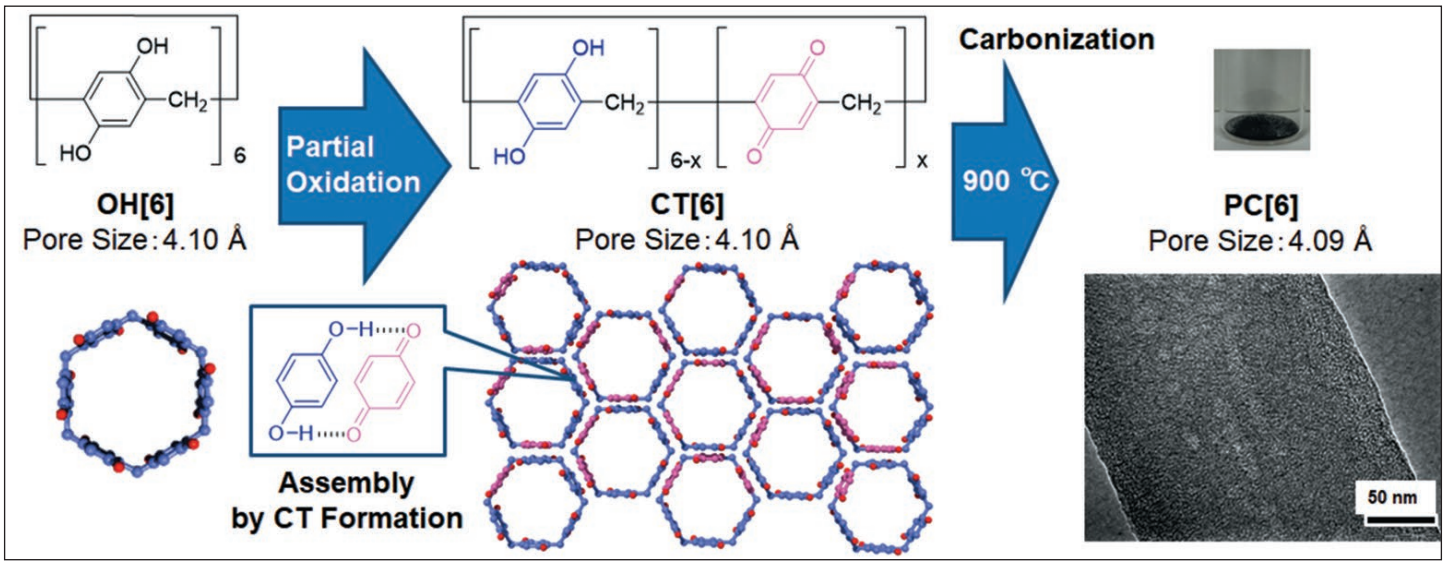

Figure 9 2D supramolecular polymerization by oxidation OH[6] and porous carbon (PC[6]) by carbonization of CT[6].

Formation of three-dimensional (3D) spheres: Fullerene (C_{60}), which is constructed from 12 pentagons and 20 hexagons, has a 3D soccer-ball spherical structure. In this structure, the pentagons provide curvature for 3D sphere formation. We successfully obtained a 2D sheet by assembly of pillar[6]arenes (Figure 9), therefore our next challenge was construction of 3D spherical structures by incorporation of pentagonal pillar[5]arenes into the 2D sheet (Figure 10).[39]

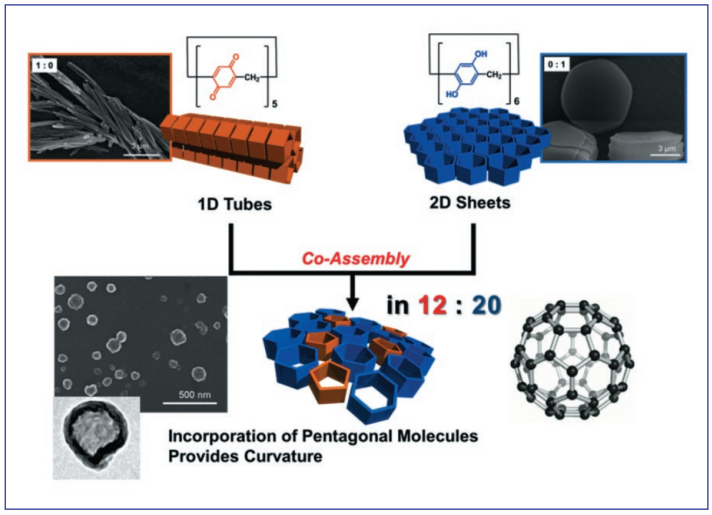

Figure 10 SEM images and schematic representation of 1D tube formation by pillar[5]quinone, 2D hexagonal sheet formation by pillar[6]arene and the vesicle formation by co-assembly of pentagon pillar[5]quinones with hexagon pillar[6]arenes.

However, a 2D sheet constructed from pillar[6]arenes was formed by simply mixing pillar[5]arene and pillar[6]arene because the more highly symmetric pillar[6]arene is easier to assemble than pillar[5]arene. Mixing of pillar[5]arene and pillar[6]arene at the molecular level was achieved by using the inter-molecular charge-transfer complex between hydroquinone and benzoquinone. Pillar[5]quinone, which was prepared by oxidation of pillar[5]arene, was mixed with pillar[6]arene. In this case, pillar[5]quinone was completely mixed with pillar[6]arene via the inter-molecular charge-transfer complex. The assembled structures were tubular that consisted of pillar[5]quinone alone, and co-assembled samples containing excess pillar[5]quinone. Disk-shaped hexagonal assemblies of pillar[6]arene alone were observed along with co-assembled samples with excess pillar[6]arene. At a 12:20 pillar[5]quinone:pillar[6]arene molar ratio, which is the magic ratio for C_{60}, 3D spheres were formed by co-assembly of pillar[5]quinone with pillar[6]arene.

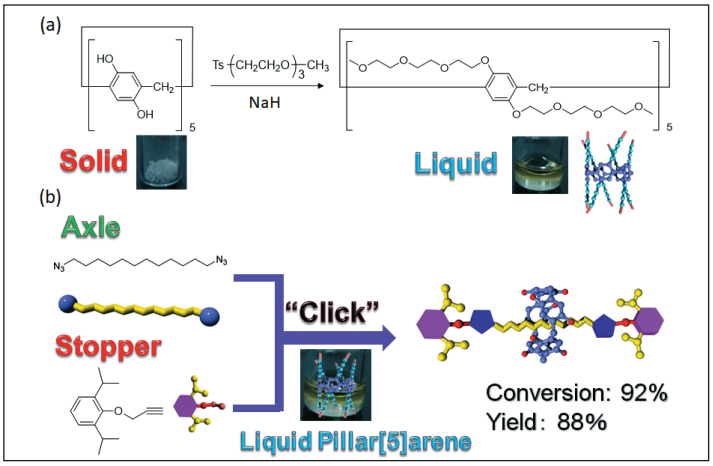

Figure 11 (a) Solid to liquid transition by modification of tri(ethylene oxide) chains on the rims of pillar[5]arene. (b) High yield synthesis of [2]rotaxane by Huisgen reaction in the liquid pillar[5]arene.

How can bulk pillar[n]arene assemblies be used?

Host–guest complexation events are generally performed in the solution state because the host molecules are solids in most cases. However, when we synthesized a pillar[5]arene with 10 tri(ethylene oxide) chains, the obtained macrocyclic compound was liquid at room temperature (Figure 11a).[40]

We therefore used the liquid pillar[5]arene not only as a macrocyclic compound but also as a solvent for synthesis of the interlocked molecule [2]rotaxane. An axle with azide groups at both ends and a stopper with an alkyne group were directly dissolved in bulk liquid pillar[5]arene (Figure 11b). The end-capping reaction was achieved by a Husigen-type copper(I)-catalyzed alkyne–azide cycloaddition "click" reaction. Surprisingly, [2]rotaxane was obtained in high yield (>88%) in the bulk system, whereas the yield of [2]rotaxane was quite low when a normal solvent system was used. In a normal solvent system, at the molecular level, the macrocyclic host and guest molecules are dispersed in a good solvent, therefore host–guest complexation takes place when the guest molecules meet the host molecules. However, host and guest solvation decrease the chance of these molecules meeting each other and decrease the stability of the host–guest complex. The yield of [2]rotaxane is therefore low in normal solvent systems. In contrast, in a bulk system, the guest molecules are directly surrounded by an excess of liquid pillar[5]arene. Inclusion of the guest molecules into the pillar[5]arene cavity is therefore maintained, which results in high-yield synthesis of [2]rotaxane.

We realized that a host–guest complexation system that uses bulk liquid pillar[5]arene is more efficient than a normal solvent system. We therefore next investigated host–guest complexation of crystalline pillar[n]arenes (Figure 12).[41,42]

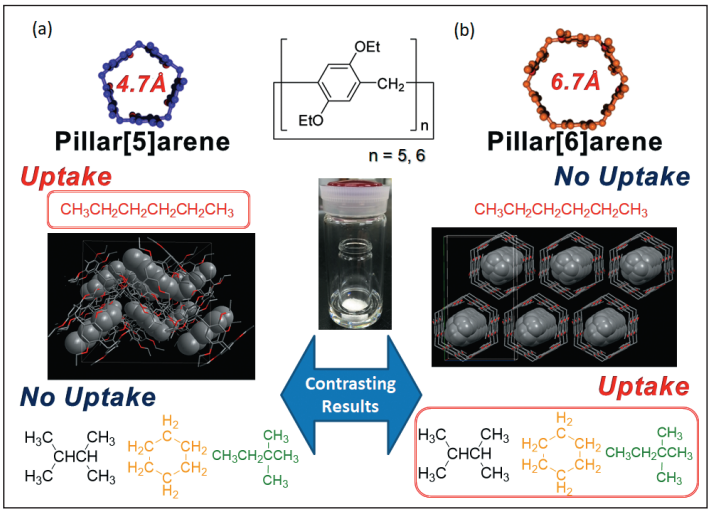

Figure 12 Alkane-shape selective vapor uptake by crystalline (a) pillar[5]arenes and (b) pillar[6]arenes.

When pillar[5]arene crystals were exposed to linear alkane vapors such as *n*-hexane vapor, the crystals took up the linear alkane vapor (Figure 12a). However, no uptake of cyclic alkanes including cyclohexane and branched alkane vapors was observed. The converse results were obtained when pillar[6]arene crystals were used (Figure 12b). Pillar[6]arene crystals took up cyclic and branched alkane vapors, but did not take up linear alkane vapors. The selectivity is the same as that for the host–guest complexation in normal solvent systems. We therefore discovered that host–guest complexation events occur even in crystalline pillar[n]arenes. Furthermore, pillar[n]arene crystals quantitatively took up alkane vapors into the crystals, whereas the association constants for host–guest complexes between pillar[n]arene and alkane guests are quite low in normal solvent systems, as a result of solvation. Crystal-state complexation is therefore superior for host–guest complex formation even in the low association constants in solvent systems.

We used the alkane-shape selective complexation to separate linear and breached alkanes (Figure 13).[42]

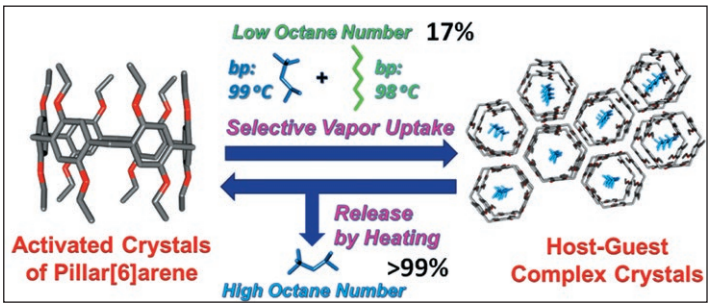

Figure 13 Representation of the method to obtain highly pure isooctane from a mixture of isooctane and *n*-heptane using crystalline pillar[6]arene as the adsorbent. Reproduced with permission from reference.[42]

Separation of linear and branched alkanes is an important technique because gasoline is mainly a mixture of the branched alkane—isooctane and linear alkane—*n*-heptane. Gasoline with a high isooctane ratio gives a good performance, therefore separation of isooctane and *n*-heptane is an important target. However, the boiling point of isooctane (99°C) is almost the same as that of *n*-heptane (98°C), therefore the separation of these alkanes by distillation is difficult, and new separation techniques are needed.

We investigated the use of pillar[6]arene crystals for the isolation of isooctane from a mixture of isooctane and *n*-heptane. When pillar[6]arene crystals were exposed to vapor mixtures containing 5% isooctane, the ratio of isooctane in the crystals was 95%. Exposure of the crystals to vapor mixtures containing >17% isooctane increased the ratio of isooctane in the crystals to >99%. The included isooctane could be stored in air at 25°C for 1 month, therefore the crystals can be used for storage of volatile isooctane. The release of high-purity isooctane (>99%) was achieved by heating the host–guest complex crystals at 110°C for 12 h. The crystals did not contain isooctane after heating, and could therefore be reused for gasoline quality improvement.

Conclusions

Research in the field of pillar[n]arene chemistry started in 2008 from our accidental discovery during phenolic polymer synthesis. The fundamental properties of pillar[n]arenes, e.g., their host–guest properties and planar chirality, were then discovered. In addition, position-selective functionalizations such as mono-, di- and per-functionalization procedures were developed. Uncovering these fundamental properties and the development of functionalization procedures triggered construction of various functional molecules at the single molecule level. Functional materials can be produced by installing functional groups on both rims of pillar[n]arenes. On the basis of their host–guest properties, pillar[n]arene-based interlocked molecules such as rotaxanes, catenanes, and polyrotaxanes were prepared. The direction of research into pillar[n]arene chemistry then turned from the single molecule level to supramolecular architectures and to supramolecular assemblies. Pillar[n]arenes have simple regular polygonal structures, therefore pillar[n]arenes are useful building blocks for creating various supramolecular assemblies with ordered structures. The pillar[n]arene structure is simple, therefore we believe that pillar[n]arenes have unlimited potential, and look forward to new directions in pillar[n]arene research, which might extend the present concept of supramolecular chemistry. ◆

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