

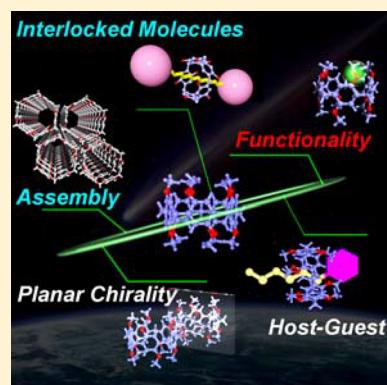
Pillar-Shaped Macrocyclic Hosts Pillar[n]arenes: New Key Players for Supramolecular Chemistry

Tomoki Ogoshi,*^{†,‡} Tada-aki Yamagishi,[†] and Yoshiaki Nakamoto[†]

[†]Graduate School of Natural Science and Technology, Kanazawa University, Kakuma-machi, Kanazawa 920-1192, Japan

[‡]Japan Science and Technology Agency, PRESTO, 4-1-8 Honcho, Kawaguchi, Saitama 332-0012, Japan

ABSTRACT: In 2008, we reported a new class of pillar-shaped macrocyclic hosts, known as “pillar[n]arenes”. Today, pillar[n]arenes are recognized as key players in supramolecular chemistry because of their facile synthesis, unique pillar shape, versatile functionality, interesting host–guest properties, and original supramolecular assembly characteristics, which have resulted in numerous electrochemical and biomedical material applications. In this Review, we have provided historical background to macrocyclic chemistry, followed by a detailed discussion of the fundamental properties of pillar[n]arenes, including their synthesis, structure, and host–guest properties. Furthermore, we have discussed the applications of pillar[n]arenes to materials science, as well as their applications in supramolecular chemistry, in terms of their fundamental properties. Finally, we have described the future perspectives of pillar[n]arene chemistry. We hope that this Review will provide a useful reference for researchers working in the field and inspire discoveries concerning pillar[n]arene chemistry.



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1. INTRODUCTION

The design and synthesis of new macrocyclic host molecules represent challenging areas of research. However, it is envisaged that new developments in this field will open the unrealized potential of supramolecular chemistry and provide access to new host molecules with unique functional characteristics that result from their unique shape, reactivity, and host–guest properties. From a historical perspective, it is clear that the arrival of new macrocyclic host systems in 1890 triggered an intense period of research and development in the field of supramolecular chemistry. The characteristics of an effective host compound are covered by the following points (Figure 1).

(1) Shape: Prospective host compounds should possess a unique shape that has not been reported previously in the literature. (2) Synthesis: Host compounds should be easy to make in large quantities from inexpensive reagents. (3) Solubility: Host compounds should be highly soluble in organic solvents and aqueous media such that they can be subject to various organic reactions to allow for the unlimited functionalization of the macrocyclic compounds. In addition, a reasonable degree of solubility is required to investigate their molecular recognition abilities. (4) Versatile functionality: Host compounds should contain reactive functional groups that can be converted to other functional groups using simple organic

reactions to maximize their assembly and molecular recognition properties in various media. (5) Homologues and host–guest ability: Macro cyclic host compounds should have at least one homologue that can accommodate guest molecules on the basis of its cyclic structure. Taken together, these points indicate that a prospective host molecule should show guest shape-selectivity and high binding ability, as well as having homologues with different cavity sizes that show different host–guest abilities depending on their cavity size. To provide a greater understanding of the five points listed above, we discussed them in detail below by taking some of the most well-known host molecules, including cyclodextrins (CDs),^{1–10} crown ethers,^{11–17} calix[n]arenes,^{18–21} and cucurbit[n]urils (CB[n]-s)^{22–32} as examples.

(1) Shape: The shape of a macrocyclic compound is one of its important characteristics. CDs and calix[n]arenes are nonsymmetrical bucket- and calix-shaped structures, respectively, whereas CB[n]-s are highly symmetrical pumpkin-like structures. Crown ethers, identified by C. J. Pedersen in 1967,¹¹ have crown-like structures on their X-ray crystal structures.

(2) Synthesis: CDs can be obtained from starch using an enzymatic process, and robust processes of this type have been developed to provide efficient access to large quantities of CD homologues consisting six, seven, and even eight glucopyranose units, (i.e., α -, β -, and γ -CDs). CD homologues with different cavity sizes can therefore be purchased at a moderate price. In contrast, crown ethers, calix[n]arenes, and CB[n]-s can only be produced by synthetic chemistry. Crown ether homologues can be produced in relatively high yields using the metal cation-template method,¹¹ while calix[n]arene homologues can be prepared by tuning temperature and base concentration conditions of the base-induced oligomerization between phenols and formaldehyde.²⁰ CB[n]-s are prepared by the condensation reaction of glycoluril and formaldehyde.²⁷ By tuning the reaction temperature of this process, it is possible to obtain a mixture of CB[n] homologues.²⁸ However, it has not yet been possible to achieve the selective synthesis of specific CB[n] homologues, and an additional purification step is therefore required to isolate CB[n] homologues from the mixture.

(3) Solubility: CDs are cyclic oligosaccharides consisting of several glucopyranose units, and consequently have many hydroxyl groups. Native CDs therefore exhibit good solubility in highly polar solvents such as water, *N,N*-dimethylformamide (DMF), and dimethyl sulfoxide (DMSO), but are insoluble in solvents with intermediate dielectric constants such as acetone, tetrahydrofuran (THF), chloroform, and dichloromethane, as well as nonpolar solvents such as *n*-hexane. CB[n]-s also exhibit poor solubility problems. The cyclic hexamer CB[6] was originally reported by Mock et al. in 1981.²⁷ Unfortunately, the poor solubility of CB[6] in aqueous media (0.018 mM) meant that research pertaining to the development of CB[n] chemistry progressed at a slow pace until 2000. In 2000, Kim et al. developed a new process for the synthesis of CB[n] homologues ($n = 5–11$) by tuning the reaction condition.²⁸ These new CB[n] homologues showed moderate solubility in water (e.g., CB[5], 420 mM; CB[7], 370 mM), which allowed for the rapid development of CB[n] chemistry following Kim's discovery in 2000. In contrast, crown ethers are soluble in a variety of solvents because they contain amphiphilic oligo(ethylene oxide) chains. Calix[n]arenes also show high solubility in a wide range of organic solvents, including chloroform, acetone, THF, DMF, and DMSO.

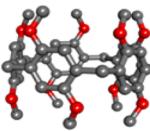
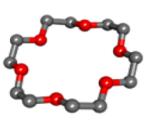
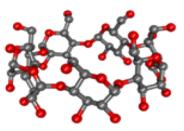
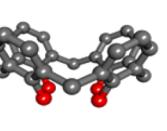
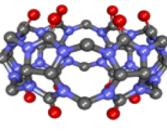
Structure					
Features	Pillar[n]arene	Crown Ether	Cyclodextrin	Calix[n]arene	Cucurbit[n]uril
Shape	Pillar	Crown	Bucket	Calix	Pumpkin
Synthesis	◎	○	◎	○	△
Solubility	High in Non-Polar Solvents	High in Various Solvents	High in Highly-Polar Solvents	High in Non-Polar Solvents	Low in Water
Functionality	◎	△	◎	○	△
Homologs	○ 5, 6	◎ 12-24	○ α, β, γ-CDs	○ 4-8	◎ 5-8
Host-Guest (Aqueous)	○	△	○	○	◎
Host-Guest (Organic)	○	○	△	○	✗
Flexibility	Flexible	Flexible	Rigid	Flexible	Rigid
Symmetry	○	✗	✗	✗	○

Figure 1. Comparison of pillar[n]arenes with several other well-known host molecules.

(4) Functionality: Native CDs have many highly reactive hydroxyl groups, which can be used to introduce a variety of functional groups.⁵ However, the poor solubility of CDs in the organic solvents typically used in synthesis means that they cannot be subjected to a large range of organic reactions, therefore limiting the number of functional groups that can be added to these macrocyclic host platforms. Reactions for the functionalization of CDs are mainly conducted in amphiphilic solvents such as DMF and DMSO, as well as aqueous media, because of their poor solubility. The yields of the reactions used for the functionalization of CDs are therefore relatively low in most cases. To overcome this problem, several organo-soluble CDs have been synthesized by introducing protecting moieties such as methyl and benzyl groups to the hydroxyl groups of the CDs.^{9,10} The resulting organo-soluble CDs can be subjected to a much wider variety of organic reactions than the parent CDs to obtain suitably functionalized CDs. Calix[n]arenes show good solubility in most typical organic solvents and have several reactive phenolic moieties, which have allowed for the preparation of various functionalized calix[n]arenes.¹⁸ In the case of simple crown ethers, there are no reactive moieties, and the design of crown ethers bearing reactive functional groups therefore requires additional functionalization steps prior to the macrocyclization of the crown ether ring. The poor functionality of CB[n]s was a long-standing problem for CB[n] chemistry, which was only confounded by their poor solubility. To overcome this limitation in CB[n] chemistry, Kim et al. developed the direct oxidation of CB[n]s in 2003, which allowed for the direct introduction of reactive hydroxyl groups into CB[n]s.²⁹ Isaacs et al. subsequently developed monofunctionalized CB[n]s by the macrocyclization of the linear glycoluril pentamer with phthalaldehydes bearing a variety of different functional groups.^{30,31}

(5) Homologues and host–guest ability: CDs are soluble in aqueous media, and the inside of the CD cavity is a hydrophobic microenvironment. CDs can therefore capture suitably sized

hydrophobic guest molecules in their hydrophobic cavity from aqueous media. The driving force for this complexation process is based on hydrophobic/hydrophilic interactions. Three kinds of CDs, α, β-, and γ-CDs, have been used for most of the research concerning the complexation of hydrophobic molecules from aqueous media. The host–guest properties of these CDs are largely dependent on their cavity sizes.³ CB[n]s are also water-soluble hosts, and have rigid structures with no conformational flexibility because of the rigidity of the double methylene bridge connecting their glycoluril units. In a manner similar to CDs, the cavity of CB[n]s is a hydrophobic environment. Furthermore, CB[n]s have two negatively charged carbonyl-laced portals. CB[n]s can therefore accommodate hydrophobic guests with positively charged ammonium cations.^{24,25} Inoue et al. reported that CB[7] formed a very stable host–guest complex with a ferrocene derivative bearing two ammonium cations ($K = 3.0 \times 10^{15} \text{ M}^{-1}$).³² The high binding affinity of this complex was similar to that of the enzyme–substrate complex formed between avidin and biotin ($K > 10^{15} \text{ M}^{-1}$). The superior host–guest ability of CB[n]s is one of the main advantages of these systems as compared to typical host molecules, and one of the main reasons that CB[n]s have been widely used in recent studies. The host–guest properties of crown ethers and calix[n]arenes have been investigated in organic media. The unpaired electrons on the oxygen atoms of the crown ethers contribute to their ability to form strong binding interactions with metal cations. Thus, the driving force for these complexation processes is the formation of a coordination interaction between the metal cations and the oxygen atoms of the crown ether. In the case of calix[n]arenes, the individual phenolic moieties act as electron-donating groups, and the calix[n]arenes consequently form host–guest complexes with cationic molecules through cation/π interactions.²⁰ The phenolic moieties situated on the lower rim of calix[n]arenes can also capture metal cations by coordination interactions.²¹

Against this historical backdrop, we successfully developed a new class of pillar-shaped macrocyclic host compounds in 2008,

which subsequently became known as pillar[n]arenes.³³ As compared to the typical host molecules mentioned above, pillar[n]arenes have characteristic highly symmetrical pillar-shaped structures, which are similar in many respects to that of highly symmetrical pumpkin-shaped hosts CB[n]s. The repeating units of pillar[n]arenes are composed of phenolic moieties, making them structurally similar to calix[n]arenes. Pillar[n]arenes also have many phenolic moieties on both rims, making them very similar to the highly functionalized macrocyclic CD compounds. It is clear from discussion that pillar[n]arenes combine many of the interesting features of the typical macrocyclic compounds discussed above. Pillar[n]arenes also have several other characteristic features such as superior host–guest abilities, planar chirality, and the ability to undergo self-assembly processes with highly symmetrical structures because of their shape. Today, almost 8 years after our initial discovery of pillar[n]arenes, new reports continue to emerge describing the remarkable properties of these compounds and their complexes following efforts of pillar[n]arene chemists.^{34–43} On the basis of their novel cross section of properties and their vast potential, pillar[n]arenes are fast becoming key players in the field of macrocyclic chemistry, as well as creating several new opportunities that give them a much greater reach over other key players in the area of research in terms of their potential applications. Figure 2 shows the number of research papers on pillar[n]arenes published by year.

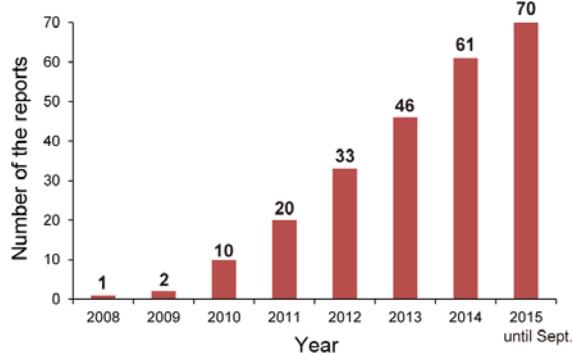
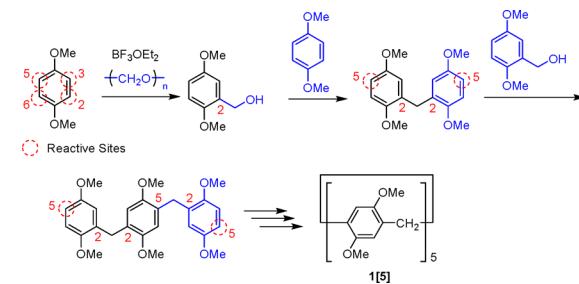


Figure 2. Number of reports concerning pillar[n]arenes from 2008 to 2015.

The area of research that we currently refer to as “pillar[n]-arene chemistry” started in 2008 with just a small group of pillar[n]arene chemists. For this reason, the total number of papers published between 2008 and 2011 was only 33. However, the level of interest in pillar[n]arene chemistry, as well as the number of researchers working in this area, has grown considerably since 2012 and now is to the point where there are now numerous pillar[n]arene chemists all over the world. This growth in the popularity and intensity of the research in this area is exemplified by the dramatic increase in the number of research paper published since 2012. Furthermore, Tokyo Chemical Industry (TCI) became the first chemical company to commercialize a pillar[5]arene product, when they started to sell per-methylated pillar[5]arene 1[5] (Scheme 1) in 2014, further emphasizing the significance of these compounds.⁴⁴

This Review covers the peer-reviewed papers published on pillar[n]arene chemistry since this area of research began 2008. First, we discuss the synthesis of pillar[n]arenes, which is the starting point of pillar[n]arene chemistry. Second, we discuss the fundamental properties of pillar[n]arenes, including their

Scheme 1. Proposed Pathway for the Preparation of the First Pillar[5]arene, Per-methylated Pillar[5]arene 1[5], by the Reaction of 1,4-Dimethoxybenzene with Paraformaldehyde in the Presence of BF_3OEt_2



structures, planar chirality, and host–guest properties. Finally, we discuss the applications of pillar[n]arenes, including pillar[n]arene-based mechanically interlocked molecules, supramolecular assemblies, hybrids, electronic, and biomedical materials.

2. SYNTHESIS OF PILLAR[n]ARENES

Pillar[n]arenes were discovered as a product of chance. The preparation of phenol–paraformaldehyde resins using a featureless and commercially available phenolic monomer, 1,4-dimethoxybenzene, led to the appearance of a fascinating macrocycle, per-methylated pillar[5]arene 1[5] (Scheme 1).³³ One of the interesting features of pillar[n]arenes is the position of the methylene bridge between 1,4-dimethoxybenzene constituent units. 1,4-Dimethoxybenzene units are connected by a methylene bridge at the 2,5-position (para-position), which contributes to the highly symmetrical pillar-shaped architecture. Historically, reaction of phenolic derivatives with aldehydes has afforded various macrocyclic compounds.²⁰ However, to obtain phenolic macrocyclic compounds, there are two key factors. One is controlling the reaction point of phenolic derivatives to inhibit the formation of three-dimensional network polymers. The other is the inhibition of the linear polymer formation and acceleration of macrocyclization.

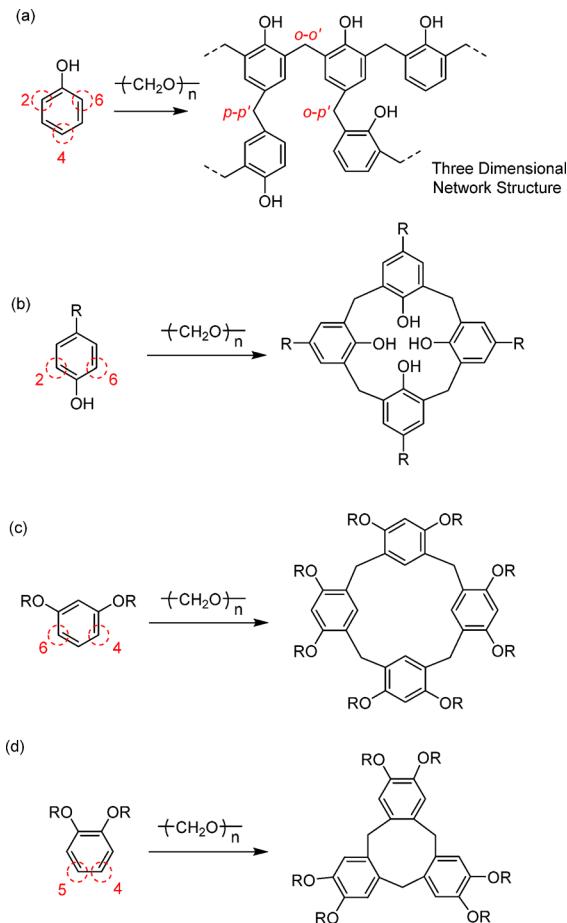
2.1. Controlling the Reaction Points of Phenolic Derivatives for the Regioselective Formation of Macroyclic Compounds

Phenol, the simplest monomer, affords three-dimensional network polymers in many cases by reaction with aldehydes because phenol has three electron-rich reaction sites at the 2, 4, 6-positions (*ortho*- and *para*-positions, Scheme 2a).

The introduction of protecting groups at the reaction sites or neighboring positions of the electron-rich reaction sites contributes to the inhibition of three-dimensional polymer formations and the generation of linear oligomers, which are intermediates for the formation of macrocyclic compounds.

Calix[n]arenes, in which *para*-substituted phenols are connected by methylene bridges at the *ortho*-positions, can be obtained by the condensation of *para*-substituted phenol derivatives with formaldehydes under appropriate conditions (Scheme 2b).^{18–20} When *para*-substituted phenols were used as the monomer, calix[n]arenes linked at the 2- and 6-positions were produced because the electron density at the 2- and 6-positions is higher than that at the 3- and 5-positions, and the electron-rich site at the 4-position is protected by the substituent. Calix[4]resorcinarenes, in which four resorcinarene molecules were connected at their 4 and 6 positions, were obtained by

Scheme 2. (a) Phenolic Resins with Three-Dimensional Network Structure by Reaction of Phenol and Aldehydes; and Macrocyclization of (b) *para*-Substituted phenol, (c) Resorcinarene, and (d) 1,2-Dimethoxybenzene Derivatives To Afford Calix[*n*]arenes, Calix[4]resorcinarenes, and Cyclotrimeratrylenes, Respectively

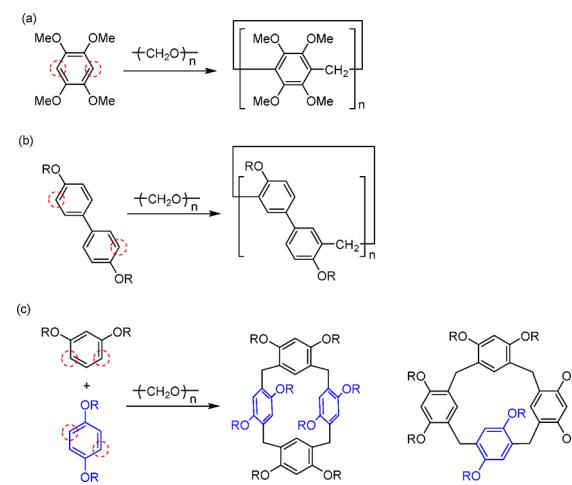


condensation of resorcinarene with aldehydes under controlled conditions (**Scheme 2c**).⁴⁵ The 2-, 4-, and 6-positions of resorcinarene are electron-rich, but steric hindrance by phenolic moieties reduces the reactivity at the 2-position. When 1,2-dialkoxybenzenes were used as monomers, the reaction sites were the 4- and 5-positions because the reactions at the 3- and 6-positions are unfavorable due to the steric hindrance. Cyclotrimeratrylenes, which are macrocyclic trimers of 1,2-dialkoxybenzenes, were obtained under controlled conditions in the 1980s (**Scheme 2d**).⁴⁶ The quest to discover new and exciting macrocyclic compounds using various phenolic derivatives is a timely topic (**Scheme 3**), which has been inspired by the discovery of pillar[*n*]arenes in 2008.

In 2013, Stoddart et al. reported a new family of macrocycles, asar[*n*]arenes, using 1,2,4,5-tetramethoxybenzene as the monomer (**Scheme 3a**).⁴⁷

In this case, the reaction sites were only at the 3- and 6-positions of 1,2,4,5-tetramethoxybenzene. Thus, *para*-bridged macrocyclic compounds were obtained. When the reaction temperature was 36 °C, a mixture of asar[*n*]arene homologues was obtained under kinetically controlled conditions; however, under heating condition at 80 °C, cyclic hexamer, asar[6]arene, was obtained as a thermodynamic product. In 2015, Li and co-workers reported biphen[*n*]arenes, which are composed of 4,4'-

Scheme 3. Recently Discovered Macroyclic Compounds Based on Phenol–Aldehyde Chemistry: (a) Asar[*n*]arenes, (b) Biphen[*n*]arenes, and (c) Hybrid[*n*]arenes



biphenol ether units linked by methylene bridges at the 3- and 3' positions under controlled conditions (**Scheme 3b**).⁴⁸ Szumna et al. reported the cocrystallization of 1,3- and 1,4-dimethoxybenzenes to produce new macrocyclic compounds, hybrid[*n*]arenes, which are composed of 1,3- and 1,4-dimethoxybenzene units (**Scheme 3c**).⁴⁹ A combination of pillar[*n*]arene and resorcinarene chemistry contributes to the synthesis of hybrid[*n*]arenes. Therefore, the numbers, electron density, and steric hindrance determine where the reaction sites will react with aldehydes. There is an unlimited potential in this field if we can design monomer structures and promote macrocyclization.

Since 2006, we have investigated the reaction of 1,4-dimethoxybenzene with paraformaldehyde to synthesize new macrocyclic compounds (**Scheme 1**). By choosing appropriate reaction conditions, new macrocyclic compounds, pillar[5]-arenes, have been obtained in 2008. In pillar[5]arene, 1,4-dimethoxybenzene units are connected by a methylene bridge at the *para*-positions (2- and 5-positions). The starting compound, 1,4-dimethoxybenzene, has four electronically equal reaction sites (2-, 3-, 5-, and 6-positions). However, steric hindrance is produced after the addition of paraformaldehyde. After the reaction of 1,4-dimethoxybenzene with paraformaldehyde at the 2-position, the second addition of paraformaldehyde selectively occurs at the 5-position, while the other reaction sites (3- and 6-positions) hardly react with paraformaldehyde. This phenomenon derives from steric hindrance. The reaction site at the 3-position between a methylene bridge and methoxy moiety is not reactive because of steric hindrance. The other reaction site at the 6-position is also affected by the steric hindrance of the methoxy moiety at the 1-position. Therefore, at the second addition step, the 5-position site is able to selectively react with paraformaldehyde.

2.2. Formation of Pillar[5]arenes under Thermodynamic Control

The synthesis of macrocyclic compounds is generally controlled kinetically and thermodynamically.⁵⁰ In a kinetically controlled process, the reaction temperature and time largely effect the yield of the macrocyclic compounds. However, a wide range of cyclic homologues and/or polymers are generally produced. Thus, macrocyclizations carried out under kinetically controlled conditions are generally low yielding reactions. For example, the macrocyclization of CB[*n*] homologues has been carried out

Table 1. Acid and Solvent Effects on the Macrocyclization of Per-methylated Pillar[5]arene 1[5]

entry	1,4-dimethoxybenzene/(CH ₂ O) _n (mol/mol)	catalyst	solvent	time (h)	yield (%)	ref
1	1	p-TsOH	CH ₂ ClCH ₂ Cl	2	38	51
2	1	AcOH	CH ₂ ClCH ₂ Cl	2	0	51
3	1	HCl	CH ₂ ClCH ₂ Cl	2	0	51
4	1	TFA	CH ₂ ClCH ₂ Cl	2	81	51
5	1	TFA+H ₂ O	CH ₂ ClCH ₂ Cl	2	77	51
6	0.67	p-TsOH	CH ₂ Cl ₂	50 ^a	66	52
7	1	TFA	CH ₂ Cl ₂	2	26	51
8	1	TFA	CHCl ₃	2	15	51
9	1	TFA	CHCl ₂ CHCl ₂	2	7	51

^aUnder reflux.

under kinetic control.²⁴ The key factor is the reaction temperature, and the reaction mixture under controlled reaction temperature yields CB[n] homologues ranging from pentamer to 11-mer. The yield of hexamer, CB[6], was highest (50–60%), while yields of CB[5], CB[7], and CB[8] were approximately 10%, and higher CB[n] homologues ($n \geq 9$) were yielded in trace amounts. This is because CB[6] has the lowest strain structure among CB[n] homologues. In the thermodynamically controlled process, additives act as a template to form a particular macrocycle. As a result, the particular macrocycle is obtained in good yield. Thus, the formation of macrocyclic compounds under thermodynamic control is extremely attractive. Crown ethers can be obtained under thermodynamic control using metal cation templates.¹¹ Particular crown ethers can be selectively formed in the presence of appropriate metal cations, which are able to fit into the cavity of the prepared crown ether.

Cyclic pentamers, pillar[5]arenes, can be obtained in high yield under optimized conditions because the formation of pillar[5]arenes should take place under thermodynamic control. We investigated the effect of the type of Lewis acid on the macrocyclization.³³ When we used BF₃OEt₂, the product was mainly pillar[5]arene 1[5], while a mixture of polymer and 1[5] was obtained using other Lewis acids such as FeCl₃, AlCl₃, and SnCl₂. Therefore, we envisioned that BF₃OEt₂ played a role as template for the formation of 1[5]. However, contrary to our expectation, Szumna et al. reported a high yield of synthesis of 1[5] using organic acids (Table 1).⁵¹

1[5] was obtained in moderate yield (38%) using *para*-toluenesulfonic acid (Table 1, entry 1), but was not obtained when acetic acid and aqueous HCl solution were used (entries 2 and 3). Using the strong organic acid, trifluoroacetic acid resulted in a high yield synthesis of 1[5] (entry 4, 81%). The yield of 1[5] was still high even in a small amount of water (entry 5), indicating that the synthesis of pillar[5]arene 1[5] can be achieved even in an air environment. Zhang and Yang et al. determined the optimized reaction conditions for the synthesis of 1[5] using *para*-toluenesulfonic acid. A long reaction time and reflux conditions allowed the formation of 1[5] in high yield (entry 6, 66%).⁵²

The other important factor is the type of solvent for the synthesis of the pillar[5]arenes. Szumna et al. investigated the solvent effect on the synthesis of pillar[5]arenes.⁵¹ When 1,2-dichloroethane was used as the solvent, the yield of 1[5] was high (Table 1, entry 4, up to 81% under optimized conditions). However, the yield was low using dichloromethane (entry 7, 26%), chloroform (entry 8, 15%), and 1,1,2,2-tetrachloroethane (entry 9, 7%). Pillar[5]arenes selectively form host–guest complexes with linear-shaped molecules (see details in section 5); thus, linear 1,2-dichloroethane acts as a template solvent for

the synthesis of pillar[5]arenes (Figure 3a). In contrast, chloroform and 1,1,2,2-tetrachloroethane have branched struc-

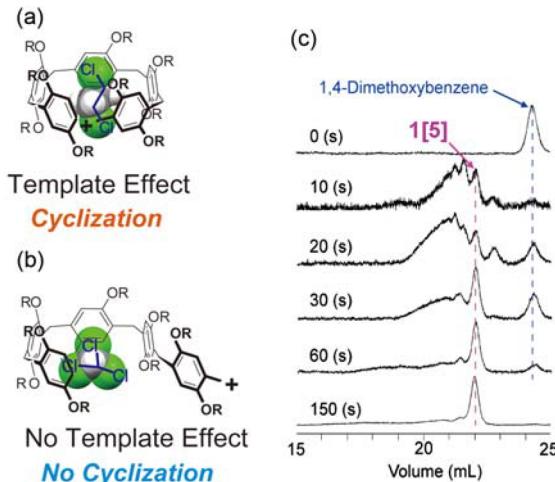
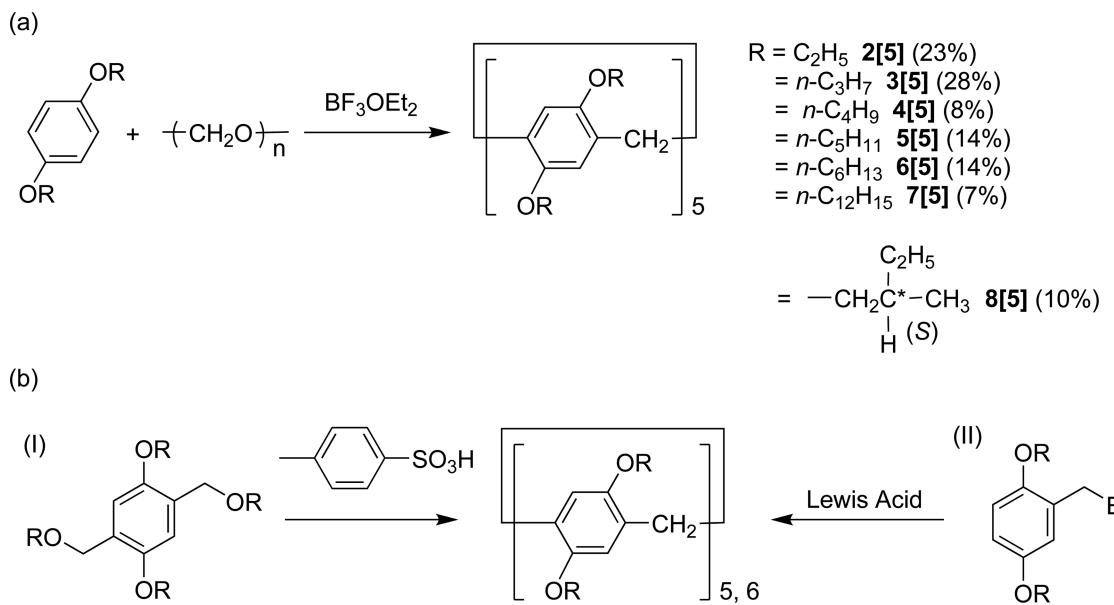


Figure 3. (a) Linear 1,2-dichloroethane acts as a template for the formation of pillar[5]arenes, while (b) branched chloroform cannot act as a template for the synthesis of particular pillar[n]arene homologues. (c) SEC traces of the products after quenching of the reaction with methanol. The feed ratio (1,4-dimethoxybenzene:parafomaldehyde) is 1:1. Reproduced with permission from ref 53. Copyright 2011 American Chemical Society.

tures (Figure 3a). Pillar[5]arenes cannot form host–guest complexes with branched molecules. Therefore, such branched structures cannot act as template solvents for the synthesis of pillar[5]arenes (Figure 3b).

The template effect for pillar[5]arene formation was confirmed by monitoring the time-dependent SEC traces (Figure 3c).⁵³ After 10 s, the peak from the 1,4-dimethoxybenzene monomer quickly decreased and peaks from the oligomer (retention volume 20–22 mL) and per-methylated pillar[5]arene 1[5] (retention volume 22 mL) were observed. A decrease in the amount of the oligomer and an increase in the amount of 1[5] were subsequently observed as the reaction time was increased. After 150 s, the peak from 1[5] was only detected, indicating the completion of the cyclization reaction. Hence, the reaction was completed in just 150 s, and thus the reaction proceeded under thermodynamic control. Pillar[5]arenes with different lengths of linear alkyl chains and branched alkyl groups, such as ethoxy 2[5], propoxy 3[5], butoxy 4[5], pentyloxy 5[5], hexyloxy 6[5], dodecanoxy 7[5], and 2(S)-methylbutoxy 8[5] groups, can also be prepared from the corresponding 1,4-

Scheme 4. (a) Simple Pillar[5]arenes with Various Lengths of Linear Alkyl and Branched Chains; and (b) Different Pathways To Produce Pillar[5]- and Pillar[6]arenes Using 1,4-Dialkoxybenzene Derivatives



dialkoxybenzene monomers using 1,2-dichloroethane as a template solvent (**Scheme 4a**).^{54,55}

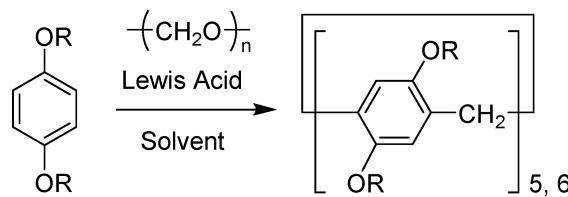
Preparation of pillar[5]arenes via different pathways was also reported by Huang et al., and Cao and Meier et al. using 2,5-bis(alkoxymethyl)-1,4-diethoxybenzene (path I, **Scheme 4b**) as monomers and 2,5-dialkoxybenzyl bromides (path II).^{56–58} Reaction of these monomers with Lewis acids or *para*-toluenesulfonic acid afforded pillar[5]arenes as the major products. In the reaction, pillar[6]arenes were also produced as minor products.

2.3. Formation of Pillar[6]arenes under Kinetic and Thermodynamic Control

The first pillar[6]arenes were reported by Cao, Meier, and co-workers in 2009 when they investigated macrocyclization of 2,5-bis(alkoxymethyl)-1,4-diethoxybenzene (**Scheme 4b**, path I).⁵⁷ However, pillar[6]arenes were obtained as minor products even under optimized conditions (yield 11%). In 2012, the same group developed a facile method for the synthesis of pillar[6]arenes (**Scheme 5a**).⁵⁹

Pillar[6]arenes were obtained as a mixture of pillar[5]- and pillar[6]arenes using 1,4-dialkoxybenzenes as monomers, FeCl₃ as catalyst, and chloroform as solvent. The highest yields of pillar[6]arenes **5[6]** and **6[6]** were 45% by this method. Zhang et al. reported the synthesis of pillar[5]- and pillar[6]arenes with high selectivity using choline chloride/FeCl₃ deep eutectic solvent in CH₂Cl₂. The yields of pillar[5]arene (**2[5]**) and pillar[6]arene (**1[6]**) were 35% and 53%, respectively, under the optimized conditions (**Scheme 5b**).⁶⁰ In their investigation, FeCl₃ was determined to be optimal to produce pillar[6]arenes. Therefore, we proposed that FeCl₃ would be effective for the formation of pillar[6]arenes, although another Lewis acid and hydrochloric acid can also be used for the synthesis of pillar[6]arenes. Hou et al. reported the reaction of 1,4-diethoxybenzene with paraformaldehyde in the presence of BF₃OEt₂ in chloroform afforded pillar[6]arene **1[6]** (yield 15%) along with various other pillar[*n*]arene homologues (**Scheme 5c**).⁶¹ In these methods, pillar[6]arenes were contained in the mixture of pillar[*n*]arene homologues, indicating that the

Scheme 5. Moderate Yield Synthetic Routes of Pillar[6]arenes Reported by (a) Cao, Meier et al.,⁵⁹ (b) Zhang et al.,⁶⁰ and (c) Hou et al.⁶¹



(a) Lewis Acid: FeCl₃, Solvent: CHCl₃

	n = 5	n = 6
R = C ₂ H ₅	30% 2[5]	34% 1[6]
R = n-C ₃ H ₇	28% 3[5]	35% 2[6]
R = i-C ₃ H ₇	31% 9[5]	30% 3[6]
R = n-C ₄ H ₉	31% 4[5]	43% 4[6]
R = n-C ₆ H ₁₃	28% 6[5]	45% 5[6]
R = n-C ₈ H ₁₇	22% 10[5]	45% 6[6]

(b) Lewis Acid: Choline Chloride 2FeCl₃, Solvent: CH₂Cl₂

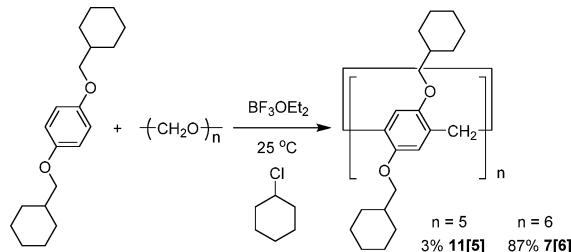
	n = 5	n = 6
R = C ₂ H ₅	35% 2[5]	53% 1[6]
R = n-C ₄ H ₉	33% 4[5]	47% 4[6]
R = n-C ₆ H ₁₃	33% 6[5]	39% 5[6]
R = n-C ₈ H ₁₇	32% 10[5]	31% 6[6]

(c) Lewis Acid: BF₃OEt₂, Solvent: CHCl₃

	n = 5	n = 6
R = C ₂ H ₅	20% 2[5]	15% 1[6]

macrocyclization proceeded under kinetic control. As shown in Table 1, the type of solvent is key for pillar[5]arene synthesis under thermodynamic control; thus we investigated several reaction solvents that are able to fit into the pillar[6]arene cavity to act as a template solvent for pillar[6]arene synthesis under thermodynamic control. Pillar[6]arenes accommodate bulky hydrocarbons because the cavity size of pillar[6]arenes is larger than that of pillar[5]arene (see details in section 5). Therefore, we envisioned that bulky hydrocarbons should act as a template solvent for the synthesis of pillar[6]arenes. When chlorocyclohexane was used as the solvent (Scheme 6), pillar[6]arene 7[6] was obtained as the major product in high yield (87%), and pillar[5]arene 11[5] was the minor product (3%).

Scheme 6. Selective Synthesis of Pillar[6]arene Using Chlorocyclohexane as the Template Solvent



The reaction was monitored by ^1H NMR (Figure 4a). In the initial stage within 1 min, the monomer reacted with

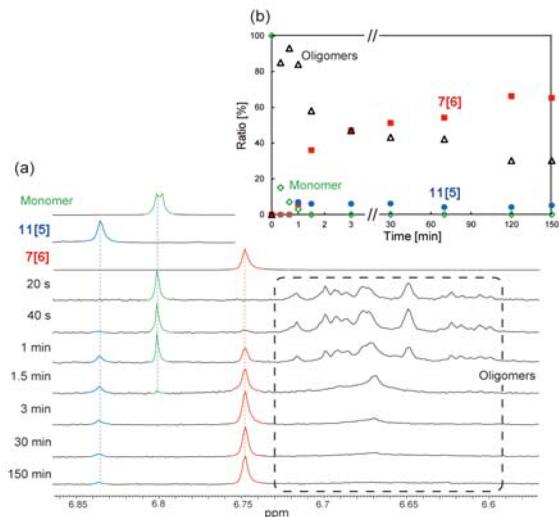


Figure 4. (a) Partial ^1H NMR spectra (CDCl_3 , 25°C) and (b) ratios of monomer (green \diamond), pillar[5]arene 11[5] (blue \bullet), pillar[6]arene 7[6] (red \blacksquare), and oligomers (\triangle) determined by ^1H NMR of the reaction mixtures over time. Reproduced with permission from ref 62. Copyright 2014 Royal Society of Chemistry.

paraformaldehyde and afforded a linear oligomer. These linear oligomers were subsequently converted to pillar[6]arene as the reaction time increased (Figure 4b). These results indicate that pillar[6]arene 7[6] is the thermodynamically stable compound in the reaction system, and that the reaction proceeds under reversible dynamic covalent bond formation between linear oligomers, pillar[5]-, and pillar[6]arenes. To clarify the dynamic covalent bond formation, we investigated dynamic interconver-

sion between pillar[5]- and pillar[6]arenes depending on the type of solvent (Figure 5).

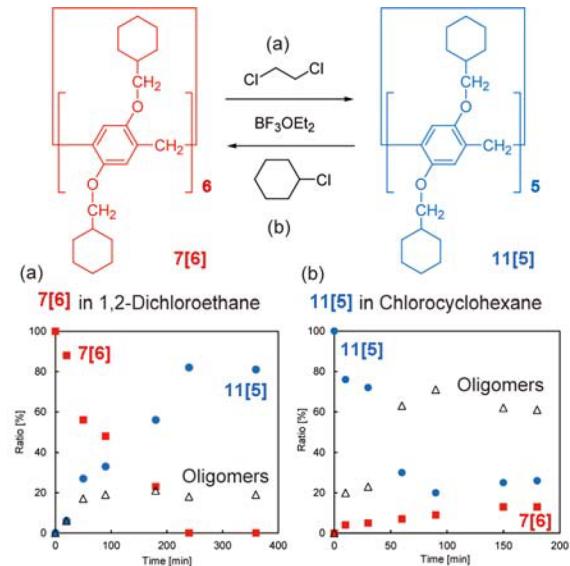
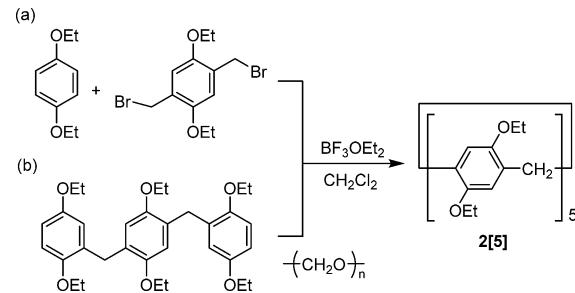


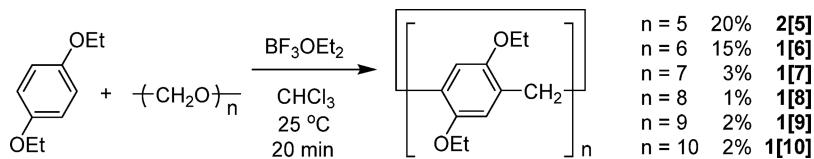
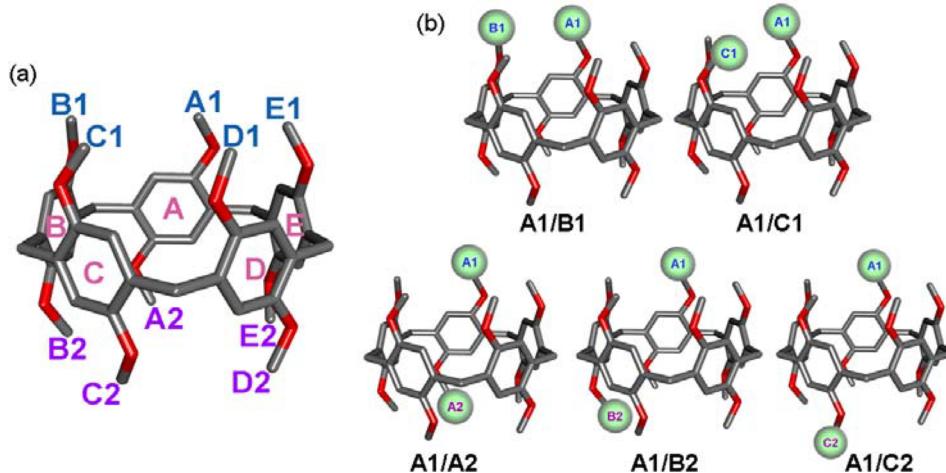
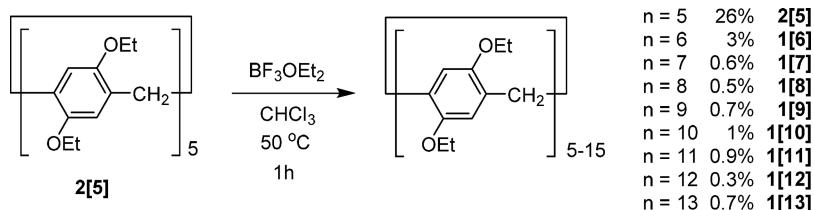
Figure 5. Inversion between pillar[5]arene 11[5] and pillar[6]arene 7[6]. Ratios of 11[5] (blue \bullet) and 7[6] (red \blacksquare) and oligomers (\triangle) by ring-opening reaction of (a) 7[6] in 1,2-dichloroethane and (b) 11[5] in chlorocyclohexane at 80°C , which were monitored by ^1H NMR analysis of the reaction mixtures over time. Reproduced with permission from ref 62. Copyright 2014 Royal Society of Chemistry.

Reaction of pillar[5]arene 11[5] with BF_3OEt_2 in chlorocyclohexane, which is a good template solvent for the synthesis of pillar[6]arene, resulted in the formation of pillar[6]arene 7[6] (Figure 5b). However, pillar[6]arene 7[6] converted to pillar[5]arene 11[5] with BF_3OEt_2 in 1,2-dichloroethane, which is a template solvent for pillar[5]arenes (Figure 5a). These experiments indicate that pillar[n]arenes were produced by dynamic covalent bond formations.⁶² Nierengarten et al. also observed that macrocyclization proceeded by dynamic covalent chemistry while they were investigating favorable synthetic procedures for the production of pillar[6]arenes (Scheme 7).⁵⁸

Scheme 7. Formation of Pillar[5]arene 2[5] from (a) Cocrystallization of Different Monomers and (b) a Trimer



To synthesize pillar[6]arenes, they investigated the cocrystallization of different monomers, 2,5-bis(bromomethyl)-1,4-diethoxybenzene and 1,4-diethoxybenzene, with a Lewis acid (Scheme 7a). However, the major product obtained was not pillar[6]arene but pillar[5]arene. Pillar[5]arene was also obtained upon macrocyclization of the trimer by reaction of paraformaldehyde with Lewis acid (Scheme 7b). These results clearly indicate that

Scheme 8. Synthesis of Pillar[*n*]arene Homologues (*n* = 5–10) from 1,4-Diethoxybenzene Reported by Hou et al.**Scheme 9.** Synthesis of Pillar[*n*]arene Homologues (*n* = 5–13) from the Ring-Opening Reaction of Pillar[5]arene 2[5]**Figure 6.** (a) Assignment of positions in pillar[5]arenes. (b) Constitutional isomers of a difunctionalized pillar[5]arene. Stereoisomers generated by rotation of units are not included.

the formation of pillar[*n*]arenes proceeded under dynamic covalent bond formation.

Recently, Zyryanov and co-workers reported the selective synthesis of pillar[6]arenes by solid-state condensation of 1,4-dialkoxybenzene and paraformaldehyde by grinding in the presence of a catalytic amount of H₂SO₄.⁶³ The highest yield of pillar[6]arene was 85% by this method; thus, the procedure will be a new useful route for the synthesis of pillar[6]arenes.

2.4. Formation of Pillar[*n*]arenes (*n* ≥ 7) under Kinetic Control

Larger pillar[*n*]arene homologues (*n* ≥ 7) were first synthesized by Hou and co-workers.⁶¹ They used 1,4-diethoxybenzene as a monomer, chloroform as a solvent, and BF₃OEt₂ as a Lewis acid (Scheme 8).

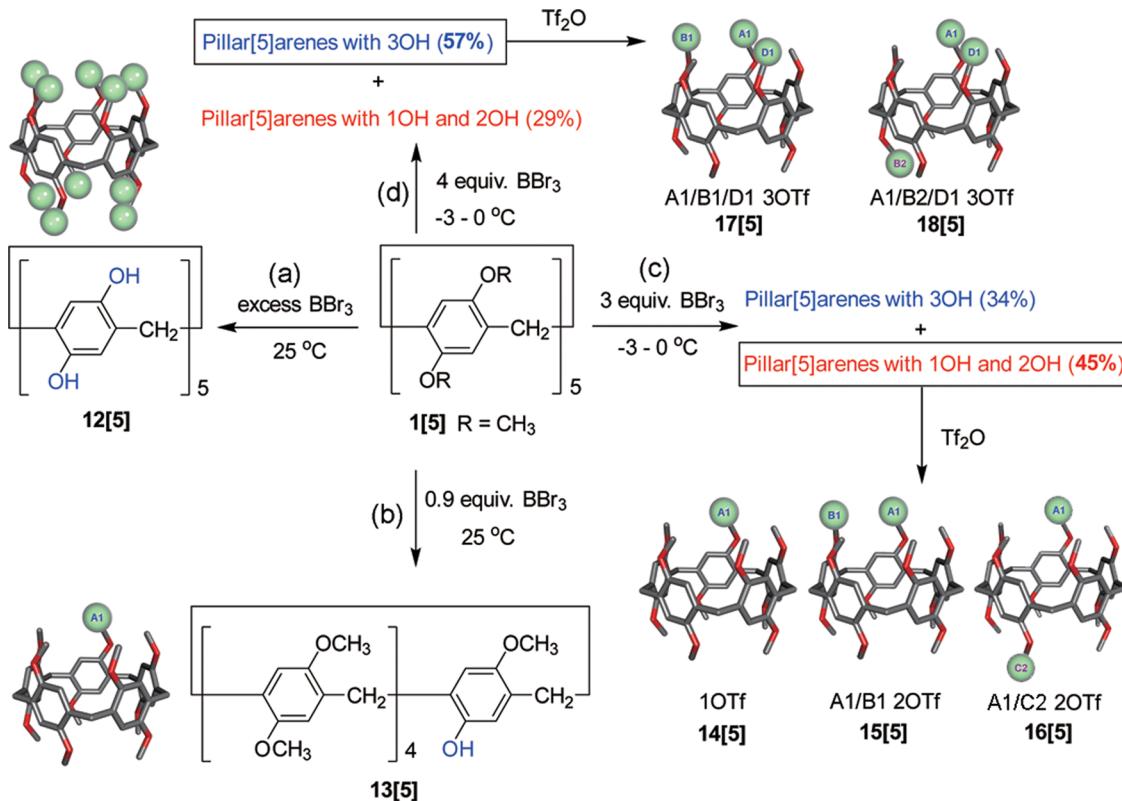
Chloroform cannot act as a template for the particular pillar[*n*]arene homologues. Therefore, the reaction in chloroform afforded not only pillar[5]- and pillar[6]arenes as major products but also larger pillar[*n*]arene homologues as minor products, pillar[7]arene 1[7], pillar[8]arene 1[8], pillar[9]arene 1[9], and pillar[10]arene 1[10] in 3%, 1%, 2%, and 2% yields, respectively. The optimized reaction time for the synthesis of larger pillar[*n*]arene homologues was 20 min. When the reaction time was longer, the larger pillar[*n*]arene homologues (*n* ≥ 7) disappeared completely. This result indicates the reaction proceeded under kinetic control. Our group also synthesized

larger pillar[*n*]arene homologues using dynamic covalent bond formation of pillar[*n*]arenes (Scheme 9).⁶⁴

We used pillar[5]arene as a monomer, and chloroform as a solvent. Again, it should be noted that chloroform did not act as a template solvent. Therefore, the reaction afforded a kinetically stable mixture of pillar[*n*]arene homologues (*n* = 5–15). Heating at 50 °C was necessary to promote ring-opening reaction of pillar[5]arene 2[5], and the optimized reaction time to produce a mixture of pillar[*n*]arene homologues (*n* = 5–15) was 1 h. New larger pillar[*n*]arene homologues (*n* = 11–13) were isolated with known pillar[*n*]arene homologues (*n* = 5–10) by silica gel chromatography. Both Hou and our protocols were carried out under kinetic control; thus, yields of larger pillar[*n*]arene homologues were quite low. One of the next challenges is the synthesis of larger pillar[*n*]arene homologues under thermodynamically controlled conditions to selectively produce larger pillar[*n*]arene homologues in high yields.

3. FUNCTIONALIZATION OF PILLAR[*n*]ARENES

Substituents on both rims of pillar[*n*]arenes affect their physical properties such as solubility, conformational, and host–guest properties. Therefore, functionalization of pillar[*n*]arenes is a very important feature in pillar[*n*]arene chemistry. Pillar[*n*]arene homologues (*n* = 5–13) have been synthesized, but the functionalization of cyclic pentamers, pillar[5]arenes, has been

Scheme 10. Synthesis of Mono-, Di-, Tri-, and Per-hydroxylated Pillar[5]arenes by Deprotection Using BBr_3 

mainly investigated because pillar[5]arenes are obtained in high yields by thermodynamic control using template solvents as compared to the other pillar[n]arene homologues ($n \geq 6$). From 2012, simple pillar[6]arenes have been obtained in moderate yields (>40%).⁵⁹ Therefore, the functionalization of pillar[6]-arenes has recently been investigated. Pillar[n]arenes have two functional groups in the constituent unit; therefore, pillar[5]- and pillar[6]-arenes have 10 and 12 functional groups, respectively. As compared to per- and monofunctionalized pillar[n]arenes, multifunctionalization of pillar[n]arenes, such as di-, tri-, tetra-, and penta-functionalized pillar[n]arenes, is quite difficult as multifunctionalized pillar[n]arenes have many constitutional isomers. Figure 6a shows the assignment of the substituent positions in pillar[5]arene.

The letters and numbers refer to the dialkoxybenzene units, and the upper and lower rims, respectively. Difunctionalized pillar[5]arenes have five isomers (Figure 6b, A1/A2, A1/B2, A1/C2, A1/B1, and A1/C1). The number of isomers increases as the increase of the substituent numbers. There are 10 constitutional isomers in trifunctionalized pillar[5]arenes (A1/B1/C1, A1/B1/D1, A1/B1/C2, A1/B1/D2, A1/A2/B1, A1/A2/B2, A1/A2/C1, A1/A2/C2, A1/B2/C1, and A1/B2/D1). Therefore, selective synthesis of multifunctionalized pillar[n]arenes is one of the challenging topics in pillar[n]arene chemistry. Position-selective functionalization of pillar[5]arenes has been intensively investigated by pillar[n]arene chemists, and their efforts have contributed to the successful synthesis of position-selective multifunctionalized pillar[5]arenes based on various organic reaction methods. Position-selective mono-, di-, tri-, tetra-, penta-, and per-functionalization of pillar[5]arenes have been achieved.^{37,38} Two approaches have been devised for the synthesis of position selective-functionalizing pillar[n]arenes: (i) exchange of the substituents by deprotection followed by

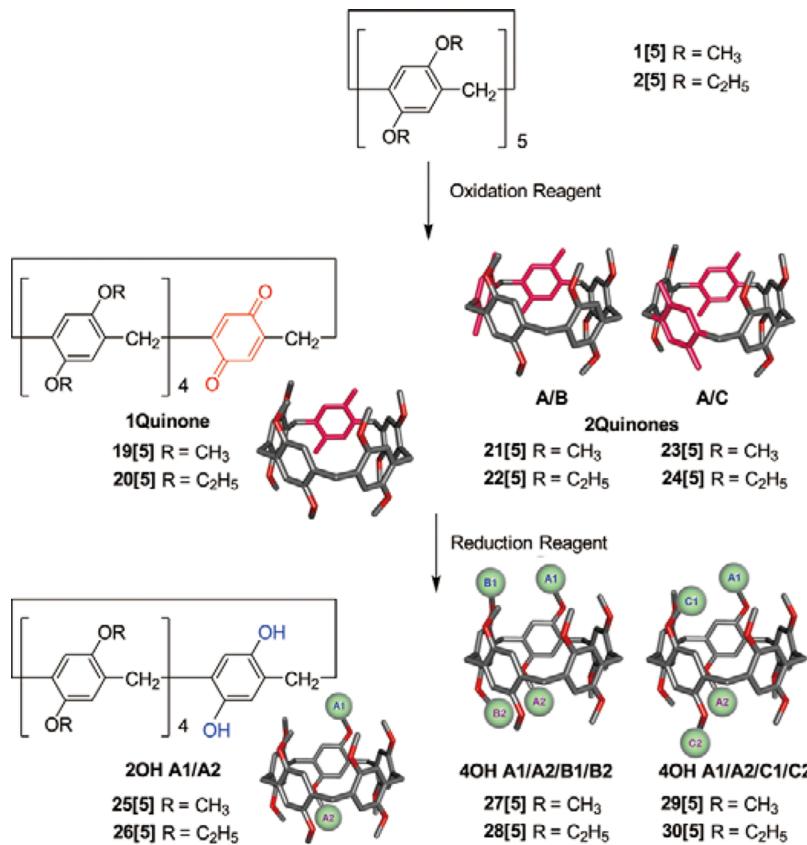
etherification of preformed pillar[n]arenes and (ii) cyclization of 1,4-dialkoxybenzene with another 1,4-dialkoxybenzene derivative with functional groups.

3.1. Deprotection of the Alkoxy Moieties of Pillar[n]arenes To Produce Key Pillar[n]arenes Bearing Phenolic Groups at Specific Positions

Deprotection of alkoxy groups to produce functionalizing pillar[5]arenes was first investigated by our group in 2008.³³ Phenolic groups, which are obtained by deprotection of alkoxy groups, are favorable reactive groups for the introduction of various functional groups. Therefore, pillar[n]arenes with phenolic groups at the desired positions are useful key compounds to produce various functionalizing pillar[n]arenes. We investigated the deprotection of methoxy groups in per-methylated pillar[5]arene 1[5]. Deprotection of the methoxy moieties of 1[5] with excess BBr₃ afforded per-hydroxylated pillar[5]arene 12[5], quantitatively (Scheme 10a).³³

However, deprotection of per-methylated pillar[5]arene 1[5] with 0.9 equiv of BBr₃ under the optimized reaction time afforded monohydroxylated pillar[5]arene 13[5] in moderate yield (22%, Scheme 10b).⁶⁵ Cao et al. optimized the reaction conditions to provide the mono-ol 13[5] in good yield (60%).⁶⁶ The effect of the amounts of BBr₃ and reaction temperature on the deprotection reaction was further investigated by Stoddart and co-workers.⁶⁷ They found that deprotection of methoxy groups of preformed per-methylated pillar[5]arene 1[5] with BBr₃ occurred in a stepwise manner at low temperatures under kinetic control (Scheme 10c and d). Therefore, conversion to mono-, di-, and trideprotected pillar[5]arenes can be controlled by reaction temperature, time, and the feed ratio between pillar[5]arene and BBr₃. The introduction of triflate groups into the phenolic moieties of the mixture of multideprotected pillar[5]arenes resulted in the separation of monotriflated

Scheme 11. Synthesis of A1/A2 Di- and Tetra-hydroxylated Pillar[5]arenes by the Oxidation Followed by Reduction Method



14[5], ditriflated, and tritriflated pillar[5]arene isomers by silica gel chromatography. Modification of the triflate groups enabled easy separation of these isomers by silica gel chromatography. New pillar[5]arene isomers, A1/B1 (**15[5]**) and A1/C2 (**16[5]**) ditriflates, and A1/B1/D1 (**17[5]**) and A1/B2/D1 (**18[5]**) tritriflates, can be produced by the protocol. They named this method the deprotection followed by activation strategy.

The other deprotection method is the oxidation followed by reduction strategy of preformed per-alkylated pillar[5]arenes to produce A1/A2 dihydroxylated pillar[5]arenes and A1/A2/B1/B2, A1/A2/C1/C2 tetra-hydroxylated pillar[5]arenes (Scheme 11).^{68,69}

Oxidation of a 1,4-dialkoxybenzene unit in per-alkylated pillar[5]arenes afforded pillar[5]arenes with a benzoquinone unit (**19[5]** and **20[5]**). Benzoquinone was easily converted to hydroquinone using a reducing agent; thus, the A1/A2 dihydroxylated pillar[5]arenes (**25[5]** and **26[5]**) were obtained by reduction of the benzoquinone unit.^{68,69} The merit of the oxidation followed by reduction method is that pillar[5]arenes with two phenolic groups at the A1 and A2 positions can be selectively produced. When BBr_3 was used to produce dihydroxylated pillar[5]arenes, the product was a mixture of multideprotected pillar[5]arenes; therefore, separation of dihydroxylated pillar[5]arene isomers from the mixture was quite difficult. Furthermore, pillar[5]arenes with two benzoquinone units at the A/B (**21[5]** and **22[5]**) and A/C (**23[5]** and **24[5]**) units can be prepared under the optimized oxidation condition, and reduction of these pillar[5]arenes with two benzoquinone units led to A1/A2/B1/B2 (**27[5]** and **28[5]**) and A1/A2/C1/C2 (**29[5]** and **30[5]**) tetra-hydroxylated pillar[5]arenes.⁶⁸ Tuning the oxidation condition enables the

synthesis of pillar[5]arenes with three and four quinone moieties. Xue et al. reported the synthesis of pillar[5]arenes consisting of three different kinds of units by selective oxidation of the units (Scheme 12).^{70,71}

They found the functional group-selective oxidation. Ether benzene units are oxidized by an oxidizing agent, but benzene units with ester moieties are not. Installation of ester groups into A1/A2/C1/C2 tetra-hydroxylated pillar[5]arene afforded pillar[5]arene with four ester groups at A1/A2/C1/C2 positions (**31[5]**). Using the functional group-selective oxidation between ether and ester groups, complex pillar[5]arene derivatives consisting of two ester units and one (**32[5]**), two (**33[5]**), and three (**34[5]**) benzoquinone units could be produced.

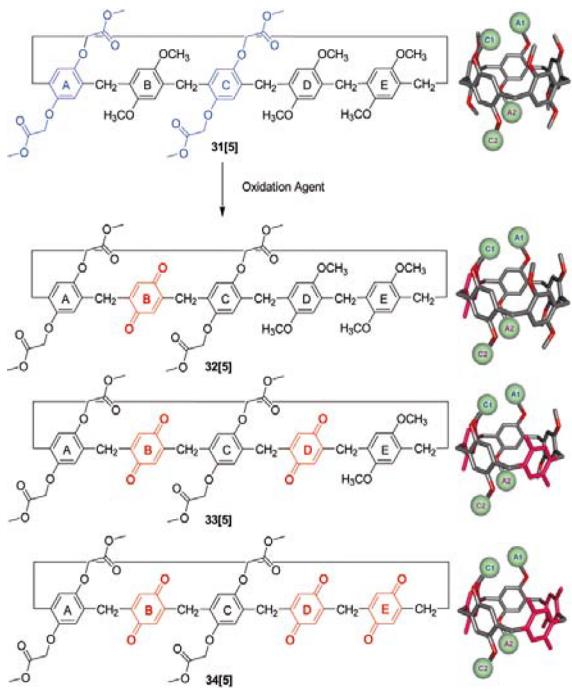
The advantages of these deprotection methods are as follows. (1) The methods can be used for pillar[5]arenes even with functional substituents such as tri(ethylene oxide) moieties.⁷² (2) The method can be used for larger pillar[n]arene homologues ($n \geq 6$). Per-hydroxylated pillar[n]arenes ($n = 6, 7, 9$, and 10) were synthesized by deprotection of ethoxy moieties with excess BBr_3 (Scheme 13a).^{73–77} Monohydroxylated pillar[6]arene **9[6]** was also obtained in moderate yield (46%) by the deprotection method (Scheme 13b).⁷⁸

A1/A2 dihydroxylated pillar[6]arene **11[6]** was also produced by the oxidation followed by reduction method (Scheme 13c).⁶⁸

3.2. Cocyclization Method To Produce Key Pillar[n]arene Derivatives Bearing Reactive Groups at Specific Positions

The other method to produce pillar[n]arenes with reactive functional groups, such as bromo and alkyne groups, is cyclization of 1,4-dialkoxybenzenes with these functional groups. Nierengarten and co-workers developed the macrocyclization procedure using 1,4-dialkoxybenzene monomers with two

Scheme 12. Synthesis of Pillar[5]arenes Containing One, Two, and Three Benzoquinone Moieties by Ester/Ether-Selective Oxidation



bromide moieties to produce pillar[5]- and pillar[6]arenes with 10 bromides 35[5] and 12 bromides 12[6], respectively, in moderate yields (**Scheme 14a**).⁷⁹

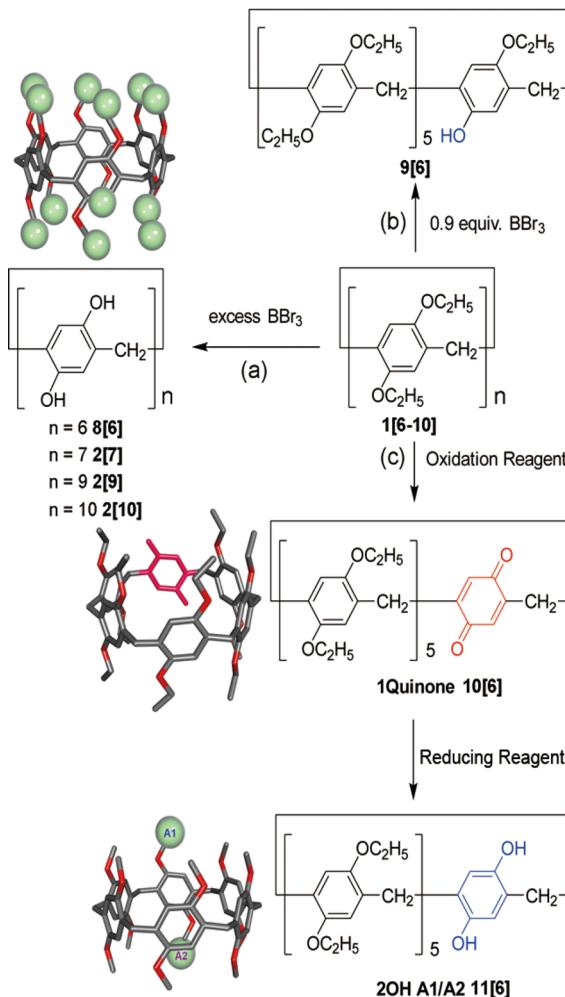
Using FeCl₃ as a Lewis acid and chloroform as a solvent under the optimized reaction condition afforded a mixture of decabromide 35[5] and dodecabromide 12[6]. A pillar[5]arene with 10 alkyne groups (36[5]) can be obtained by macrocyclization of a monomer with two alkyne groups (**Scheme 14b**).⁸⁰

Cocyclization of two kinds of 1,4-dialkoxybenzene monomers allowed mono-, di-, and tetra-functionalized pillar[5]arenes. Cocyclization was first developed by Huang et al. (**Scheme 15**).⁸¹

Cocyclization of two different 1,4-dialkoxybenzenes with dimethoxy, dibutoxy, and dioctyloxy groups afforded pillar[5]arenes containing a different 1,4-dialkoxybenzene unit (37[5] and 38[5]). Monoreactive pillar[5]arene was first introduced by Stoddart and co-workers based on the cocyclization method.⁸² Co-pillar[5]arene 39[5], in which are one 2-bromoethoxy and nine methoxy groups, was prepared by cocyclization of 1,4-dimethoxybenzene and nonsymmetric dialkoxybenzene with one bromide group. Tuning the feed ratio between the two different monomers was very important for the efficient synthesis of the monobromide 39[5], which was developed by Cao and Meier et al.⁸³ Wang et al. applied the cocyclization method to obtain a A1/A2 dibromo-functionalized pillar[5]arene 40[5].⁸⁴ Cocyclization of 1,4-bis(2-bromoethoxy)benzene with 1,4-dialkoxybenzene afforded dibromide 40[5]. Tetra-functionalized pillar[5]arenes with four bromides can also be produced by tuning the feed ratio of different monomers in the cocyclization method.⁸⁵

The cocyclization method is a useful approach to obtain useful key pillar[n]arenes with bromide groups at desired positions by a one-step reaction, but is limited because the functional groups in the monomers sometimes inhibit the macrocyclization. In addition, the cocyclization cannot be used for the synthesis of functionalizing pillar[n]arenes with larger homologues ($n \geq 6$) in

Scheme 13. Synthesis of Mono- and A1/A2 Di- and Perhydroxylated Pillar[n]arenes by (a,b) Deprotection with BBr₃ and (c) the Oxidation Followed by Reduction Method



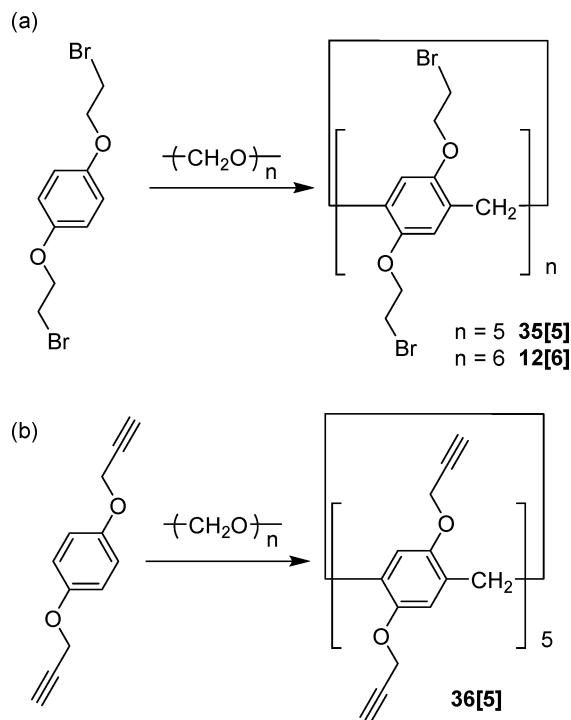
many cases because these larger pillar[n]arene homologues are only obtained as minor products under kinetically controlled processes. It is necessary to use both the deprotection and the cocyclization methods depending on the type of functional groups in the monomer and targeting numbers of rings.

3.3. Combination of Deprotection and Cocyclization Methods To Produce Key Pillar[n]arene Derivatives with Phenolic Groups

Combination of the cocyclization and deprotection methods also affords useful key pillar[5]arenes. First, dihydroxylated pillar[5]arene was accidentally obtained by our group in macrocyclization of 1,4-dimethoxybenzene using different Lewis acids.⁸⁶ For the synthesis of pillar[5]arenes, BF₃OEt₂ was a good Lewis acid in many cases to produce pillar[5]arenes in good yields.⁸³ However, the deprotection reaction of methoxy groups took place concurrently with macrocyclization when AlBr₃ was used as a Lewis acid. AlBr₃ acts as a Lewis acid for both macrocyclization and deprotection of the methoxy groups. A regioselective A1/B2 dihydroxylated pillar[5]arene 41[5] could be isolated by silica gel chromatography and washing with methanol (**Scheme 16a**).

Stoddart et al. reported the synthesis of A1/A2 hydroxylated pillar[5]arene 25[5] by the cocyclization followed by deprotection method (**Scheme 16b**).⁸⁷ The A1/A2 dibromo-functionalized pillar[5]arene 42[5] was first synthesized by cocyclization

Scheme 14. Macrocyclization of 1,4-Dialkoxybenzenes with (a) Two Bromide or (b) Two Alkyne Moieties To Produce Decabromide 35[5], Dodecabromide 12[6], or Decaalkyne 36[5]



of 1,4-bis(3-bromopropoxy)benzene with 1,4-dimethoxybenzene. Elimination of bromide moieties in **42**[**S**] resulted in the A1/A2 diallylated pillar[**5**]arene **43**[**S**]. Deprotection of the allyl groups afforded A1/A2 dihydroxylated pillar[**5**]arene **25**[**S**].

3.4. Functionalization of Pillar[n]arenes Bearing Phenolic Groups by Etherification

Pillar[n]arenes with phenolic groups at desired positions could be produced by various methods, such as deprotection, oxidation followed by reduction method of preformed pillar[5]arenes, and *in situ* macrocyclization and deprotection, and the cocrystallization followed by deprotection method. Pillar[n]arenes with phenolic groups are very important key compounds, because etherification between the pillar[n]arenes and alkyl-halide in the presence of appropriate bases can afford various functionalizing pillar[n]-

arenes. Various per-functionalized pillar[5]arenes have been synthesized by etherification (**Scheme 17**).

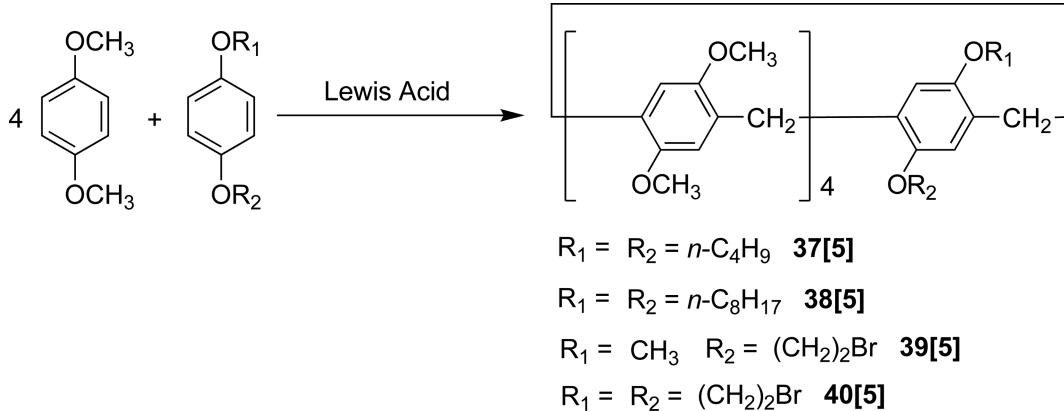
The first water-soluble pillar[5]arene with 10 carboxylate anions **46**[5] was introduced by our group.⁸⁸ A pillar[5]arene with 10 ester groups **44**[5] was synthesized by installing 10 ester groups through etherification. Hydrolysis of the deca-ester **44**[5] afforded the first water-soluble pillar[5]arene **46**[5]. Hou et al. reported that **44**[5] converted to a water-soluble pillar[5]arene with 10 amine groups **49**[5].⁸⁹ Our group reported that synthesis of pillar[5]arenes with nonionic moieties, such as ethylene oxide **50**[5] and tri(ethylene oxide) groups **51**[5] by etherification.⁹⁰ Pillar[5]arene with 10 tri(ethylene oxide) **51**[5] was completely soluble in aqueous media, but pillar[5]arene with 10 ethylene oxide **50**[5] was insoluble, indicating that the long water-soluble moieties are necessary to gain water solubility. Pillar[5]arene with 10 cyclohexylmethyl moieties **11**[5] was also synthesized by etherification.⁹¹ The other method to functionalize pillar[n]-arene is by palladium-catalyzed reactions, such as Sonogashira, Suzuki, and Heck reactions, which have been widely used for the synthesis of π -conjugated molecules and polymers. A reactive intermediate pillar[5]arene with 10 triflate groups **52**[5] was synthesized by reaction of per-hydroxylated pillar[5]arene **12**[5] and Tf₂O. Sonogashira coupling between the decatriflate **52**[5] and ethynylbenzene afforded a highly π -conjugated pillar[5]-arene **53**[5], which exhibited through-space π -delocalization.⁹² The etherification protocol is a straightforward and reliable process, and thus is applicable for the functionalization of larger pillar[n]-arene homologues ($n \geq 6$, Scheme 18).

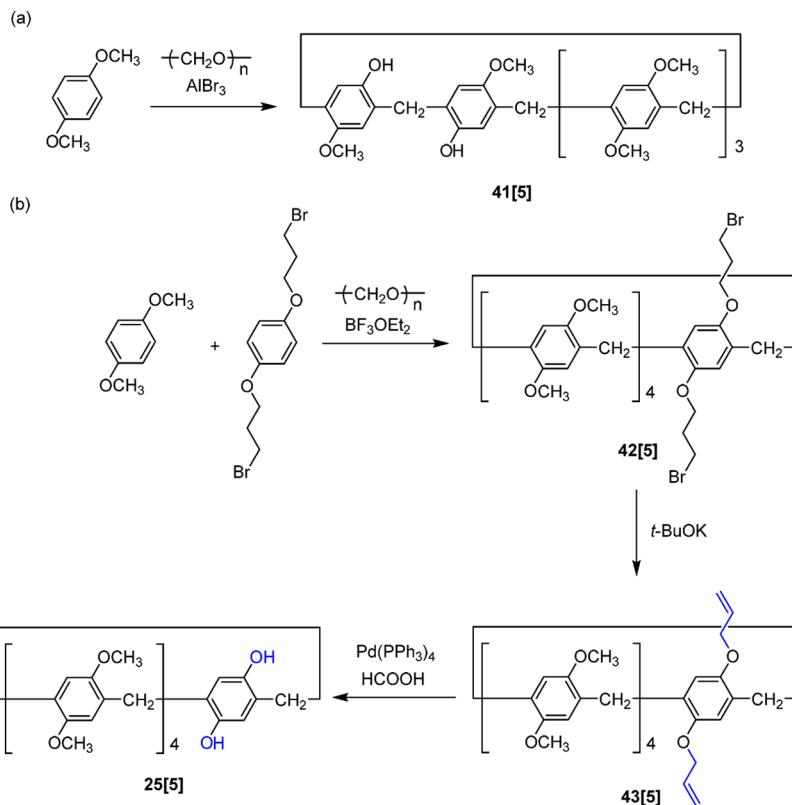
As with per-functionalization of pillar[5]arenes by esterification, water-soluble pillar[n]arenes with carboxylate anions (13[6], 3[7], 3[9], and 3[10]),^{74–76,93} and amphiphilic pillar[n]arenes with ethylene oxide and tri(ethylene oxide) moieties (14[6], 15[6], 4[7], and 4[10]),^{90,93–97} have been synthesized from per-hydroxylated pillar[n]arenes.

Monofunctionalized pillar[5]arenes with one trimethylammonium **54**[5],⁶⁵ DABCO cation **55**[5],⁷⁸ and phosphoryl groups **56**[5]⁶⁶ were accessible by etherification of monohydroxylated pillar[5]arene **13**[5] with the corresponding monohalides (Scheme 19).

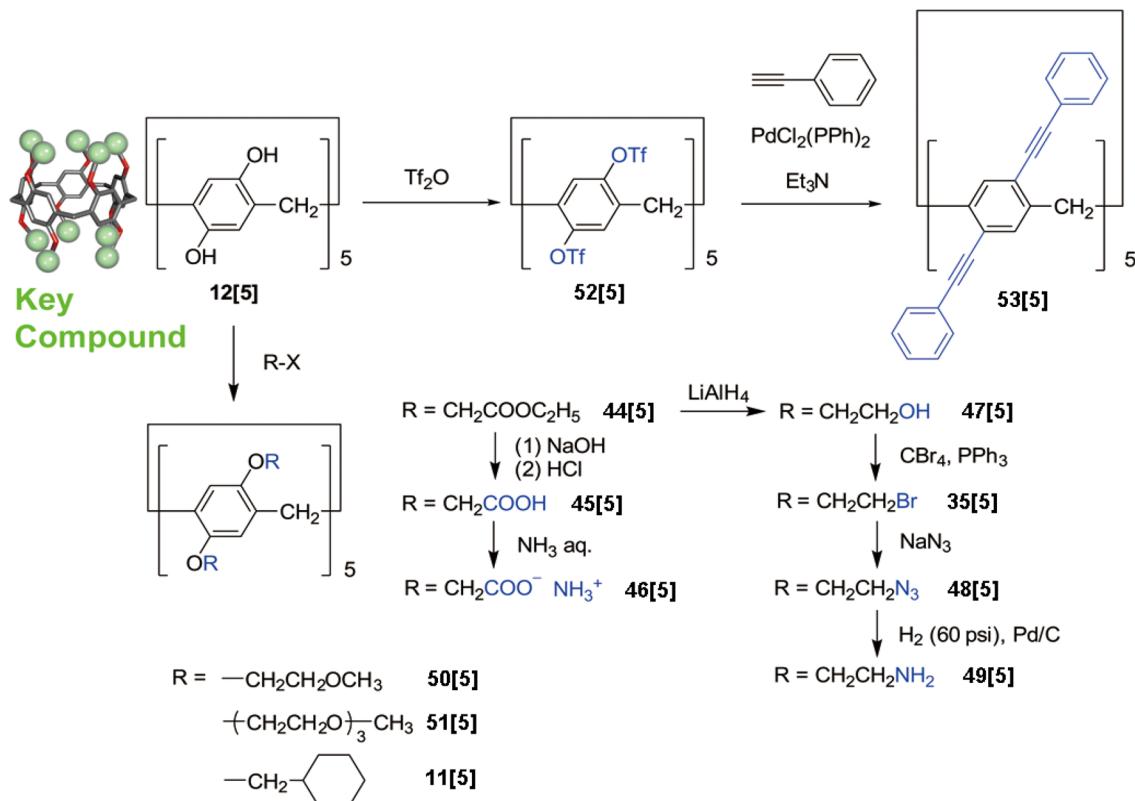
As compared to the cocyclization method, this approach required multistep reactions to produce the monofunctionalized pillar[n]arenes, but can be used for the synthesis of the larger homologues ($n \geq 6$) of monofunctionalized pillar[n]arenes. In an approach similar to that for the production of monofunction-

Scheme 15. Ccocyclization of Two Different 1,4-Dialkoxybenzene Monomers with Paraformaldehyde To Produce Co-piller[5]arenes

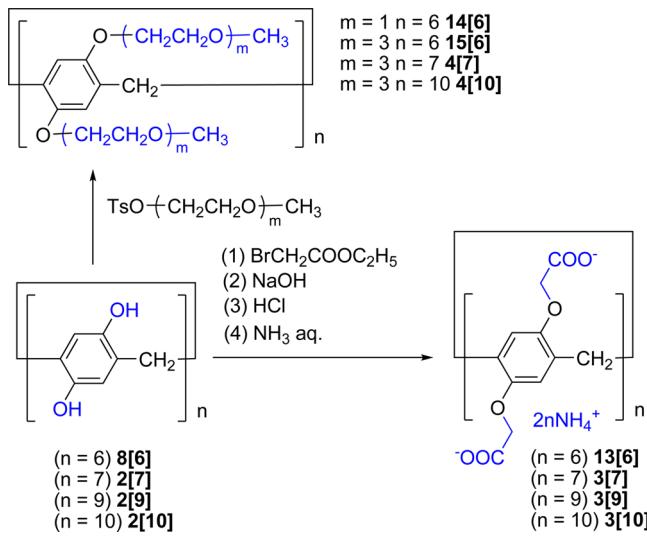


Scheme 16. Combination of the Cocyclization and Deprotection Methods^a

^a(a) In situ macrocyclization and deprotection to produce A1/B2 di-hydroxylated pillar[5]arene **41[5]**. (b) Cocyclization followed by deprotection to produce A1/A2 di-hydroxylated pillar[5]arene **25[5]**.

Scheme 17. Synthesis of Per-functionalized Pillar[5]arenes from Preformed Per-hydroxylated Pillar[5]arene **12[5]**

Scheme 18. Synthesis of Per-functionalized Pillar[*n*]arene Homologues from Preformed Per-hydroxylated Pillar[*n*]arenes (*n* ≥ 6)



alized pillar[5]arenes, monofunctionalized pillar[6]arene with a pyridinium cation **16[6]** was produced by etherification.⁷⁸

Pillar[5]arene with two functional groups can also be produced by etherification. Pillar[5]arene with two carboxylic acid groups **57[5]** was prepared by the modification of two ester groups by etherification, followed by hydrolysis of an ester bond (Scheme 20).⁹⁸

Introduction of a π-conjugated unit into pillar[5]arenes can be achieved by the palladium-catalyzed reaction. The A1/A2 ditriflate **58[5]** was prepared from A1/A2 dihydroxylated pillar[5]arene, as reported by Stoddart et al., to produce a terphenyl substituted pillar[5]arene **60[5]**.⁸⁷ In a similar approach,

our group also synthesized a pillar[5]arene incorporating π-conjugated units **61[5]** between A1/A2 ditriflate **59[5]** and (5-bithienyl)boronic acid by palladium-catalyzed Suzuki coupling.⁹⁹

Stoddart et al. successfully introduced two bromide groups at the ortho positions (A1' and A2') **62[5]** by bromination of **25[5]**.¹⁰⁰

The dibromide **62[5]** can be functionalized by palladium-catalyzed coupling reactions, and thus is a useful key compound to produce difunctionalized pillar[5]arenes at the A1' and A2' positions.

3.5. Functionalization of Pillar[*n*]arenes Bearing Bromide Groups by Etherification, Cationation, and Amination

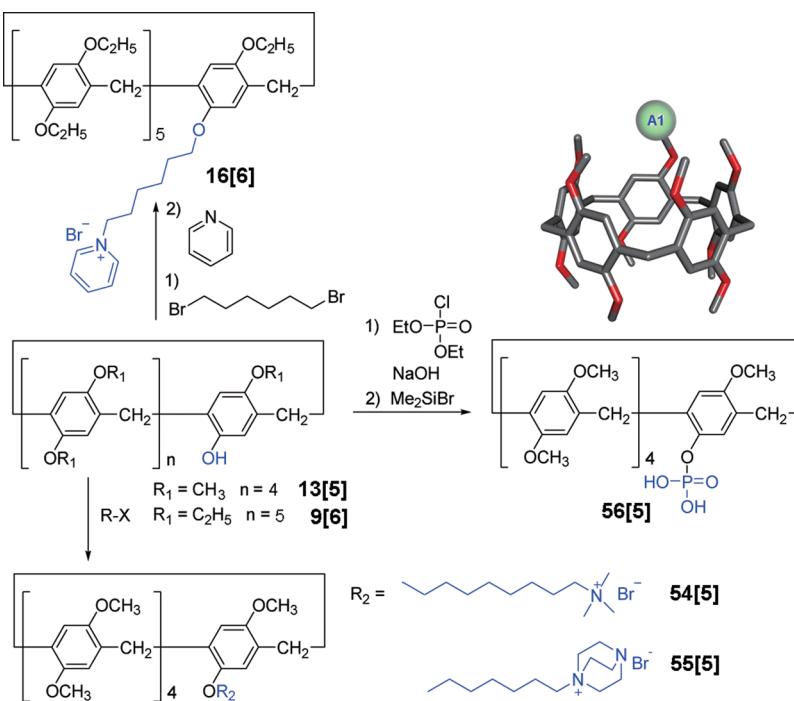
Pillar[5]- and pillar[6]arenes with bromide moieties, which can be produced by cyclization of 1,4-dialkoxybenzene with two bromide groups (Scheme 14), are good key compounds because various per-functionalized pillar[5]- and pillar[6]arenes were accessible by cationation and etherification (Scheme 21).

Reaction of the decabromides and dodecabromide with pyridine,¹⁰¹ 1-methylimidazole,^{102,103} amine,¹⁰⁴ and tributylphosphine¹⁰⁵ afforded cationic pillar[5]arenes **65[5]**–**68[5]** and pillar[6]arene **18[6]**. Etherification of the decabromide **64[5]** and coumarin derivative with phenolic moiety gave a pillar[5]-arene with 10 coumarin moieties **69[5]**.¹⁰⁶

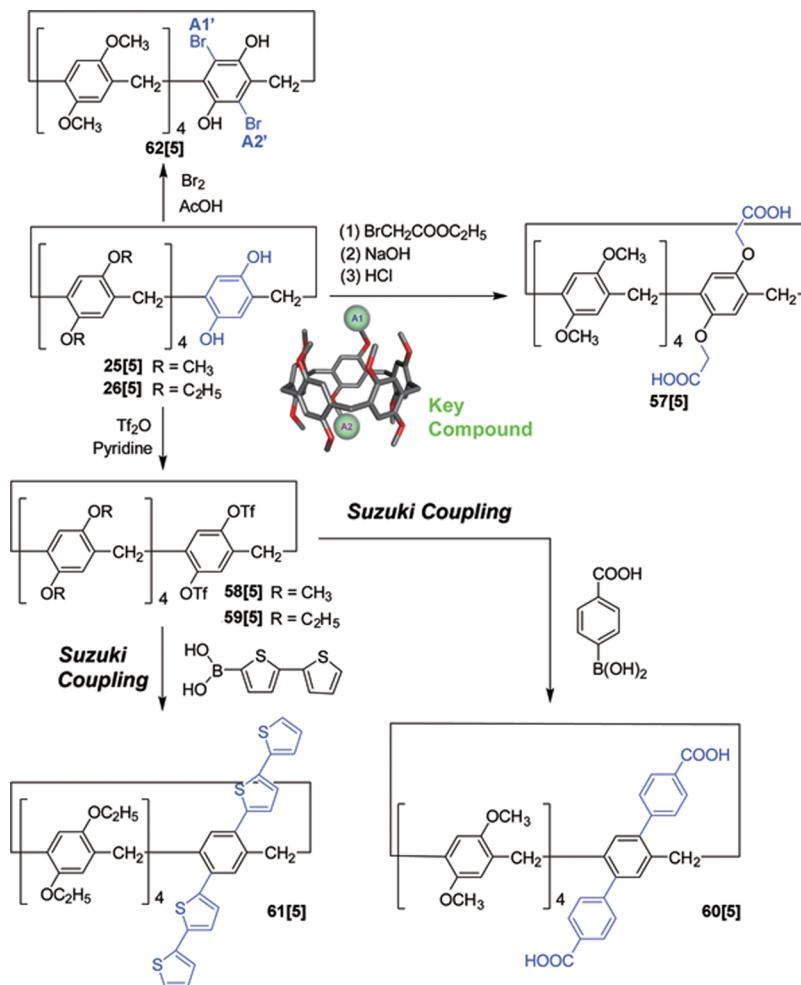
The monobromide **39[5]** and dibromide **40[5]**, which are prepared by cocrystallization method (Scheme 15), were converted to monoamine **70[5]** and diamine **71[5]**, respectively, by Gabriel synthesis (Scheme 22).^{84,107}

Mono- **72[5]** and diureidopyrimidinone **73[5]** were synthesized from the monoamine **70[5]** and A1/A2 diamine **71[5]**, respectively.

Scheme 19. Monofunctionalized Pillar[5]- and Pillar[6]arenes from Monohydroxylated Pillar[5]arene **13[5] and Pillar[6]arene **9[6]** by Etherification**



Scheme 20. Di-functionalized Pillar[5]arenes from Di-hydroxylated Pillar[5]arenes 25[5] and 26[5] by Etherification, Bromination, and Palladium-Catalyzed Cross-Coupling Reactions



3.6. Functionalized Pillar[n]arenes from Pillar[n]arenes Bearing Alkyne and Azide Groups by the Copper(I)-Catalyzed Huisgen Alkyne–Azide 1,3-Dipolar Cycloaddition Reaction

Reaction between azides and alkynes with copper(I), the copper(I)-catalyzed Huisgen alkyne–azide 1,3-dipolar cycloaddition reaction (CuAAC reaction), is a very efficient and quick reaction.¹⁰⁸ Pillar[n]arenes with azide moieties are easily accessible from pillar[n]arenes with bromide groups. Bromide groups in pillar[n]arenes are converted to azide groups by reaction of bromide moieties in pillar[n]arenes with sodium azide. These pillar[n]arenes with azide groups are useful key compounds because CuAAC reaction of these azides with alkyne derivatives affords various functionalizing pillar[n]arenes.

Nierengarten and co-workers synthesized pillar[5]- and pillar[6]arenes with azide groups. The CuAAC reaction of the decaazide and dodecaazide with corresponding alkyne derivatives afforded pillar[n]arenes with mesogens (75[5] and 20[6]) and mannose moieties 76[5] (Scheme 23).^{79,109}

Pei et al. synthesized a pillar[5]arene with 10 ferrocene moieties 77[5] by CuAAC reaction between decaazide and ferrocene with an alkyne moiety.¹¹⁰

Per-alkynylated pillar[5]arene 36[5] is also a useful key compound because CuAAC reaction of per-alkynylated pillar[5]arene with monoazide derivatives afforded per-functionalized pillar[5]arenes. The decaalkyne 36[5] was accessible by not only

etherification of preformed per-hydroxylated pillar[5]arene 12[5] with propargyl bromide¹¹¹ but also macrocyclization of dialkoxybenzene monomer with two alkyne groups (Scheme 14b).⁸⁰

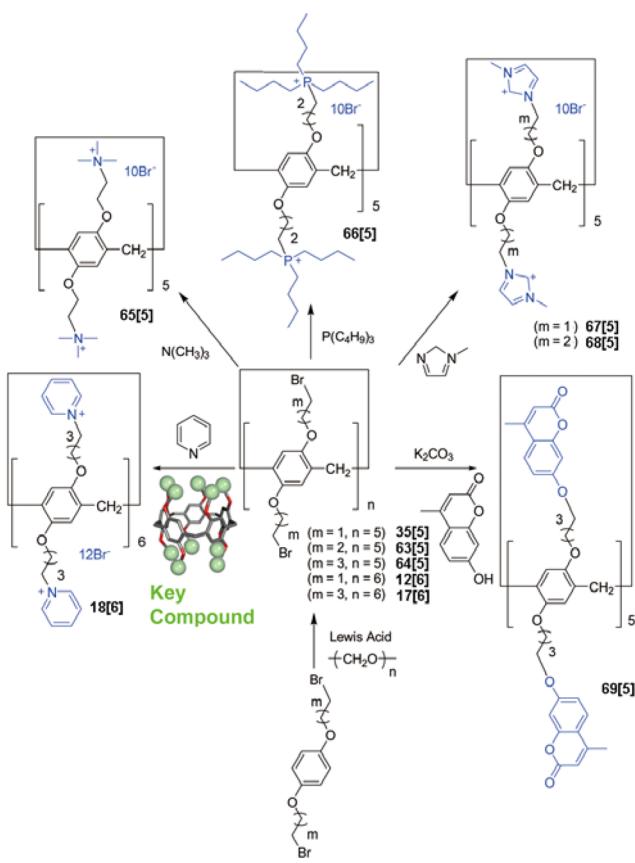
Reaction of decaalkyne 36[5] with azide derivatives such as hexylazide, benzylazide, phenylazide, naphthylazide, pyrenylazide, oligo(ethylene oxide), and cationic dendrons with an azide moiety afforded various per-functionalizing pillar[5]arenes with corresponding functional groups 78[5]–84[5] (Scheme 24).^{80,111–114}

Reaction of the copillar[5]arene with one bromide group 39[5] with sodium azide produced a copillar[5]arene with an azide group 85[5]. The monoazide 85[5] was an important key compound to synthesize monofunctionalized pillar[5]arenes through the CuAAC reaction (Scheme 25).⁸²

Monofunctionalized pillar[5]arenes with pyrene 86[5],⁸² azobenzene 87[5],¹¹⁵ viologen 88[5],¹¹⁶ and fluorescein 89[5]¹¹⁷ were produced by the CuAAC reaction of the monoazide 85[5] with the corresponding monoalkynes.

The A1/A2 dialkyne 90[5] and A1/A2/C1/C2 tetra-alkyne 91[5] were produced by etherification of A1/A2 diol 26[5] and A1/A2/C1/C2 pentanol 30[5] with propargyl bromide. The dialkyne and tetraalkyne can be reacted with pyrene with an azide moiety through the CuAAC reaction to afford a pillar[5]arene with two 92[5] and four pyrenyl moieties 93[5] (Scheme 26).⁶⁸

Scheme 21. Per-functionalized Pillar[5]- and Pillar[6]arenes from Decabromides and Dodecabromide by Cationation and Etherification



Thus, the dialkyne **90[5]** and tetraalkyne **91[5]** are useful key compounds to produce various A1/A2 di- and A1/A2/C1/C2 tetra-functionalized pillar[5]arenes.

Yang and co-workers synthesized an A1/A2 difunctionalized pillar[5]arene with a bromide and an alkyne moiety at the A1 and A2 positions **94[5]** by cocrystallization of a nonsymmetric

dialkoxybenzene monomer possessing a bromide and an alkyne group with 1,4-dialkoxybenzene (**Scheme 27**).¹¹⁸

An anthracene moiety can be installed in **94[5]** using the CuAAC reaction between the alkyne moiety and an anthracene derivative with an azide group. The reaction between the bromide moiety in **95[5]** and dimethylamine then afforded a pillar[5]arene with an anthracene and a cationic moiety at the A1 and A2 positions **96[5]**. Combination of CuAAC and another reaction expands the functionality of pillar[5]arenes.

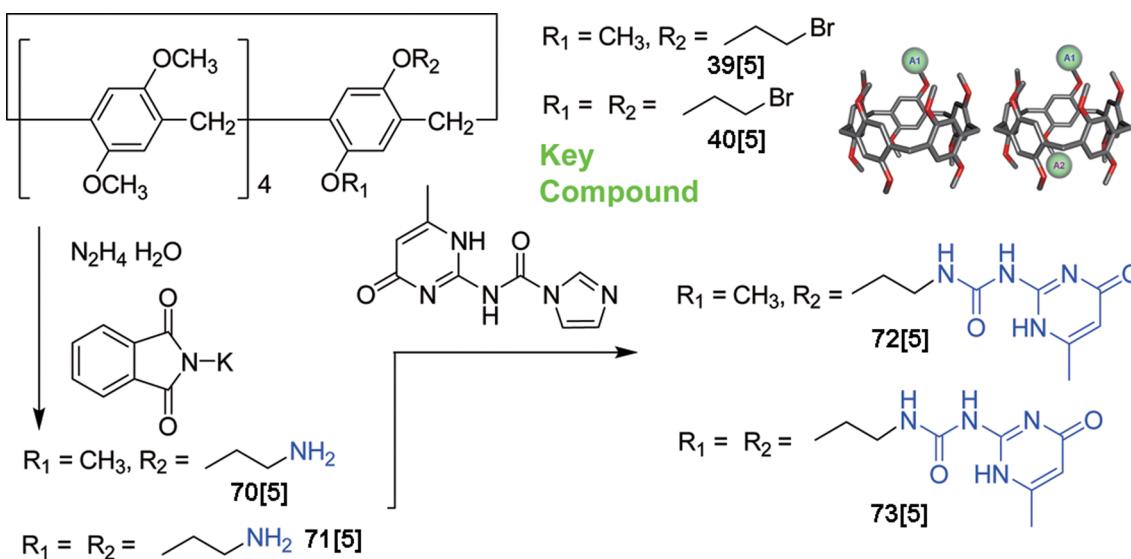
3.7. Pillar[5]arene Dimers, Tetramers, and Pentamers from Monoreactive Pillar[5]arenes

Monofunctionalized pillar[n]arenes are useful building blocks to produce molecules containing more than one pillar[n]arene, such as dimers, trimers, and tetramers. Our group synthesized a pillar[5]arene dimer **97[5]** by connecting the monohydroxylated pillar[5]arenes **13[5]** with 1,4-bis(bromomethyl)benzene (**Scheme 28**).¹¹⁹

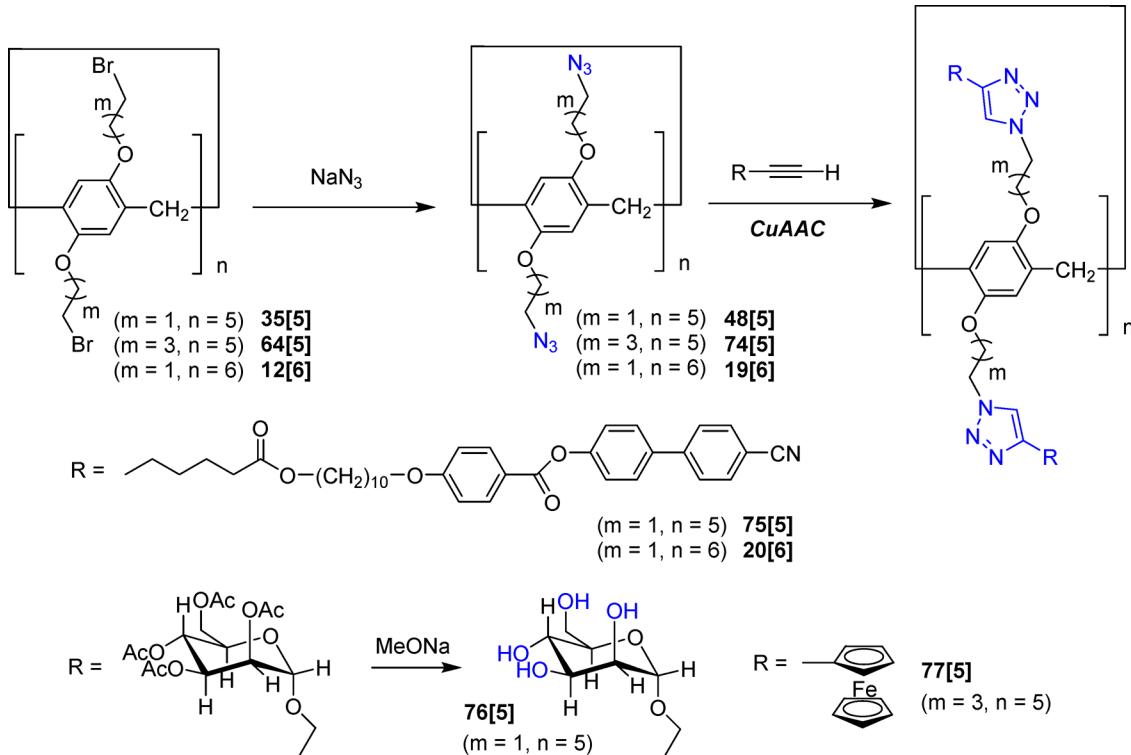
The other pillar[5]arene dimers (**98[5]** and **99[5]**) connecting the monohydroxylated pillar[5]arene molecules by other linkers, such as 1,2-bis(bromomethyl)benzene and 1,4-diiodobutane, were synthesized by Li, Jia, and co-workers.¹²⁰ An azobenzene bridged pillar[5]arene dimer **101[5]** was synthesized by the CuAAC reaction between monoalkyne-functionalized pillar[5]arene **100[5]** and azobenzene with two azide moieties.¹²¹ Yang et al. and Yu et al. synthesized pillar[5]arene dimer **104[5]** and tetramer **105[5]** by etherification of di- and tetra-ol compounds with monobromides (**102[5]** and **103[5]**), respectively, which were produced by cocrystallization of 1,4-dimethoxybenzene and 1,4-dialkoxybenzene with one bromide group (**Scheme 29**).^{122–124}

Reaction between the monobromide **102[5]** and NaSeSeNa afforded a pillar[5]arene dimer linked by an Se–Se bond **106[5]**.¹²⁵ A pillar[5]arene with an azide moiety **107[5]**, which was produced by reaction of monobromide **102[5]** and sodium azide, is also a good key compound to produce pillar[n]arene oligomers. CuAAC reaction of di- and tetra-alkynes with pillar[5]arenes possessing an azide moiety **107[5]** produced a pillar[5]arene dimer **108[5]** and a tetramer.^{126,127} The other process for the synthesis of pillar[5]arene dimers is the cocrystallization method. Huang et al. and Xiao, Jiang et al.

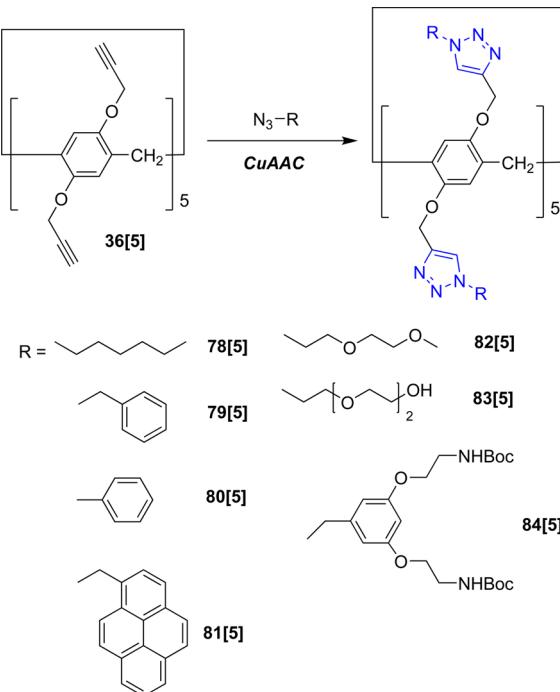
Scheme 22. Mono- and A1/A2 Di-functionalized Pillar[5]arenes from Monobromide **39[5]** and A1/A2 Dibromide **40[5]**



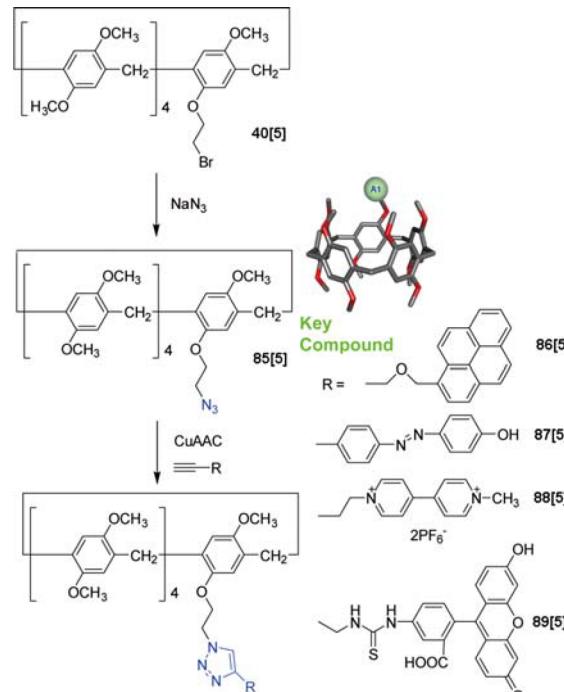
Scheme 23. Per-functionalized Pillar[5]- and Pillar[6]arenes from Decaazide and Dodecaazide by CuAAC Reaction



Scheme 24. Per-functionalized Pillar[5]arenes from Decaalkyne 36[5] by CuAAC Reaction



Scheme 25. Monofunctionalized Pillar[n]arenes from Monoazide 85[5] by CuAAC Reaction



synthesized pillar[5]arene dimers by cocrystallization of 1,4-dimethoxybenzene monomer with dimeric monomer, in which two monomers are connected by flexible aliphatic chains.^{128,129}

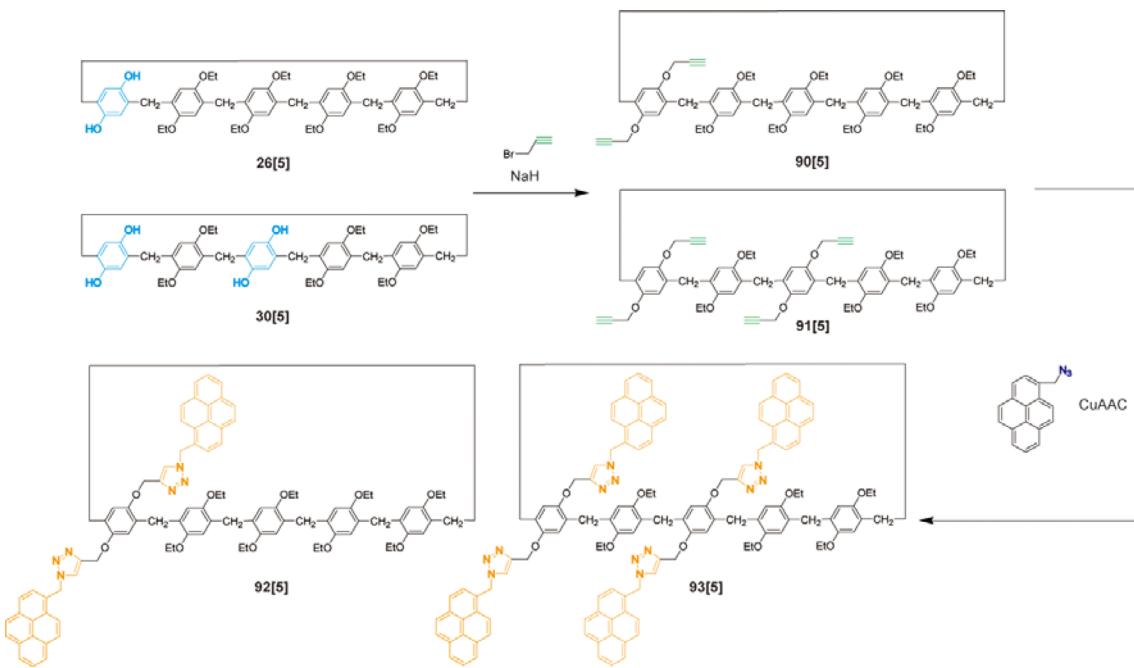
3.8. Penta-functionalization of Pillar[n]arenes

Penta-functionalized pillar[5]arenes can be synthesized by macrocyclization of nonsymmetric dialkoxybenzene monomers.

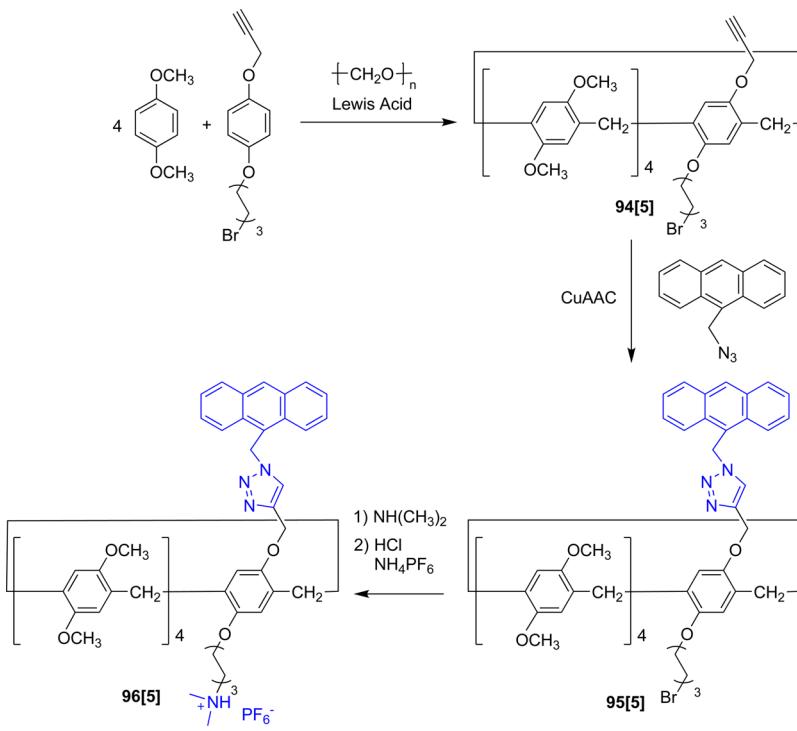
However, four constitutional isomers are formed by macrocyclization (Scheme 30).

This is a serious problem because isolation of these conformers is quite difficult by silica gel chromatography. Among these isomers, the highly symmetric C_5 -isomer shows a rim-different structure; thus it should be useful for various applications. However, yields of the C_5 -symmetric isomers were quite low.

Scheme 26. A1/A2 Di- and A1/A2/C1/C2 Tetra-functionalized Pillar[*n*]arenes from Dialkyne 90[5] and Tetraalkyne 91[5] by the CuAAC Reaction



Scheme 27. Synthesis of A1/A2 Di-functionalized Pillar[5]arene with Two Different Functional Groups 96[5] by a Combination of Cocyclization, CuAAC Reaction, and Cationation

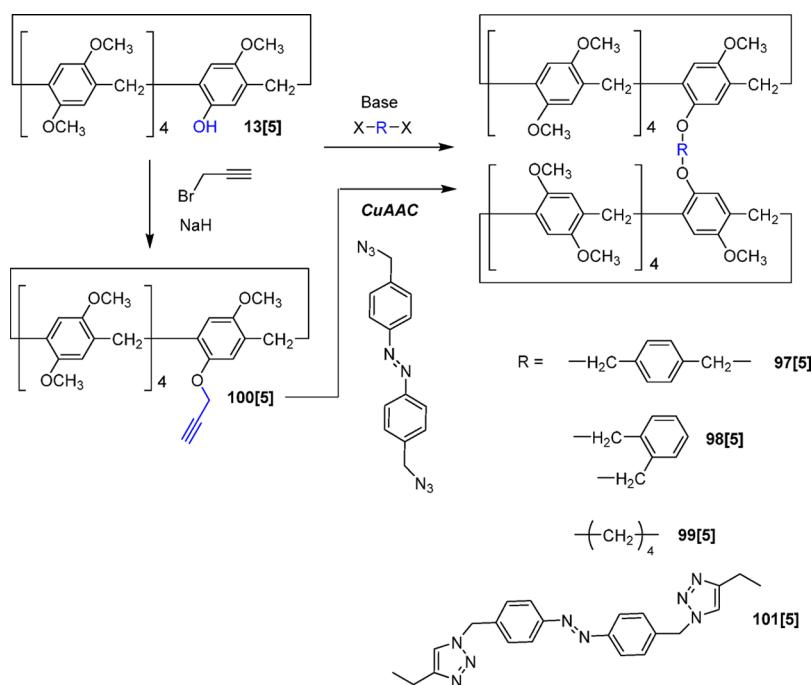


Our group reported the first nonsymmetrical pillar[5]arene **109a–d[5]** by cyclization of nonsymmetrical dialkoxybenzene monomer, 1-ethoxy-4-methoxybenzene.¹³⁰ However, we could not separate four isomers **109a–d[5]**. Huang et al. and Meier et al. successfully isolated the nonsymmetrical pillar[5]arene isomers **110a–d[5]**, which are composed of 1-butoxy-4-methoxybenzene units, by silica gel chromatography, but the

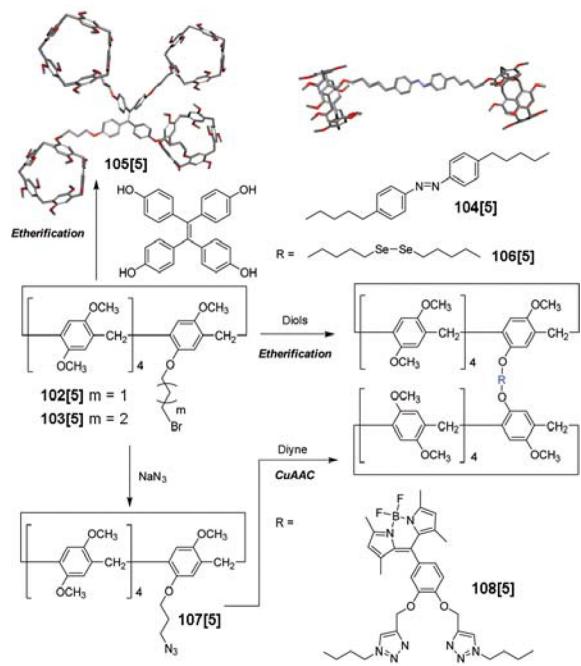
yield of the C_5 -symmetric isomer **110a[5]** was quite low (Scheme 30, 6%).^{131,132}

Huang et al. developed a C_5 -symmetric pillar[5]arene with five functional groups by the CuAAC reaction.¹³³ First, they produced a nonsymmetric pillar[5]arene containing four isomers **111a–d[5]** by macrocyclization of the nonsymmetrical monomer, 1,4-dialkoxybenzene with an alkyne group. These isomers could not be separated because separation of these isomers was

Scheme 28. Synthesis of Pillar[5]arene Dimers from Mono-ol 13[5] and Monoalkyne 100[5] by Esterification and CuAAC Reaction, Respectively



Scheme 29. Synthesis of Pillar[5]arene Dimers and Tetramers from Monobromides (102[5] and 103[5]) and Monoazide 107[5] by Etherification and CuAAC Reactions, Respectively



quite difficult. The CuAAC reaction between a mixture of the isomers 111a–d[5] and a naphthalene containing an azide moiety afforded pillar[5]arene isomers 112a–d[5] with five naphthalene moieties. A *C*₅-symmetric isomer 112a[5] was successfully isolated from the other isomers by silica gel chromatography. Modification of naphthalene moieties contributes to the easy separation of the target compound *C*₅-symmetric isomer. The same group also discovered isolation of the *C*₅-symmetric isomer by recrystallization. Macrocyclization of the

nonsymmetric monomer with an ester group afforded a mixture of pillar[5]arene isomers 113a–d[5] (Scheme 31).¹³⁴

Isolation of the *C*₅-symmetric pillar[5]arene 113a[5] was achieved by recrystallization of a mixture of the isomers. Because the *C*₅-symmetric isomers cannot be selectively formed in these methods, yields of the *C*₅-symmetric isomers were low. Selective synthesis of the *C*₅-symmetric isomer is one of the next challenging topics in pillar[*n*]arene chemistry.

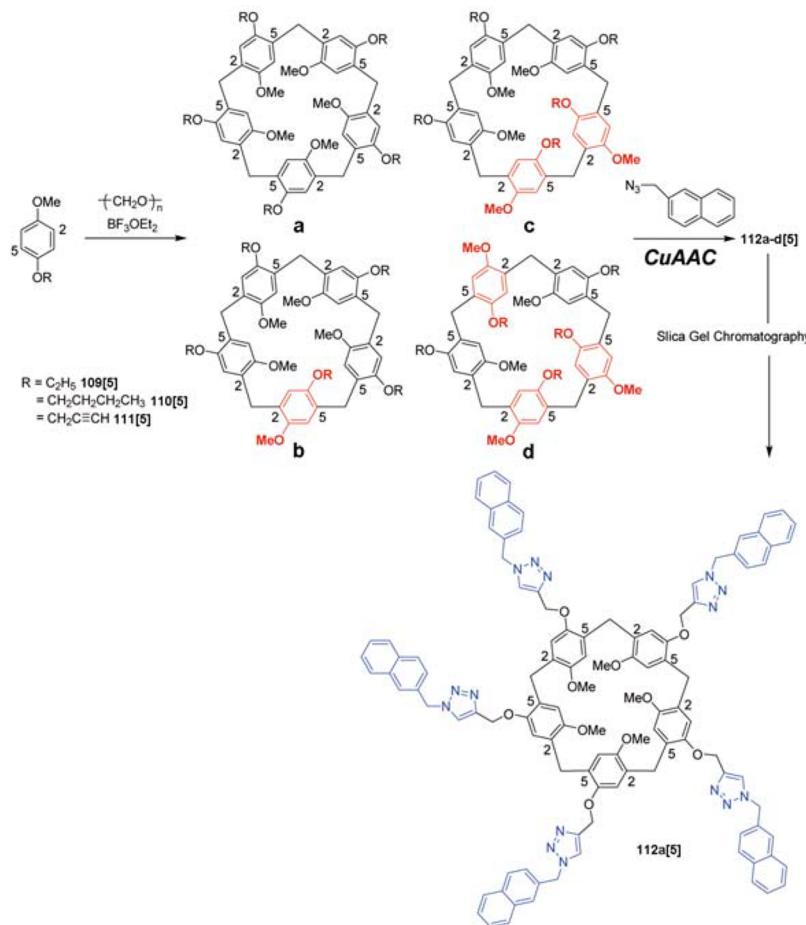
4. STRUCTURE OF PILLAR[*n*]ARENES

4.1. X-ray Crystal Structures of Simple Pillar[*n*]arene Homologues

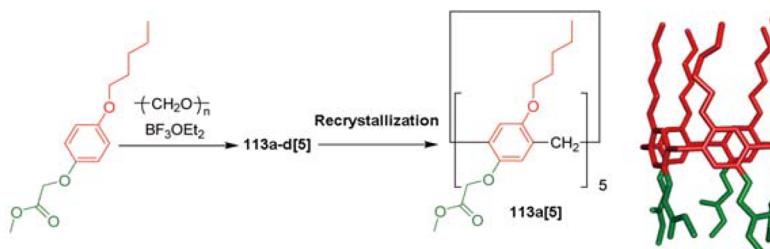
One of the important features of pillar[*n*]arenes is their structure. We were the first to report the X-ray crystal structure of cyclic pentamer pillar[*n*]arenes, pillar[5]arene with 10 methoxy groups 1[5] (Figure 7a).³³

Pillar[5]arene 1[5] showed a completely symmetric cylindrical structure from the side view, and a highly symmetrical regular pentagonal structure from the top view. 1,4-Dimethoxybenzene units consisting of 1[5] were connected by methylene linkages at the 2- and 5-positions (*para*-positions). The position of the methylene bridge linkage contributed to these highly symmetrical structures. On the basis of the highly symmetric pillars that constitute the Parthenon in Athens, we named this type of paracyclophane “pillar[*n*]arenes”. The first X-ray crystal structure of cyclic hexamer, pillar[6]arene with 12 diisobutoxy groups 3[6], was reported by Huang and co-workers.¹³⁵ The same group also reported the X-ray crystal structure of pillar[6]arene with 12 propoxy groups 2[6] (Figure 7b).¹³⁶ 2[6] has a hexagonal-like cyclic structure from the top view. From the side view, as with pillar[5]arene 1[5], pillar[6]arene 2[6] has a highly symmetrical structure. X-ray crystal structures of pillar[8]-, pillar[9]-, and pillar[10]arenes were first reported by Hou and co-workers (Figure 8),⁶¹ while that of pillar[7]arene

Scheme 30. Four Constitutional Isomers Generated from Macrocyclization of Nonsymmetric Monomers and Separation of the C_5 -Symmetric Isomer by the Cyclization Followed by Activation Strategy



Scheme 31. Isolation of the C_5 -Symmetric Isomer 113a[5] from a Mixture of Isomers by Crystallization



has not been reported because pillar[7]arenes would have a low symmetry structure.

These larger pillar[n]arenes have two cavities, while pillar[5]- and pillar[6]arenes have a single pentagonal and hexagonal cavity, respectively. Pillar[8]arene with 16 ethoxy groups 1[8] have two pentagonal cavities. From the top view of the X-ray crystal structure of pillar[9]arene with 18 ethoxy groups 1[9], one pentagonal and one hexagonal cavity were observed. Pillar[10]arene with 20 ethoxy groups 1[10] have two hexagonal cavities. To reduce the ring strain, they should have two cavities. The same trend was also reported in calix[n]arene chemistry. Calix[8]arene has two tetragonal calix-shaped cavities because the tetragonal calix-shape is the most stable structure.¹³⁷ As with pillar[5]- and pillar[6]arenes, these larger pillar[n]arenes exhibit a highly symmetrical pillar-shaped structure from their side views.

4.2. Conformational and Planar Chirality Characteristics of Pillar[n]arenes

From the viewpoint of conformational mobility, macrocyclic molecules are divided into two categories: conformationally fixed and conformationally flexible. Calix[n]arenes and crown ethers are assigned as conformationally flexible macrocyclic compounds. For example, calix[4]arenes have four conformational isomers: cone, partial cone, 1,2-alternate, and 1,3-alternate. In contrast, CB[n]s are conformationally fixed macrocyclic compounds because their units are connected by double methylene bridges.

Pillar[n]arenes are assigned as conformationally flexible macrocyclic compounds because their benzene units can rotate around 180° (Figure 9a).

The pillar[n]arene constituent units are composed of two substituents at the 2 and 5 positions of the benzene units.

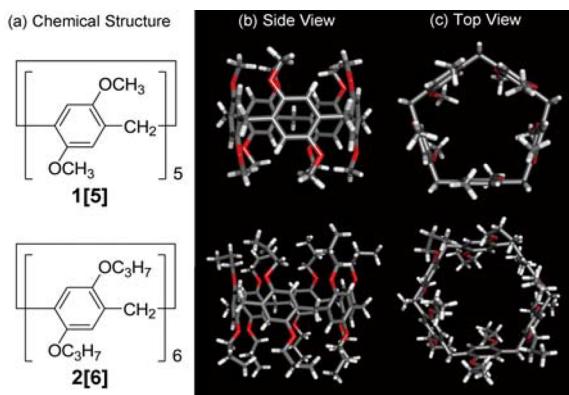


Figure 7. (a) Chemical structures and (b) side and (c) top views of per-methylated pillar[5]arene **1[5]** and per-propylated pillar[6]arene **2[6]**.

Therefore, pillar[n]arenes have conformational isomers resulting from rotation of the benzene units. Pillar[5]arenes have an odd number of constituent units (five); therefore, they have four diastereomers (**Figure 9b**, **a**, **b**, **c**, and **d**): Diastereomer **a** has C_5 symmetry, while the other three diastereomers (**b**, **c**, and **d**) have C_2 symmetry. Furthermore, they have the corresponding enantiomers (**a'**, **b'**, **c'**, and **d'**). Thus, pillar[5]arenes have a total of eight conformers.¹³⁸ In the case of pillar[6]arenes, they have an even number of constituent units (six); therefore, they have five diastereomers (**Figure 9c**, **a**, **b**, **c**, **d**, **e**) and three meso forms (**f**, **g**, **h**). **a**, **b**, **c**, **d**, **e**, **f**, **g**, and **h** forms are assigned with C_6 , C_1 , C_{2v} , C_{2h} , C_2 , C_3 , C_{3v} , and C_{2h} symmetries, respectively. Furthermore, **a**, **b**, **c**, **d**, and **e** forms have the corresponding enantiomers (**a'**, **b'**, **c'**, **d'**, and **e'**). Therefore, there are a total of 13 conformers in pillar[6]arenes.¹³⁹ These conformers are interconverted by rotation of the benzene units of pillar[n]arenes because the rotation of the benzene unit leads to the positional changes of the substituents.

The conformational structure in the crystal state is a “snapshot” of one of the conformations of pillar[n]arenes, but this structure will be the most stable conformation of pillar[n]arenes. From the X-ray crystal structure of simple alkyl-substituted pillar[n]arenes, shown in **Figures 7** and **8**, their structures exhibit C_n symmetry, indicating that C_n symmetric structures are most stable among all possible conformers. The possible reason for this is that there are no strong interactions between neighboring units in per-alkylated pillar[n]arenes. Simple alkyl-substituted pillar[n]arenes form C_n symmetric **a** and **a'** conformations to reduce the steric hindrance between the alkyl substituents. **Figure 10** shows the energy diagrams of per-methylated pillar[5]arene **1[5]** conformers obtained from calculations.

The C_5 -symmetric conformers **a/a'** are the most stable structures among the **1[5]** conformers. However, their conformation dramatically changed by replacing the substituents from methoxy to hydroxyl groups. **Figure 11** shows the X-ray crystal structure of per-hydroxylated pillar[5]arene **12[5]**.⁵³

Flipping of the two hydroquinone moieties at the A and C units is observed to form intramolecular hydrogen bonds between the neighboring units. However, pillar[5]arenes have an odd number of units; thus hydroquinone moieties at the D and E units cannot form intramolecular hydrogen bonds. Hence, per-hydroxylated pillar[5]arene forms conformational isomers **d/d'** in the solid state. Formation of isomers **d/d'** in the frozen state of **12[5]** is also suggested by ^1H NMR of **12[5]** at low temperature (**Figure 12**).

The proton signals from phenol, phenyl, and the methylene bridge of per-hydroxylated pillar[5]arene **12[5]** were observed as singlets at 25 °C. In contrast, the signals broadened around –50 °C, and split as the measurement temperature decreased under –60 °C. The split signals at low temperature suggest that the nonsymmetrical diastereomers **d/d'** are the most stable conformers in the case of per-hydroxylated pillar[5]arene **12[5]**. Peerannawar and Gejji supported the experimental

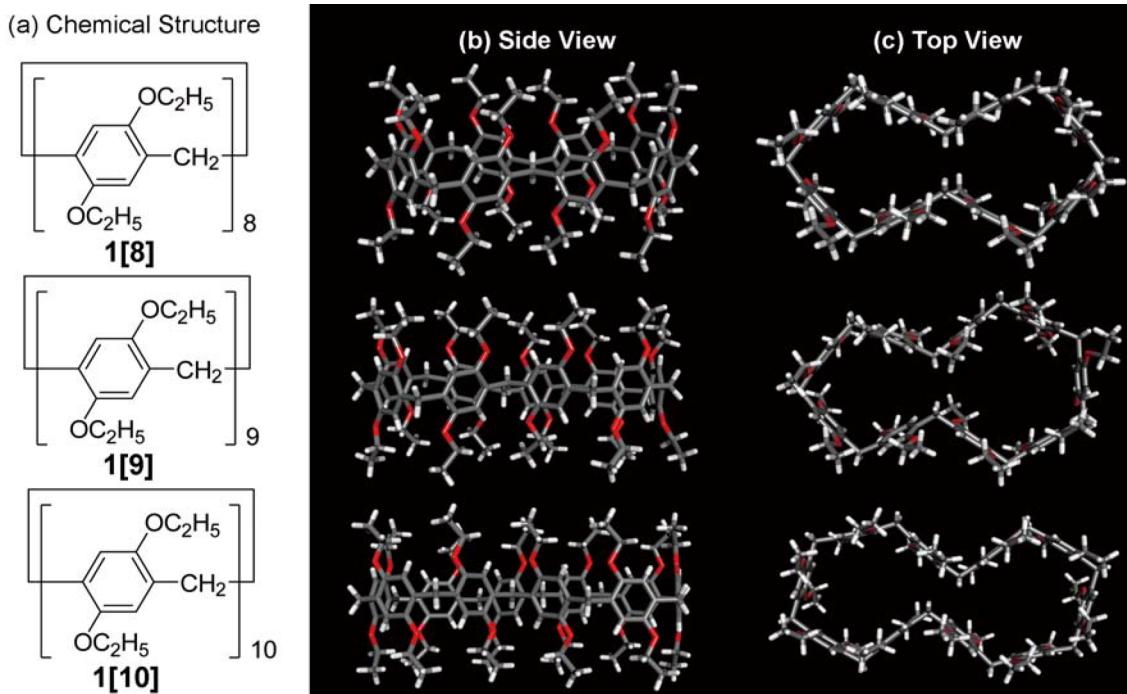


Figure 8. (a) Chemical structures and (b) side and (c) top views of per-ethylated pillar[8]-, pillar[9]-, and pillar[10]arenes (**1[8]**, **1[9]**, and **1[10]**).

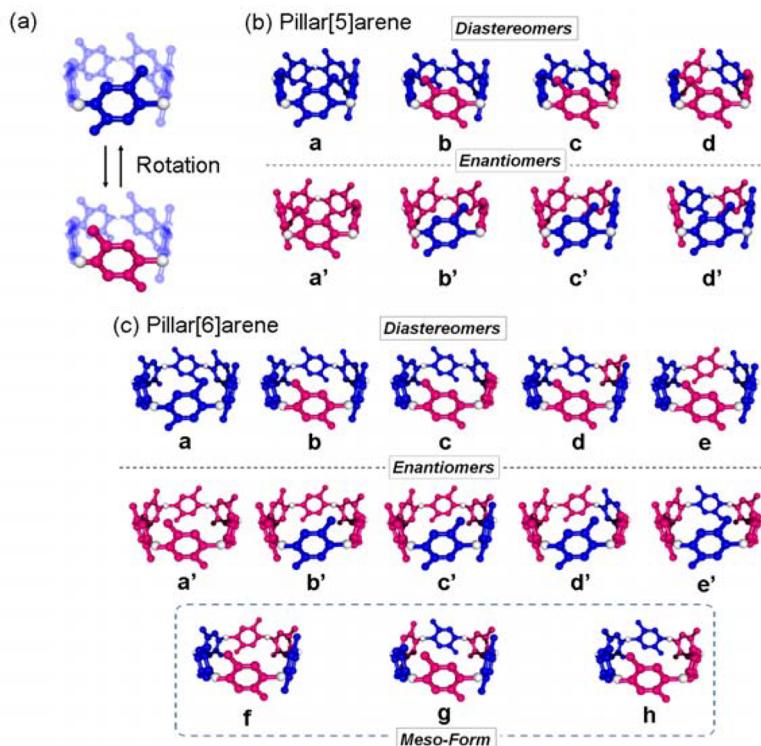


Figure 9. (a) Rotational mode of the benzene units of pillar[n]arenes. Conformers of (b) pillar[5]arene and (c) pillar[6]arene caused by rotation of the benzene units. Reproduced with permission from ref 139. Copyright 2013 Royal Society of Chemistry.

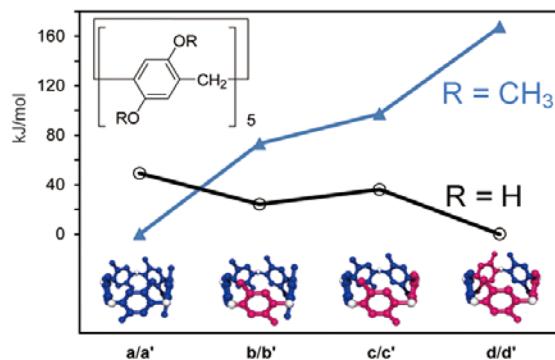


Figure 10. Energy diagrams of per-methylated 1[5] and per-hydroxylated pillar[5]arenes 12[5].

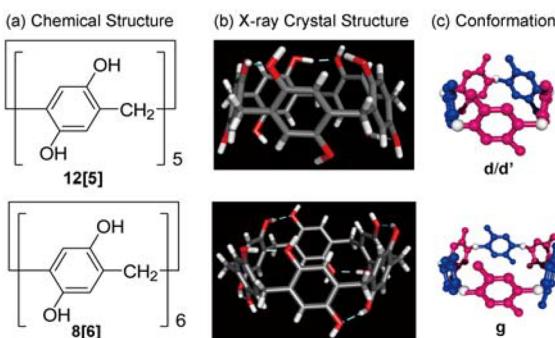


Figure 11. (a) Chemical, (b) X-ray crystal structures, and (c) conformations of per-hydroxylated pillar[5]arene 12[5] and pillar[6]-arene 8[6].

observations with calculations (Figure 10).¹⁴⁰ The most stable diastereomers of per-hydroxylated pillar[5]arene 12[5] were the

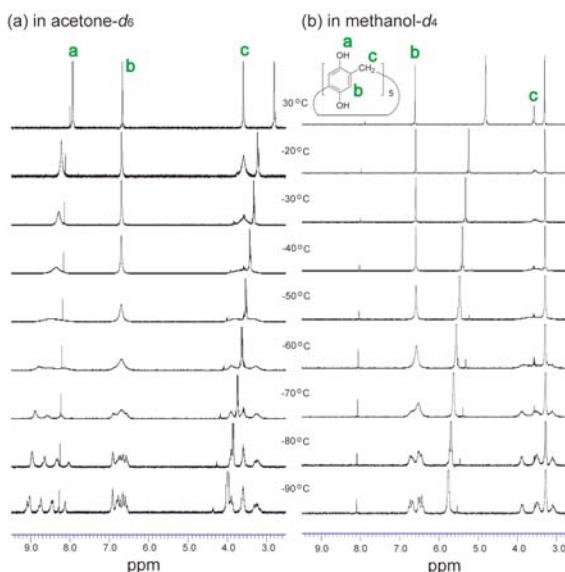


Figure 12. Variable-temperature ¹H NMR spectra of per-hydroxylated pillar[5]arene 12[5] in (a) acetone-d₆ and (b) methanol-d₄. Reproduced with permission from ref 138. Copyright 2010 American Chemical Society.

d/d' conformers, which is the exact opposite result as compared to the simple per-methylated pillar[5]arene 1[5]. Per-hydroxylated pillar[5]arene 12[5] forms up-and-down d/d' conformations to form an intramolecular hydrogen-bond network between units, while per-methylated pillar[5]arene 1[5] forms highly regular a/a' conformations to reduce the steric hindrance between substituents.

Per-hydroxylated pillar[6]arene 8[6] also formed intramolecular hydrogen bonds between adjacent units; therefore,

flipping of hydroquinone moieties at the A, C, and E units was observed in the X-ray crystal structure of **8[6]** (Figure 11).⁷³ The conformation of **8[6]** was assigned as isomer g. Cyclic hexamer, pillar[6]arenes have an even number of units; thus, the intramolecular hydrogen-bond network is completely continuous in an alternating up-and-down manner. The relative stabilization energies of the different conformers, which have been reported by Gejji and co-workers, supported the X-ray crystal structure of per-hydroxylated pillar[6]arene **8[6]**.¹⁴¹ The meso-form of conformer g is the most stable, and the energies (in kJ/mol) of the different conformers relative to conformer g are calculated to be 21.4 (**d/d'**) < 41.3 (**c/c'**) < 45.5 (**b/b'**) < 61.9 (**h**) < 72.4 (**a/a'**).

X-ray crystal structures of A1/B2 and A1/A2 dihydroxylated pillar[5]arenes (**41[5]** and **25[5]**) were reported by our group and the Stoddart group, respectively.^{86,87} Flipping of two units (A and B units) was observed in A1/B2 dihydroxylated pillar[5]arene **41[5]** (Figure 13a).

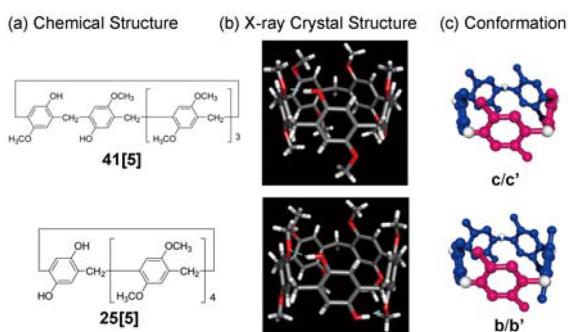


Figure 13. (a) Chemical and (b) X-ray crystal structures and (c) conformations of A1/B2 41[5] and A1/A2 dihydroxylated pillar[5]-arenes 25[5].

The flipping occurred to form intramolecular hydrogen bonds between B and C units, and between A and E units. Therefore, isomers **c/c'** were the most stable conformers in A1/B2 dihydroxylated pillar[5]arene **41**[5]. In contrast, in the crystal structure of A1/A2 dihydroxylated pillar[5]arene **25**[5] (Figure 13b), flipping of one hydroquinone unit A was observed to form intramolecular hydrogen bonds between the A and B units, and between the A and E units. Therefore, isomers **b/b'** were the most stable in A1/A2 dihydroxylated pillar[5]arene **25**[5]. Both A1/B2 and A1/A2 diols have two phenolic moieties, but the conformation of the A1/B2 diol is different from that of the A1/A2 diol, indicating that the position of the phenolic moieties dominates the most stable conformation of pillar[5]arenes.

Pillar[n]arene enantiomers should be useful compounds for chiral molecular recognition and catalysts because pillar[n]arene enantiomers have pores to capture guest molecules. However, interconversion between isomers occurred by rotation of the units. To isolate the pillar[n]arene enantiomers, inhibition of the rotation of the units is necessary. We first synthesized various lengths of alkyl chains, such as ethyl, propyl, butyl, pentyl, hexyl, and dodecyl chains (**1[5]**–**7[5]**), at both rims to inhibit the rotation of the units.⁵⁴ Figure 14a shows the rotational barrier of the units, which was determined by variable-temperature ^1H NMR.

As the length of the alkyl chain increased, the rotational barrier also increased. However, these substituents were too small to stop the rotation of the units. Therefore, a pillar[5]arene with 10 bulky cyclohexylmethyl groups **11[5]** was produced.⁹¹ For **11[5]**, rotation of the units could not be observed by variable ¹H NMR. Thus, **11[5]** was characterized by chiral HPLC (Figure 14b). Two peaks with equal areas were observed by injection of **11[5]** into a chiral column, indicating that **11[5]** was a mixture of two enantiomers, and exhibited a rotational barrier to observe two enantiomers as separated peaks. When the first fraction collected was reinjected, the original peak was detected but the pair peak from an enantiomer was not observed. After the first

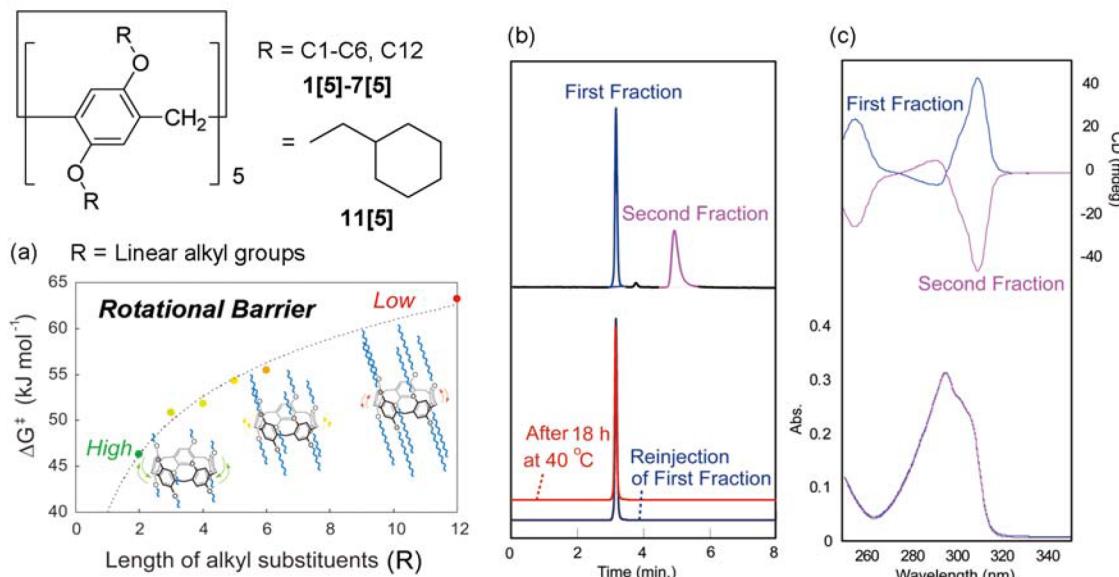


Figure 14. (a) Plot of the ΔG^\ddagger values for pillar[5]arenes with different lengths of alkyl chains **1**[5]–**7**[5] in toluene-*d*₈. Reproduced with permission from ref 54. Copyright 2010 American Chemical Society. (b) Chiral HPLC traces of pillar[5]arene with 10 cyclohexylmethyl groups **11**[5] and the first fraction of the pillar[5]arene by maintaining at 40 °C for 18 h. Hexane/EtOH = 97/3 (vol %) was used as eluent. (c) UV–vis and CD spectra of the first and second fractions of **11**[5] (14 μ L mol⁻¹ cm⁻¹) in hexane at 25 °C. Reproduced with permission from ref 91. Copyright 2011 American Chemical Society.

fraction was maintained at 40 °C for 18 h, the second peak was also not detected, indicating **11[5]** did not racemize. The CD spectra of the first and second fractions were completely mirror image (Figure 14c), and stable at 25 °C, and the conformation of the enantiomers determined by ¹H NMR was shown to be the C₅-symmetric isomer **a/a'**. Therefore, we successfully stopped the rotation of the units, and isolated the enantiomers **a** and **a'** by introducing bulky cyclohexylmethyl groups at both rims of pillar[5]arene.

Stoddart et al. reported the separation of enantiomers by introducing one π -conjugated unit (Figure 15).⁸⁷

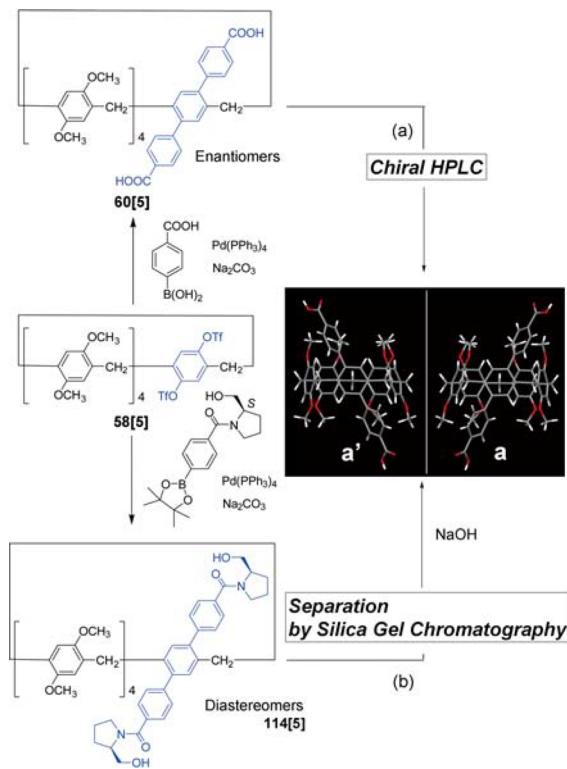


Figure 15. Pillar[5]arene enantiomers with one π -conjugated unit isolated by (a) chiral HPLC and (b) diastereomer method.

Introduction of bulky monosubstituted phenyl rings at the A1/A2 positions of pillar[5]arene **60[5]** contributes to inhibit the rotation of the units and separate the **a** and **a'** forms of planar chiral pillar[5]arenes by chiral column chromatography. Introduction of bithienyl moieties to the pillar[5]arene at the A1/A2 positions **61[5]** (Scheme 20) also prevented the rotation of the units, and resulted in the isolation of enantiomers **a** and **a'** by chiral column chromatography.⁹⁹ Stoddart et al. also successfully synthesized the planar chiral pillar[5]arenes by the diastereomer method (Figure 15b).¹⁴² First, bulky monosubstituted phenyl rings with chiral resolving agent were introduced at the A1/A2 positions of pillar[5]arene. The compounds **114[5]** are diastereomers; thus, the two diastereomers can be easily separated by silica gel chromatography. Removal of the resolving agent afforded **60[5]** enantiomers in the **a** and **a'** forms.

Introduction of chiral substituents is another pathway to induce the planar chirality. We synthesized pillar[5]arene with 10 2(S)-methylbutoxy groups **8[5]** (Figure 21).⁵⁵

The diastereomeric excess (de%) of **8[5]** was changed by solvent, temperature, and inclusion of a guest molecule. The

dynamic planar chirality change will be applied in chiral molecular recognition and as catalysts (Figure 16).

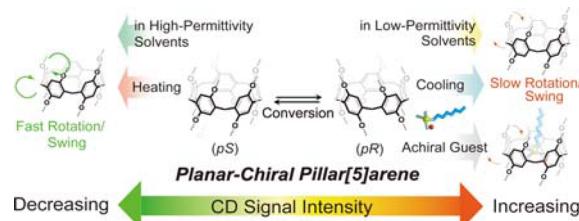


Figure 16. Dynamic changes of a diastereomeric excess of pillar[5]-arene with 10 chiral substituents **8[5]** depending on solvent, temperature, and inclusion of guest molecules. Reproduced with permission from ref 55. Copyright 2011 American Chemical Society.

Enantiomers **a** and **a'** have been successfully isolated, but the isolation of the other enantiomers has not been accomplished. The inhibition of units of pillar[6]arenes has not been achieved, and thus remains another challenging topic. We synthesized pillar[6]arene with 12 cyclohexylmethyl groups **7[6]** to inhibit the rotation of the pillar[6]arene units (Figure 17).¹³⁹

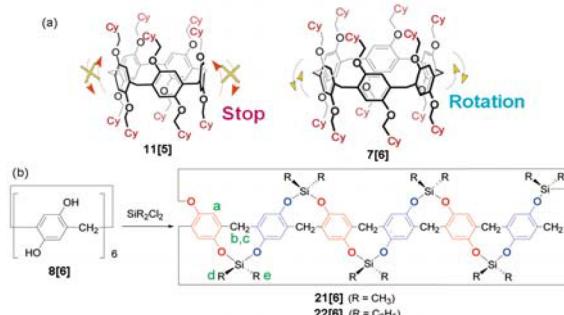


Figure 17. (a) Rotational property of pillar[5]arene with 10 cyclohexylmethyl groups **11[5]** and pillar[6]arenes with 12 cyclohexylmethyl groups **7[6]**. (b) Bridging of the adjacent units in **8[6]** by dialkylsilanes to inhibit the rotation of the units.

However, rotation of the units occurred even after the introduction of 12 bulky cyclohexylmethyl groups because the cavity size of pillar[6]arene is larger than that of pillar[5]arene. Introduction of more bulky substituents would therefore be necessary to stop the rotation of the units. The other method to stop the rotation of the units was bridging the even number of benzene rings in pillar[6]arenes.¹³⁹ The most stable conformation of per-hydroxylated pillar[6]arene **8[6]** is the g, meso-form C_{3v}-symmetric structure, as determined by X-ray crystal analysis of **8[6]** (Figure 11).⁷³ The meso-form pillar[6]arenes were fixed by bridging units by reaction of adjacent phenolic units of pillar[6]arene with dialkyldichlorosilanes (Figure 17b, **21[6]** and **22[6]**). The bridged pillar[6]arene cavitands are conformationally fixed macrocyclic compounds, and thus should have superior host–guest ability as compared to conformationally flexible pillar[6]arenes.

4.3. Assembled Structure of Pillar[n]arenes

Pillar[n]arenes exhibit highly symmetrical structures. Therefore, clarification of the assembled structures of pillar[n]arene molecules in the crystal state is an interesting topic, and will result in the solid-state complexation with guests. Pillar[n]arenes mainly form three assembled structures in the crystal state:

herringbone, one-dimensional channels, and slipped-stacked structures. The ring size, substituents on the pillar[*n*]arene rims, and type of solvent to produce pillar[*n*]arene crystals dominate the assembled structures of pillar[*n*]arenes.

Single crystals of per-methylated pillar[5]arene **1[5]**, which is the first pillar[*n*]arene derivative, were produced by slow evaporation of its acetonitrile solution. In the crystal structure, one acetonitrile molecule was incorporated in the cavity of pillar[5]arene. The complexes were arranged perpendicular to each other, in a herringbone structure (Figure 18a).³³

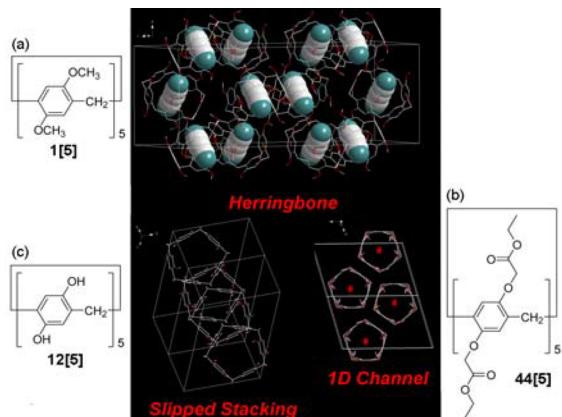


Figure 18. (a) Herringbone crystal structure formed by per-methylated pillar[5]arene **1[5]** crystallized from its acetonitrile solution. (b) One-dimensional channels formed by pillar[5]arene with 10 ester moieties **44[5]** crystallized from a mixture of ethylene glycol and chloroform. (c) Slipped-stacked structure formed by per-hydroxylated pillar[5]arene **12[5]** crystallized from its acetone solution.

The one-dimensional channel structure constructed by the assembly of pillar[5]arenes was first reported by Hou and co-workers.¹⁴³ Pillar[5]arene with 10 ester moieties **44[5]** formed one-dimensional channels by crystallization from a mixture of ethylene glycol and chloroform (Figure 18b). Water molecules were arranged in one-dimensional channels. The slipped-stacked structure was observed in the crystal of per-hydroxylated

pillar[5]arene **12[5]** (Figure 18c). **12[5]** formed rigid structures due to the intramolecular hydrogen bonds between adjacent units.⁵³ However, because of the odd number of benzene rings, the decanol cannot form perfect intramolecular hydrogen bonds. Therefore, the decanol forms intermolecular hydrogen bonds, which should cause the slipped-stacked structure of **12[5]**.

Our group found that per-ethylated pillar[5]arene **2[5]** formed two assembled structures depending on the solvents for crystallization (Figure 19a).¹⁴⁴

By crystallization of **2[5]** from acetone, their assembled structure was the herringbone structure. In contrast, one-dimensional channels were constructed by crystallization of **2[5]** from chloroform under hexane vapor. The type of solvent included in the cavity of pillar[5]arenes determined the assembled structure of **2[5]**. Danylyuk and Sashuk reported hydrogen-bonded polymeric chains of pillar[5]arene with 10 carboxylic acid groups **45[5]** (Figure 19b).¹⁴⁵ Slipped-stacked structures were observed by crystallization of the 10 carboxylic acids **45[5]** by a 1:1 water–ethanol mixture, but they assembled into one-dimensional channels by crystallization of **45[5]** with the guest tetracaine hydrochloride. The inclusion of the guest molecules also changed their assembled structure.

Pillar[*n*]arene crystal structures can be categorized into three assembled structures, herringbone, one-dimensional channels, and slipped-stacked structures, while various pillar[5]arene crystal structures have been reported. Herringbone assemblies were observed in per-methylated pillar[5]arenes with one benzoquinone unit **19[5]** crystallized from isopropyl ether,⁶⁹ one hydroquinone unit **25[5]** crystallized from dichloromethane,⁸⁷ per-ethylated pillar[5]arene **2[5]**–4-dichlorobutane complex crystallized from dichloromethane,¹⁴⁶ and per-methylated pillar[5]arene **1[5]**–1,6-dibromohexane complex.¹⁴⁶ Per-propylated pillar[5]arene **3[5]** crystallized from a mixture of dichloromethane and acetonitrile,¹³⁶ pillar[5]arene with 10 triflate moieties **52[5]** crystallized from 1,2-dichloroethane,¹⁴⁷ pillar[5]arene with one benzoquinone unit **20[5]** crystallized from methanol,⁶⁸ pillar[5]arene containing one triphenyl unit **60[5]** crystallized from DMF under methanol vapor,⁸⁷ nonsymmetric pillar[5]arene isomers consisting of nonsymmetric dialkoxybenzene monomer with methoxy and butoxy moieties

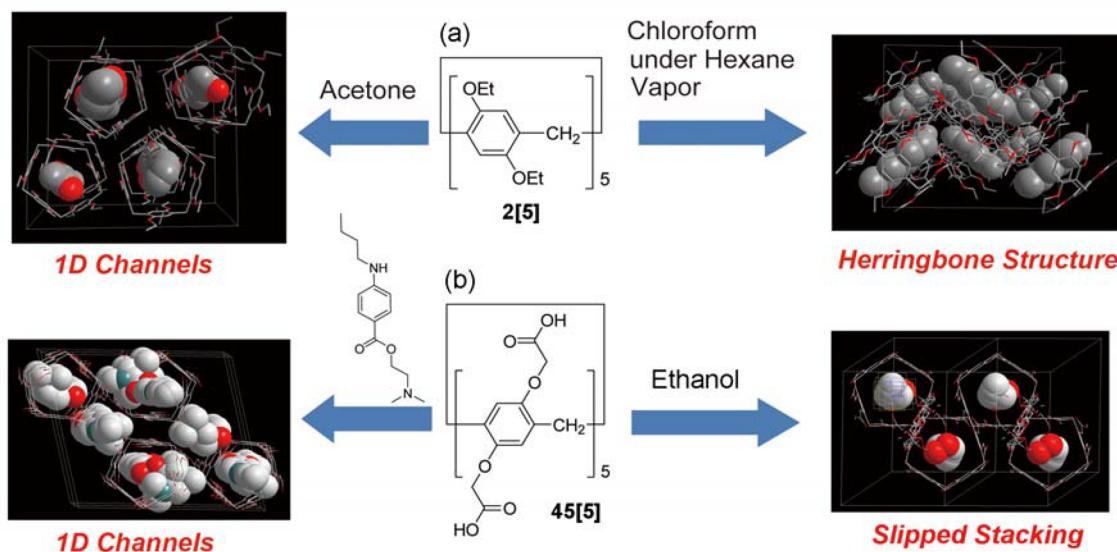


Figure 19. Crystal transformation of (a) **2[5]** depending on solvents and (b) **45[5]** depending on guest molecules for crystallization.

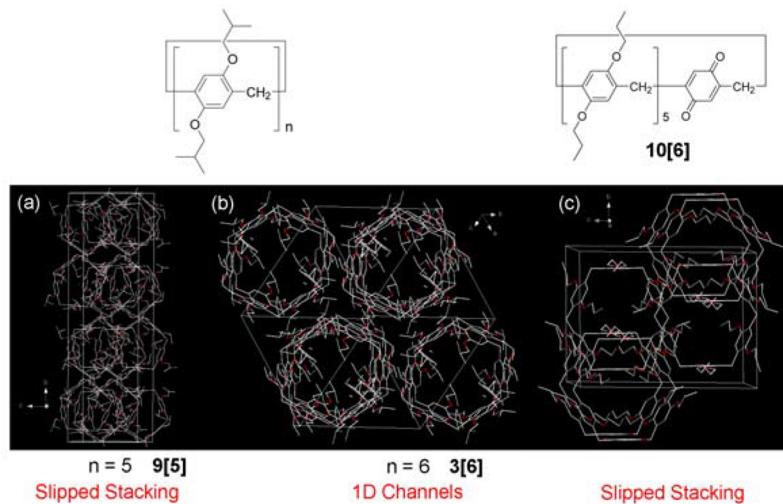


Figure 20. (a,b) Effect of the number of the repeating units on assembled structures of pillar[n]arenes 9[5] and 3[6]. (c) Slipped-stacked structure of pillar[6]arene with one benzoquinone unit 10[6].

110[5]¹³¹ and nonsymmetric amphiphilic pillar[5]arene 113a[5] crystallized from a mixture of dichloromethane and methanol¹³⁴ assembled into one-dimensional channels. Examples of slipped-stacked structures constructed from the assembly of pillar[5]arene molecules were per-pentylated pillar[5]arene 5[5] crystallized from acetone,⁵⁴ per-isobutylated pillar[5]arene 9[5] crystallized from a mixture of dichloromethane and acetonitrile,¹³⁵ pillar[5]arenes with two benzoquinones (22[5] and 24[5]) from a mixture of dichloromethane and acetonitrile,¹⁴⁸ and pillar[5]arene with 10 ethylene oxide 50[5] Δ paraquat complex from a mixture of isopropyl ether and acetonitrile.¹⁴⁹

Assembled structures of pillar[6]arenes are more regular than those of pillar[5]arenes because pillar[6]arenes are highly symmetric hexagonal molecules. Huang and co-workers obtained single crystals of pillar[5]- and pillar[6]arenes with 10 and 12 diisobutyl moieties (9[5] and 3[6], Figure 20a and b).¹³⁵

In the case of the pillar[5]arene 9[5], they assembled into slipped-stacked structures. Considering that pillar[5]arene with linear propyl groups 3[5] formed one-dimensional channels,¹³⁶ the branched substituents, such as diisobutyl moieties of the pillar[5]arene rims, should disturb the one-dimensional channel assemblies. In contrast, one-dimensional channels formed by the assembly of pillar[6]arene with 12 diisobutyl moieties 3[6]. The hexagonal structure of pillar[6]arene should enable ordering of their assembled structure even though the pillar[6]arene has bulky 12 diisobutyl groups. One-dimensional channel assemblies were also observed in per-propylated pillar[6]arene 2[6] crystallized from a mixture of dichloromethane and acetonitrile,¹³⁶ per-hydroxylated pillar[6]arene 8[6] and its complex with paraquat,⁷³ and pillar[6]arene with 12 ethylene oxide groups 14[6] Δ diquat complex crystallized from a mixture of isopropyl ether and acetonitrile.⁹⁶ As the exception, the assembled structure of pillar[6]arene with one benzoquinone unit 10[6] formed a slipped-stacked structure by crystallization from a mixture of petroleum ether and ethyl acetate (Figure 20c).¹⁵⁰ A possible reason for this observation is either reduction of the symmetry of pillar[6]arene by incorporation of one benzoquinone unit, or intermolecular formation of a charge-transfer complex between benzoquinone and 1,4-dialkoxybenzene units.

5. HOST PROPERTY OF PILLAR[n]ARENES

A variety of interactions can be used to form stable host–guest complexes. Coordination interactions between unpaired electrons and empty electron orbitals, electrostatic interactions between cationic and anionic groups, and charge-transfer (CT) interactions between electron donors and acceptors are all classified in terms of the strength of the physical interactions. In contrast, van der Waals, π/π , and hydrogen-bonding interactions, including OH/O, NH/O, CH/O, OH/N, NH/N, CH/N, CH/ π , NH/ π , and OH/ π interactions, are characterized as weak physical interactions when they occur in isolation. However, multiple versions of these weak physical interactions can effectively enhance host–guest complexation processes in some cases. All of the physical interactions listed above can play a role in the host–guest complexation of pillar[n]arenes because a variety of functional groups can be installed on the rim of pillar[n]arenes to provide suitable interaction sites for a variety of guests. In this section, we will discuss the host–guest complexation process between pillar[n]arenes and guests using various physical interactions.^{40,43}

5.1. Complexation by Charge-Transfer Interactions

Pillar[n]arenes are composed of electron-donating dialkoxybenzene units and can consequently form host–guest complexes with electron-accepting molecules. With this in mind, our group initially investigated these host–guest complexation processes as CT interactions.³³ To enhance the electron-donating ability of the host molecule, we used pillar[5]arene bearing a series of 5 hydroquinone units 12[5] (Figure 21 and Table 2).

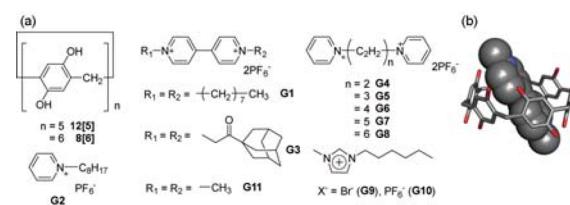


Figure 21. (a) Chemical structures of the per-hydroxylated pillar[5]- and pillar[6]arenes and the electron-accepting guest molecules. (b) X-ray crystal structure of 8[6]G11 CT complex.

Table 2. Host–Guest Complexes of Per-hydroxylated Pillar[5]arene 12[5] and Pillar[6]arene 8[6] with Their Electron-Accepting Guests in Terms of Their CT Interactions

run	host	guest	solvent	association constant (K) (M^{-1})	method	ref
1	12[5]	G1	methanol	$(1.2 \pm 0.2) \times 10^4$	FL	33
2	12[5]	G2	methanol	$(1.2 \pm 0.3) \times 10^3$	FL	33
3	12[5]	G3	acetone- d_6	— ^a	NMR	33
4	12[5]	G4	DMSO	— ^a	NMR	151
5	12[5]	G5	DMSO	$(8.8 \pm 0.7) \times 10$	NMR	151
6	12[5]	G6	DMSO	$(4.5 \pm 0.4) \times 10^2$	NMR	151
7	12[5]	G7	DMSO	$(3.7 \pm 0.3) \times 10^2$	NMR	151
8	12[5]	G8	DMSO	$(1.2 \pm 0.1) \times 10^2$	NMR	151
9	12[5]	G9	acetone- d_6	$K_1 = 1.1 \times 10^2, K_2 = 2.0 \times 10$	NMR	152
10	12[5]	G10	acetone- d_6	$K_1 = 7.0 \times 10^2, K_2 = 1.7$	NMR	152
11	8[6]	G11	acetone- d_6	$(2.2 \pm 0.3) \times 10^2$	NMR	73

^aThe K value was too small to be calculated.

Viologen **G1** and pyridinium salt **G2** were selected as suitable electron-acceptor guest molecules. The color of the solution changed from colorless to yellow during the mixing of **G1** and 12[5], indicating the formation of a CT complex. In contrast, the mixing of **G2** and 12[5] did not lead to any significant color changes. The lack of a color change in the latter of these two cases was attributed to the pyridinium salt **G2** being a weaker electron acceptor than the viologen salt **G1**. The association constant of the pyridinium salt **G2** with 12[5] (run 2), which was determined by fluorescence measurements, was 10 times smaller than that of the viologen salt **G1** with 12[5] (run 1). The host compound 12[5] did not form a host–guest complex with a viologen salt bearing bulky adamantyl moieties **G3** (run 3) because the adamantyl groups were too bulky to fit into the pillar[5]arene cavity. Li and co-workers investigated host–guest complexation abilities of various pyridinium and viologen salts with the per-hydroxylated pillar[5]arene 12[5] by UV–vis and ¹H NMR spectroscopy.¹⁵¹ In a manner similar to our own results, the UV–vis spectra of mixtures of the different viologen salts with 12[5] showed a CT band (about 450 nm), whereas mixtures that contained dipyridinium guests did not afford a CT band. The authors of this study also investigated the host–guest abilities of a series of linear alkyl chains bearing pyridinium moieties at both ends of the chain (runs 4–8, **G4**–**G8**) by ¹H NMR spectroscopy. Compound **G6** (run 6), which consisted of a C4 alkyl chain with pyridinium moieties at either end of the chain, formed the most stable host–guest complex with 12[5] of all of the compounds tested because the length of the C4 alkyl chain provided the best fit to the height of the pillar[5]arene cavity. Typical imidazolium ionic liquids are also good guests for 12[5] because of the electron-accepting nature of imidazolium cations.¹⁵² 1-Hexyl-3-methylimidazoliums with Br[−] **G9** and BF₄[−] **G10** anions both formed 1:2 host–guest complexes with 12[5] through a series of CT interactions (runs 9 and 10).

The per-hydroxylated pillar[6]arene 8[6] may also form host–guest complexes with electron-acceptor systems. Huang et al. reported that 8[6] formed host–guest complexes with viologen and pyridinium derivatives.⁷³ However, the binding ability of 8[6] toward these electron-accepting guests was weaker than that of the per-hydroxylated pillar[5]arene 12[5] because the cavity size of the former was too large to form stable host–guest complexes with these guest molecules. The association constant for the 8[6]–viologen salt **G11** complex (run 11) was determined to be $(2.2 \pm 0.3) \times 10^2 M^{-1}$ based on the results of ¹H NMR titration in acetone- d_6 . Notably, this result was almost 100 times lower than that of the 12[5]–viologen salt **G1**.

complex (run 1), which was determined by fluorescence measurements. An X-ray crystal structure of the 8[6]–**G11** complex is shown in Figure 21b. The viologen moiety of **G11** was found to be in the cavity of 8[6]. Furthermore, the complex was stabilized by hydrogen bonding and edge-to-face π-stacking interactions between the host and the guest.

Per-alkylated pillar[n]arenes may also form host–guest complexes through CT interactions because the constituent 1,4-dialkoxybenzene units also exhibit electron-donating properties (Figure 22 and Table 3).

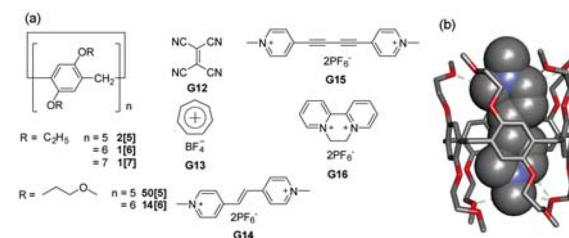


Figure 22. (a) Chemical structures of pillar[5]arenes (2[5] and 50[5]), pillar[6]arenes (1[6] and 14[6]), and pillar[7]arene 1[7], and their electron-accepting guest molecules. (b) X-ray crystal structure of the 50[5]–**G11** CT complex.

The addition of the electron-acceptor tetracyanoethylene (**G12**, TCNE) to per-ethylated pillar[5]arene 2[5] in chloroform changed the solution from colorless to dark green, indicating the occurrence of a CT complexation process between **G12** and 2[5].¹⁰² The association constant (K) of the 1:1 2[5]–**G12** complex was determined by UV–vis measurements to be $62 \pm 10 M^{-1}$ (run 12). Li et al. reported the formation of a CT complex between the tropylium cation **G13** and the per-ethylated pillar[6]arene 1[6].¹⁵³ A 1:1 mixture of **G13** and 1[6] afforded a CT band (run 14), whereas no CT band was observed for 1:1 mixtures of **G13** with per-ethylated pillar[5]arene 2[5] (run 13) or pillar[7]arene 1[7] (run 15). The lack of a CT band in the latter of these two cases was attributed to **G13** being too big and small to fit inside the cavities of pillar[5]- and pillar[7]arenes, respectively.

Per-functionalized pillar[5]- and pillar[6]arenes also form host–guest complexes through CT interactions. Huang and co-workers reported the formation of a host–guest complex using a pillar[5]arene bearing 10 ethylene oxide substituents 50[5].¹⁴⁹ Mixing viologen salt **G11** with 50[5] (run 16) resulted in a change in the color of the solution from colorless to yellow,

Table 3. Host–Guest Complexes of Pillar[5]-, Pillar[6]-, and Pillar[7]arenes Carrying Alkyl and Ethylene Oxide Chains with Electron-Accepting Guests through CT Interactions

run	host	guest	solvent	association constant (K) (M^{-1})	method	ref
12	2[5]	G12	CHCl ₃	62 ± 10	UV	102
13	2[5]	G13	1:1 acetone–CHCl ₃	— ^a	UV	153
14	1[6]	G13	1:1 acetone- <i>d</i> ₆ –CDCl ₃	(1.8 ± 0.3) × 10 ³	NMR	153
15	1[7]	G13	1:1 acetone–CHCl ₃	— ^a	UV	153
16	50[5]	G11	CH ₃ CN	(3.35 ± 0.22) × 10 ⁴	ITC	149
17	50[5]	G14	CH ₃ CN	(4.7 ± 0.3) × 10 ⁴	ITC	154
18	50[5]	G15	CH ₃ CN	(5.0 ± 0.8) × 10 ⁴	UV	155
19	14[6]	G16	CH ₃ CN	(2.5 ± 0.2) × 10 ⁵	UV	96

^aThe K value was too small to be calculated.

indicating the occurrence of a CT complexation process between G11 and 50[5]. The association constant (K) of the complex was determined by isothermal calorimetry (ITC) experiments to be $(3.35 \pm 0.22) \times 10^4 M^{-1}$, which was much larger than that of the complex formed between G11 and the per-hydroxylated pillar[6]arene 8[6] (run 11).⁷³ The X-ray crystal structure of this host–guest complex revealed that G11 was positioned inside the cavity of 50[5] (Figure 22b). The complex was stabilized by multiple interactions, including CH/O, CH/π interactions, and face-to-face π-stacking interactions between the host and guest. For the host–guest complex between G11 and the per-hydroxylated pillar[6]arene 8[6], the viologen salt G11 was stabilized by edge-to-face π-stacking interactions (Figure 21b). These results therefore indicated that the viologen salt G11 was a much better fit for the cavity of pillar[5]arene 50[5] than it was for the cavity of pillar[6]arene 8[6]. The vinylogous viologen salt G14 (run 17) and the bis-pyridinium guest G15 bearing a rigid π-conjugated structure (run 18) also formed stable CT host–guest complexes with 50[5] with associated constants (K) in the range of 10^3 – $10^4 M^{-1}$.^{154,155} Huang and co-workers also reported the formation of CT host–guest complex between diquat G16 and pillar[6]arene 14[6] bearing 12 ethylene oxide chains (run 19).⁹⁶ The mixing of G16 with pillar[6]arene 14[6] led to a dramatic change in the color of the solution, whereas the mixing of G16 and pillar[5]arene 50[5] did not induce a color change. These results therefore indicate that pillar[6]arene 14[6] formed a stable host–guest complex with G16, whereas pillar[5]arene 50[5] did not.

5.2. Complexation by Cation/π Interactions

Cation/π interactions are defined as physical interactions between an electron-rich π-electron system and a cation. Pillar[n]arenes are composed of 1,4-dialkoxybenzene units and can therefore form cation/π interactions with suitable cationic molecules to give the corresponding host–guest complexes. Huang and co-workers first investigated the formation of cation/π interactions between per-alkylated pillar[5]arene and ammonium cations as guest molecules (Figure 23 and Table 4).

The quaternary ammonium salt, octatrimethylammonium hexafluorophosphate G17, has been included in per-alkylated pillar[5]arenes.⁸¹ The results revealed that the nature of the substituents on the rim of the pillar[5]arene had a pronounced impact on the host–guest ability. Pillar[5]arene 4[5] bearing 10 butyl substituents formed a stable host–guest complex with G17 [run 20, $K = (4.1 \pm 0.4) \times 10^3 M^{-1}$], which was larger than those of the complexes formed between pillar[5]arenes 8[5] and 11[5] bearing 10 (S)-methylbutyl⁵⁵ (run 21) and 10 cyclohexylmethyl groups (run 22),⁹¹ respectively. The introduction of steric hindrance around the rim of the pillar[5]arene would lead to a

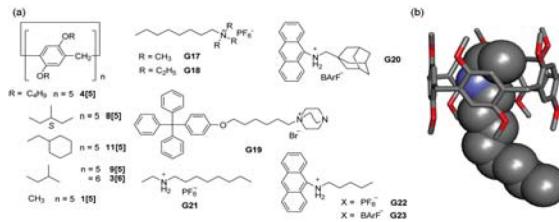


Figure 23. (a) Chemical structures of the per-alkylated pillar[5]- and pillar[6]arenes and their cationic guest molecules. **(b)** X-ray crystal structure of the 1[5]–G21 complex.

decrease in the stability of the host–guest complex by attenuating the cationic/π interactions. The per-isobutylated pillar[6]arene 3[6] formed a host–guest complex with *n*-octatriethylammonium hexafluorophosphate G18 (run 24), whereas the per-isobutylated pillar[5]arene 9[5] did not (run 23).¹³⁵ The triethylammonium moiety, which is much bulkier than the trimethylammonium moiety, was a much better fit for the cavity of the pillar[6]arene host. However, this group was too big to fit into the cavity of the pillar[5]arene host. Cations containing bulky hydrocarbon groups such as adamantyl G20 (run 26) and DABCO cations G19 (run 25) are good guest molecules for per-alkylated pillar[6]arenes.^{78,156} Pillar[5]- and pillar[6]arenes also form host–guest complexes with secondary ammonium cations. Huang and co-workers reported the complexation of per-methylated pillar[5]arene 1[5] with *n*-octylethylammonium G21 bearing a hexafluorophosphate anion (run 27).¹⁵⁷ Figure 23b shows the X-ray crystal structure of the resulting complex, which revealed that the secondary ammonium moiety of the guest was located in a cavity composed of five 1,4-dimethoxybenzene units. Three NH/π interactions were observed between the host and guest. The nature of the counteranion had a pronounced impact on the complexation ability of the ammonium cation. For example, changing the anion from PF₆[−] to Cl[−] resulted in very little complexation. The Cl[−] anion is smaller than the PF₆[−] anion and can therefore form a stronger ion pair with the *n*-octylethylammonium cation in chloroform, which would lead to a decrease in the ability of this cation to form cation/π interactions. In contrast, the PF₆[−] anion forms a much looser ion pair with the *n*-octylethylammonium cation in chloroform, which makes it much easier for the cation to form cation/π interactions. Secondary ammonium cations bearing weakly coordinating counter-anions can therefore form highly stable host–guest complexes with per-ethylated pillar[5]- and pillar[6]arenes because weakly coordinating anions effectively afford free “naked” secondary ammonium cations. Li et al. reported that pillar[5]arene formed a very stable host–guest complex with the secondary ammonium cation G23

Table 4. Host–Guest Complexes of the Per-alkylated Pillar[5]- and Pillar[6]arenes with Cationic Guests through Cation/π Interactions

run	host	guest	solvent	association constant (K) (M^{-1})	method	ref
20	4[5]	G17	CDCl ₃	(4.1 ± 0.4) × 10 ³	NMR	81
21	8[5]	G17	CDCl ₃	1.3 × 10 ³	NMR	55
22	11[5]	G17	CDCl ₃	8.3 × 10 ²	NMR	91
23	9[5]	G18	CDCl ₃	— ^a	NMR	135
24	3[6]	G18	CDCl ₃	(3.34 ± 0.24) × 10 ²	NMR	135
25	1[6]	G19	CDCl ₃	(5.52 ± 0.65) × 10 ²	NMR	78
26	1[6]	G20	CDCl ₃	(3.4 ± 0.2) × 10 ³	NMR	156
27	1[5]	G21	CDCl ₃	(1.09 ± 0.41) × 10 ³	NMR	157
28	2[5]	G22	CDCl ₃	(6.1 ± 0.8) × 10	NMR	156
29	2[5]	G23	CDCl ₃	(3.4 ± 0.4) × 10 ⁴	NMR	156

^aThe K value was too small to be calculated.

containing a linear butyl chain with a tetrakis[3,5-bis(trifluoromethyl)phenyl] borate (BArF⁻) anion (run 29, $K > 10^4 M^{-1}$).¹⁵⁶ Notably, this result was almost 5000 times larger than that of the complex formed with the corresponding PF₆⁻ salt **G22** (run 28). The association constant (K) for the complexation of pillar[6]arene **1[6]** with the secondary ammonium cation **G20** containing a bulky adamantyl moiety with a BArF⁻ anion was also high (run 26, $K = 3.4 \times 10^3 M^{-1}$), whereas very little complex was formed with the corresponding PF₆⁻ salt.

5.3. Complexation by Hydrophobic/Hydrophilic Interactions

Hydrophobic/hydrophilic interactions mean the aggregation of nonpolar molecules in polar solvents such as water. The cavity of pillar[n]arenes is hydrophobic because it is composed of hydrophobic benzene moieties. The introduction of hydrophilic substituents such as cationic, anionic, or nonionic moieties to the rims of the pillar[n]arenes makes them much more soluble in water. Hydrophobic guests in aqueous media therefore are encapsulated in the hydrophobic cavity of pillar[n]arenes to escape the hydrophilic environment. The first water-soluble pillar[5]arene to be reported in the literature was synthesized by our group as pillar[5]arene **46[5]** bearing 10 carboxylate moieties (Figure 24 and Table 5).⁸⁸

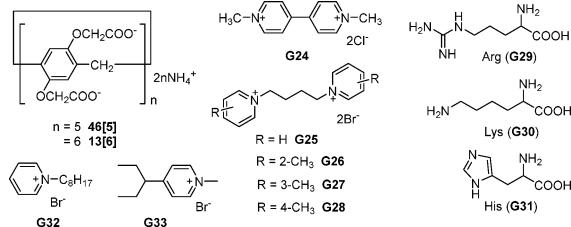


Figure 24. Chemical structures of anionic water-soluble pillar[5]- and pillar[6]arenes and their guest molecules.

Pillar[n]arenes **46[5]** captured paraquat **G24** with a high association constant [run 30, $K = (8.2 \pm 1.7) \times 10^4 M^{-1}$], which was determined by fluorescence measurements. It is noteworthy that this association constant was almost 70 times higher than that of the complex formed between paraquat and per-hydroxylated pillar[5]arene **12[5]** in methanol (Table 2, run 1).³³ Cooperative physical bond interactions, including hydrophobic/hydrophilic, $\pi-\pi$, and multiple electrostatic interactions between the anionic carboxylate moieties on the pillar[5]arene rims and the cationic paraquat guest, contributed to the high

Table 5. Host–Guest Complexes of Water-Soluble Pillar[5]- and Pillar[6]arenes with Hydrophobic Guests Formed through Hydrophobic/Hydrophilic Interactions

run	host	guest	solvent	association constant (K) (M^{-1})	method	ref
30	46[5]	G24	H ₂ O	(8.2 ± 1.7) × 10 ⁴	FL	88
31	46[5]	G25	H ₂ O	(1.1 ± 0.2) × 10 ⁶	FL	158
32	46[5]	G26	H ₂ O	(1.9 ± 0.4) × 10 ⁴	FL	158
33	46[5]	G27	H ₂ O	(3.5 ± 0.1) × 10 ⁵	FL	158
34	46[5]	G28	H ₂ O	(3.6 ± 0.5) × 10 ⁵	FL	158
35	46[5]	G29	D ₂ O	(5.9 ± 0.4) × 10 ³	NMR	159
36	46[5]	G30	D ₂ O	(1.5 ± 0.2) × 10 ³	NMR	159
37	46[5]	G31	D ₂ O	(1.8 ± 0.2) × 10 ³	NMR	159
38	13[6]	G24	H ₂ O	(1.02 ± 0.10) × 10 ⁸	FL	161
39	13[6]	G32	H ₂ O	(3.26 ± 0.28) × 10 ⁵	FL	160
40	13[6]	G33	D ₂ O	(1.67 ± 0.13) × 10 ⁵	NMR	162
41	65[5]	G34	D ₂ O	(1.33 ± 0.94) × 10 ⁴	NMR	104
42	65[5]	G35	D ₂ O	(1.03 ± 0.37) × 10 ²	NMR	165
43	65[5]	G36	D ₂ O	(4.61 ± 0.43) × 10	NMR	165
44	65[5]	G37	D ₂ O	(2.07 ± 0.59) × 10	NMR	165
45	65[5]	G38	D ₂ O	(1.90 ± 0.33) × 10	NMR	165
46	65[5]	G39	D ₂ O	(9.68 ± 0.60) × 10	NMR	165
47	65[5]	G40	D ₂ O	(4.26 ± 0.52) × 10 ²	NMR	165
48	18[6]	G41	H ₂ O	(3.8 ± 0.2) × 10 ⁴	FL	101
49	18[6]	G42	H ₂ O	(2.1 ± 0.3) × 10 ⁵	FL	101

binding affinity of this host–guest complex. Li and co-workers investigated the nature of these host–guest interactions using the water-soluble pillar[5]arene **46[5]**.¹⁵⁸ The results revealed that the 1,4-bis(pyridinium)butane derivatives **G25–G28** were good guests for the water-soluble pillar[5]arene **46[5]** (runs 31–34, $K > 10^4 M^{-1}$) because the length of the hydrophobic C4 linker was a good fit to the pillar[5]arene cavity, and the pyridinium cation of the guest formed multiple electrostatic interactions with the carboxylate anions on both rims of the host. Water-soluble pillar[5]arene **46[5]** selectively encapsulated arginine (**G29**), lysine (**G30**), and histidine (**G31**) from a mixture of 20 basic amino acids (runs 35–37).¹⁵⁹ It is noteworthy that all three of these amino acids had two or more basic N-containing groups, whereas all of the other amino acids contain only one such group. This result therefore demonstrates that the formation of multiple electrostatic interactions between the carboxylate anions of the host and the basic cations of these amino acids made a considerable contribution to their selective and strong binding as compared to the other amino acids.

Huang and co-workers synthesized the water-soluble pillar[6]arene **13[6]** by the introduction of 12 carboxylate anions and

subsequently investigated its host–guest ability.¹⁶⁰ The results revealed that **13[6]** formed highly stable host–guest complexes with paraquat [run 38, **G24**, $K = (1.02 \pm 0.10) \times 10^8 \text{ M}^{-1}$]¹⁶¹ and the pyridinium salts **G32** and **G33** (runs 39 and 40, $K > 10^5 \text{ M}^{-1}$).^{160,162–164} Pillar[6]arene **13[6]** showed a higher guest binding ability in aqueous media as compared to water-soluble pillar[5]arene **46[5]**.⁸⁸

Huang and co-workers also reported the preparation of water-soluble cationic pillar[5]arene **65[5]** bearing 10 trimethylammonium bromide moieties (Figure 25).¹⁰⁴

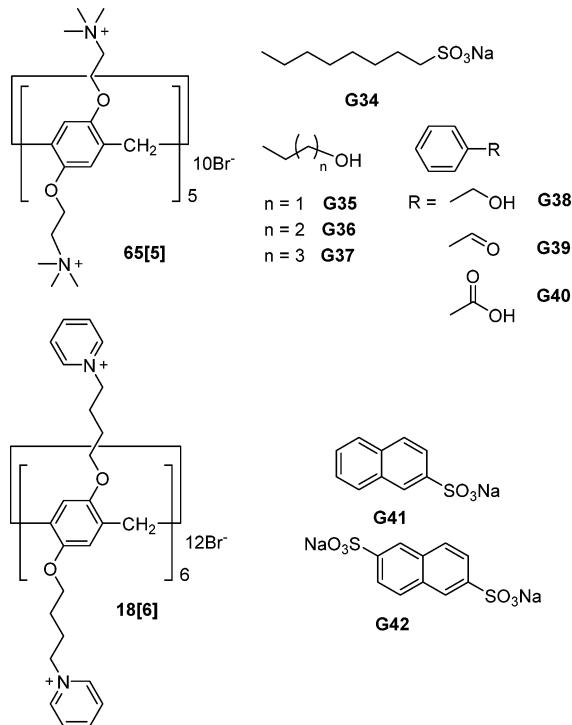


Figure 25. Chemical structures of cationic water-soluble pillar[5]- and pillar[6]-arenes and their guest molecules.

Pillar[5]arene **65[5]** possesses cationic substituents and can therefore form strong host–guest complexes with anionic molecules bearing hydrophilic moieties. The anionic guest molecule sodium 1-octanesulfonate (**G34**) was strongly encapsulated in the hydrophobic cavity of **65[5]** [run 41, $K = (1.33 \pm 0.94) \times 10^4 \text{ M}^{-1}$] because the resulting complex was stabilized by hydrophobic and electrostatic interactions. Pillar[5]arene **65[5]** also encapsulated several neutral molecules (runs 42–44, **G35–G37**) and monosubstituted benzene systems (runs 45–47, **G38–G40**), but their association constants were determined to be in the range of 20–500 M^{-1} , and therefore lower than that of the complex formed between **G34** and **65[5]** (run 41).¹⁶⁵ The main driving force for the formation of the host–guest complexes between the neutral and monosubstituted benzene guests and **65[5]** was hydrophobic/hydrophilic interactions with no electrostatic interactions. These results therefore indicate that the formation of electrostatic interactions is important to stabilize the complexation. Li and co-workers synthesized pillar[6]arene **18[6]** bearing 12 pyridinium cations.¹⁰¹ In this case, anionic naphthalene derivatives bearing sulfonate groups (runs 48 and 49, **G41** and **G42**) were determined to be good guests. Hou and co-workers reported

the water-soluble neutral pillar[5]arene **49[5]** bearing 10 amino moieties (Figure 26).⁸⁹

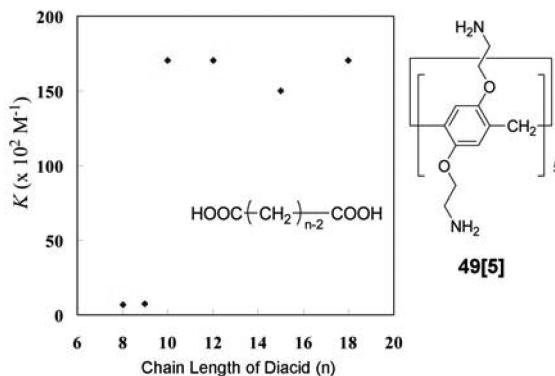


Figure 26. Plot of association constants (K) versus the chain length of the diacid guests (n), indicating that the formation of hydrophobic interactions made a considerable contribution to the binding of **49[5]** to the diacids.

Pillar[5]arene **49[5]** also formed stable host–guest complexes with long-chain linear diacids ($n \geq 10$), but not with shorter diacids ($n = 8$ and 9). This trend indicated that the hydrophobic interaction of the chain with the host was playing an important role in the complexation process in addition to the electrostatic interaction between the carboxylic acid moieties of the guest and the amino moieties on the pillar[5]arene rims.

5.4. Complexation by Cationic/Anionic Interactions

Pillar[n]arenes bearing ionic moieties on all of their substituents are water-soluble, and their complexation with a variety of different guest molecules has consequently been investigated in aqueous media. When oppositely charged ionic molecules were evaluated as guest molecules for host systems of this type, cationic/anionic electrostatic interactions made a significant contribution to the stabilization of the resulting complexes. However, the complexation abilities of these systems through electrostatic interactions were more pronounced in nonpolar solvents than they were in polar solvents because the dissociation of the ionic interaction was suppressed considerably in nonpolar solvents. Yu et al. reported the formation of complexes between alkylamines and pillar[5]arene **57[5]** bearing dicarboxylic acid moieties at its A1/A2 positions (Figure 27 and Table 6).⁹⁸

These complexes were quite stable (runs 50–55, $K = 10^5 \text{ M}^{-1}$) in a 1:1 (v/v) mixture of chloroform and methanol. Figure 27b shows the X-ray crystal structure of the **57[5]**–pentylamine **G43** complex. This result showed that the ammonium groups at both ends of the guest pointed toward the carboxylate anion to form electrostatic interactions. Furthermore, the pentyl chain of

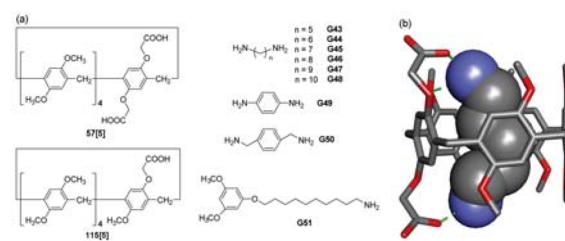


Figure 27. (a) Chemical structures of pillar[5]arenes with carboxylic acid moieties and their amine guests. (b) X-ray crystal structure of the **57[5]**–**G43** complex.

Table 6. Formation of Host–Guest Complexes between Pillar[5]arenes Bearing Carboxylic Acid Moieties and Their Amine Guests through Electrostatic Interactions

run	host	guest	solvent	association constant (K) (M^{-1})	method	ref
50	57[5]	G43	CHCl ₃ :CH ₃ OH = 1:1	(2.84 ± 0.232) × 10 ⁵	ITC	98
51	57[5]	G44	CHCl ₃ :CH ₃ OH = 1:1	(2.39 ± 0.237) × 10 ⁵	ITC	98
52	57[5]	G45	CHCl ₃ :CH ₃ OH = 1:1	(3.13 ± 0.210) × 10 ⁵	ITC	98
53	57[5]	G46	CHCl ₃ :CH ₃ OH = 1:1	(2.89 ± 0.212) × 10 ⁵	ITC	98
54	57[5]	G47	CHCl ₃ :CH ₃ OH = 1:1	(3.45 ± 0.228) × 10 ⁵	ITC	98
55	57[5]	G48	CHCl ₃ :CH ₃ OH = 1:1	(3.06 ± 0.232) × 10 ⁵	ITC	98
56	57[5]	G49	CHCl ₃ :CH ₃ OH = 1:1	(9.93 ± 1.92) × 10 ³	ITC	166
57	57[5]	G50	CHCl ₃ :CH ₃ OH = 1:1	(5.89 ± 1.43) × 10 ⁵	ITC	166
58	115[5]	G51	CDCl ₃	(1.52 ± 0.075) × 10 ⁴	NMR	167

the guest was located inside the cavity, where it formed multiple CH/π interactions to stabilize the complexation process. Diacid 57[5] also formed stable host–guest complexes with benzene moieties bearing *para*-substituted amino groups such as *p*-xylylenediamine (run 56, G49) and *p*-phenylenediamine (run 57, G50).¹⁶⁶ Xue et al. reported the formation of a stable host–guest complex between pillar[5]arene 115[5] bearing one carboxylic acid group and linear alkane G51 bearing a single amino group at one end of its chain.¹⁶⁷ The association constant of this complex was determined to be $(1.52 \pm 0.075) \times 10^4 M^{-1}$ (run 58), which was higher than that of the complexes formed between per-alkylated pillar[5]arenes and linear alkylamines. The electrostatic interactions formed between the carboxylate anion and ammonium cation of the host and guest molecules, respectively, in organic solvents made a considerable contribution to the stabilization of this complex.

5.5. Complexation by Hydrogen-Bond Interactions

In 2011, IUPAC defined hydrogen-bond interactions as follows: the hydrogen bond is an attractive interaction between a hydrogen atom from a molecule or a molecular fragment X–H in which X is more electronegative than H, and an atom or a group of atoms in the same or a different molecule, in which there is evidence of bond formation.¹⁶⁸ In the broadest possible sense, CH/π interactions may be defined as the weakest possible hydrogen bond. Huang and co-workers reported the existence of CH/π hydrogen-bonding interactions between *n*-hexane and per-butylated pillar[5]arene 4[5] by X-ray crystallography (Figure 28a).⁸¹ The important pillar[5]arene/alkyl chain recognition motif first established by them has been widely used in pillar[*n*]arene supramolecular chemistry.

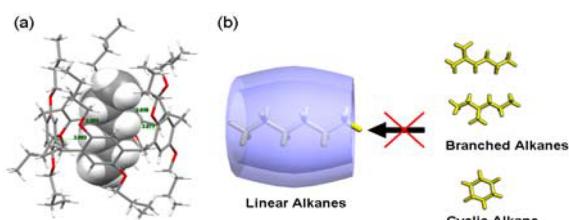


Figure 28. (a) X-ray crystal structure of the 4[5]D_n-hexane complex. (b) Alkane shape-selective host–guest complexation process.

The inclusion of an *n*-hexane molecule in the cavity of 4[5] has also been observed. Four of the hydrogen atoms of the *n*-hexane molecule were less than 3.05 Å away from the π-plane of the pillar[5]arene, therefore indicating the existence CH/π interactions. We found that pillar[5]arenes showed good alkane-shape selectivity (Figure 28b).¹¹⁹ Pillar[5]arenes formed host–

guest complexes with linear hydrocarbons, but did not form complexes with branched- or cyclic-shaped hydrocarbons. Li et al. investigated the complexation of linear hydrocarbons with pillar[5]arenes.¹⁶⁹ The complexation ability of pillar[5]arene with linear alkane such as *n*-octane (G54) was very weak (run 61, $K < 2 M^{-1}$), and much lower than those of 1,7-octadiyne (run 59, G52) and 1,7-octadiene (run 60, G53) (Figure 29 and Table 7).

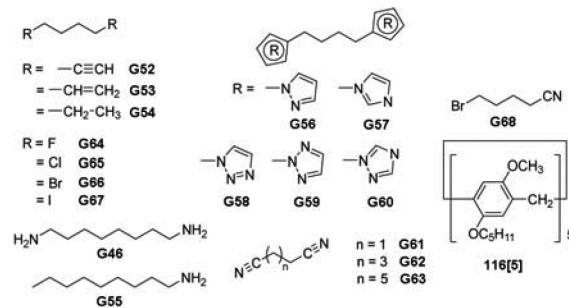


Figure 29. Chemical structures of nonsymmetric pillar[5]arene 116[5] and the neutral guests G51–G68.

Stoddart and co-workers investigated the neutral guest recognition ability of pillar[5]arene using 1,8-diaminoctane (G46) and *n*-octylamine (G55) as guests.⁸² The association constant between G46 and the per-methylated pillar[5]arene 1[5] was determined to be $70 \pm 10 M^{-1}$ (run 62) by ¹H NMR spectroscopy, which was 3 times higher than the association constant between *n*-octylamine (G55) and per-methylated pillar[5]arene 1[5] (run 63, $K = 20 \pm 2 M^{-1}$). These results therefore indicated that the terminal groups of the linear alkanes were contributing to the stabilization of the complexation process. Li and co-workers reported that simple per-alkylated pillar[5]arenes can form stable host–guest complexes with the neutral 1-substituted 1,3-imidazole guest G57.¹⁷⁰ A butyl linker bearing two imidazole groups formed the most stable host–guest complex with pillar[5]arene [run 65, $K = (2.0 \pm 0.4) \times 10^4 M^{-1}$] of all of the alkane linkers tested bearing 1,3-imidazoles groups at either end of the chain. The complexation of 1,4-butylene guests substituted with nitrogen heterocycles with pillar[5]arenes was also investigated by Li and co-workers.¹⁷¹ Nitrogen heterocycles containing outer N atoms such as 1-substituted 1,2,3-triazole G58 and 1,2,4-triazole G60 were good guests for pillar[5]arenes (runs 66 and 68), whereas heterocycles without an outer N atom such as 1,2-imidazole G56 and 1,2,5-triazole G59 were not (runs 64 and 67). Figure 30a shows the X-ray crystal structure of the per-ethylated pillar[5]arene 2[5]D G57 complex.

In addition to CH/π and CH/O hydrogen-bonding interactions, several CH/N hydrogen bonds were observed

Table 7. Formation of Host–Guest Complexes between Pillar[5]arenes and the Neutral Guests through Hydrogen-Bond Interactions

run	host	guest	solvent	association constant (K) (M^{-1})	method	ref
59	2[5]	G52	CDCl ₃	(8.2 ± 0.5) × 10	NMR	169
60	2[5]	G53	CDCl ₃	(1.2 ± 0.2) × 10	NMR	169
61	2[5]	G54	CDCl ₃	<2	NMR	169
62	1[5]	G46	CDCl ₃	(7.0 ± 1.0) × 10	NMR	82
63	1[5]	G55	CDCl ₃	(2.0 ± 0.2) × 10	NMR	82
64	2[5]	G56	CDCl ₃	(6.6 ± 0.2) × 10	NMR	171
65	2[5]	G57	CDCl ₃	(2.0 ± 0.4) × 10 ⁴	NMR	170
66	2[5]	G58	CDCl ₃	(1.6 ± 0.3) × 10 ⁴	NMR	171
67	2[5]	G59	CDCl ₃	(1.1 ± 0.1) × 10	NMR	171
68	2[5]	G60	CDCl ₃	(6.6 ± 0.4) × 10 ³	NMR	171
69	2[5]	G61	DMSO-d ₆ –CDCl ₃ (1:9)	— ^a	NMR	172
70	2[5]	G62	DMSO-d ₆ –CDCl ₃ (1:9)	(1.5 ± 0.3) × 10 ⁴	NMR	172
71	2[5]	G63	DMSO-d ₆ –CDCl ₃ (1:9)	(6.5 ± 0.5) × 10 ⁴	NMR	172
72	2[5]	G64	CDCl ₃	(8.6 ± 0.5) × 10	NMR	146
73	2[5]	G65	CDCl ₃	(1.9 ± 0.2) × 10 ³	NMR	146
74	2[5]	G66	CDCl ₃	(4.9 ± 0.3) × 10 ³	NMR	146
75	2[5]	G67	CDCl ₃	(1.0 ± 0.1) × 10 ⁴	NMR	146
76	1[5]	G68	CDCl ₃	(1.7 ± 0.2) × 10 ⁴	NMR	173
77	5[5]	G68	CDCl ₃	(1.6 ± 0.3) × 10 ⁴	NMR	173
78	116[5]	G68	CDCl ₃	(8.4 ± 0.6) × 10 ⁴	NMR	173

^aThe K value was too strong to be calculated.

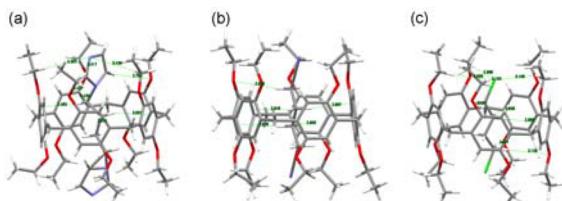


Figure 30. X-ray crystal structures of the (a) 2[5]⊃G57, (b) 2[5]⊃G62, and (c) 2[5]⊃G65 complexes.

between the ethyl substituents on the rims of the pillar[5]arene and the outer N-3 atom of the guest. The CH/N hydrogen bonds, in particular, played an important role in the stabilization of the complex. Li and co-workers also reported the formation of highly effective binding interactions between neutral dinitriles and simple per-alkylated pillar[5]arenes.¹⁷² The association ability in these cases was found to be largely dependent on the length of the alkyl chain between the two nitrile groups. Dinitrile G62 with a C4 linker was the best fit of all of the dinitriles tested for the cavity of per-ethylated pillar[5]arene [run 70, $K = (1.5 \pm 0.3) \times 10^4 M^{-1}$] in terms of its length. Figure 30b shows the crystal structure of the per-ethylated pillar[5]arene-1,4-dicyanobutane G62 complex. This structure revealed that 1,4-dicyanobutane was located inside of the pillar[5]arene cavity, and the guest formed multiple CH/π interactions with the host, as well as several CH/O and CH/N interactions. These multiple weak hydrogen-bonding interactions made a considerable contribution to the stabilization of the complex. Butylene linkers bearing two electron-withdrawing groups are good guests for pillar[5]arenes. With this in mind, Li et al. investigated the complexation of per-alkylated pillar[5]arenes with 1,4-dihalobu-

tanes.¹⁴⁶ The results revealed that the association constants increased in the order of F < Cl < Br < I (runs 72–75), indicating that the main driving force for the complexation of these guests was the dispersion force, which is dependent on the movement of electrons to produce temporary dipoles. Figure 30c shows the crystal structure of the per-ethylated pillar[5]arene 2[5]⊃1,4-dichlorobutane G65 complex. The structure revealed the presence of several CH/π and CH/O hydrogen bonds, as well as a series of CH/Cl hydrogen bonds, which resulted in the stabilization of the complex.

Li et al. reported the regioselective host–guest complexation of the nonsymmetric pillar[5]arene 116[5] bearing methyl and pentyl substituents on its rims with the nonsymmetric butylene guest G68 bearing cyano and bromide groups at either end of its chain (Figure 31).¹⁷³

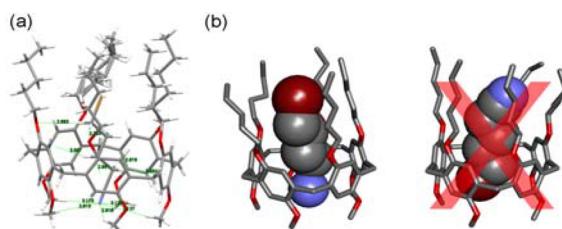


Figure 31. (a) X-ray crystal structure of 116[5]⊃G68 complex. (b) Regioselective formation of a host–guest complex between the nonsymmetric pillar[5]arene 116[5] and the nonsymmetric neutral guest G68.

The association constant of the complex formed between the nonsymmetric guest G68 and the nonsymmetric pillar[5]arene 116[5] was $(8.4 \pm 0.6) \times 10^4 M^{-1}$ (run 78), which is around 5 times higher than those obtained for the symmetric pillar[5]-arenes 1[5] and 5[5] bearing methyl and *n*-pentyl substituents on their rims (runs 76 and 77), respectively. Taken together, these results indicated that the binding to the pillar[5]arenes occurring in a regioselective manner. Figure 31a shows the X-ray crystal structure of the complex formed between the nonsymmetric guest G68 and the nonsymmetric pillar[5]arene 116[5]. The structure showed that the CN side of the guest was positioned in close proximity to the methyl rim of the pillar[5]arene, while the pentyl rim exhibited a preference for the Br side. Five CH/O, seven CH/π, and several CH/N hydrogen-bonding interactions accounted for the observed regioselectivity (Figure 31b).

5.6. Pillar[n]arene-Based Stimuli-Responsive Host–Guest Complexation/Decomplexation Systems

Stimuli-responsive host–guest complexation systems are very useful because they can be used as switches to control supramolecular assemblies. The stimuli-induced switching of the electronic distribution properties of guests is a useful strategy for inducing complexation/decomplexation processes, because electrostatic effects are very important factors for determining the strength of host–guest interactions. Li et al. reported the development of a stimuli-responsive host–guest system using acid–base stimulus.¹⁷⁴

Alternating the addition of acid and base allowed for the switching of the complexation/decomplexation of the host–guest complex formed between pillar[5]arene 12[5] and 1,4-bis(imidazolium)butane G69. Pillar[5]arene formed a host–guest complex with the protonated state of the 1,4-bis(imidazolium) dication, because of the formation of an active



Figure 32. (a) Acid–base and (b) photocontrolled threading/dethreading processes.

cation/π interaction between the 1,4-bis(imidazolium)dication and pillar[5]arene. The addition of a suitable base led to the deprotonation of the guest, which subsequently triggered the dethreading of the guest from the pillar[5]arene cavity. Li et al. also reported the development of a pH-responsive molecular switch based on the same concept using pillar[6]arene as a host and a bis(1,2,3-triazolium)butane cation as the guest.¹⁷⁵ Silver(I) ions can form a complex with imidazolinium cations, and the addition of Ag⁺ to host–guest complexes based on imidazolinium cations can also lead to the dissociation of these complexes.¹⁷⁶

We reported that the time scale for the photoresponsive transformations involved in the complexation/decomplexation of host–guest complexes extended from seconds to hours (Figure 32b).¹⁷⁷ We synthesized the axle-type system G70 bearing a bulky adamantyl stopper at one end of the axle and a photoresponsive azobenzene group at the other. The exchange rate between the complexation/decomplexation of the complex formed between *trans*-G70 and 12[5] was quite fast with a half-life of 3.33 ± 0.21 s. In contrast, the exchange rate of the complex formed between *cis*-G70 and 12[5] was much slower with a half-life of 9.13 ± 1.2 h, which allowed the process to be readily monitored. The photoinduced isomerization of G70 from its *trans* form to its *cis* form led to an increase in the free energy of activation, which in turn led to the observed photoresponsive time-scale transformation.

The photoresponsive host–guest complexation of an azobenzene guest with a pillar[6]arene host was investigated by Huang and co-workers (Figure 33a).¹³⁶

The simple per-propylated pillar[6]arene 2[6] strongly encapsulated the *trans*-form of the azobenzene guest G71 [$K = (2.22 \pm 0.34) \times 10^3 \text{ M}^{-1}$]. In contrast, the binding affinity of 2[6] to the corresponding *cis*-form of the azobenzene guest was much

less pronounced [$K = (2.64 \pm 0.29) \times 10^2 \text{ M}^{-1}$]. This difference in the association constants of these complexes could be used as a photoinduced switching mechanism for supramolecular assemblies constructed from these host–guest complexes. Photoresponsive complexation systems in organic media using azobenzene guests and pillar[6]arene hosts have been expanded to aqueous media.⁹⁷

Lin and co-workers constructed a photoresponsive host–guest system using photoresponsive carbamate derivatives (Figure 33b).¹⁷⁸ The association constant for the complex formed between the axle-type compound G72 bearing a photoresponsive *ortho*-nitrobenzene group at one end and an unsubstituted benzyl group at the other and the per-ethylated pillar[5]arene 2[5] was determined to be $(8.56 \pm 0.05) \times 10^2 \text{ M}^{-1}$. The photoirradiation of this system led to the precipitation of a photocleavage product, which appeared as a consequence of the poor solubility of the photocleavage product in the medium.

Wang and co-workers reported the development of a redox-responsive host–guest complexation system (Figure 33c).¹⁷⁹ In this case, the simple per-butylated pillar[6]arene 4[6] formed a strong host–guest complex with the oxidized form of the ferrocenium cation G73, while the reduced form of the ferrocene formed much weaker host–guest complexes with pillar[6]arene 4[6]. The redox reaction of ferrocene is completely reversible; thus the redox-responsive complexation can be used as a switching mechanism for the complexation/decomplexation of these systems.

5.7 Application of Pillar[n]arene-Based Host–Guest Systems

Pillar[5]arenes form host–guest complexes with linear hydrocarbons but not with branched or cyclic hydrocarbons. On the basis of the alkane-shape selectivity of these systems, we reported the shape-selective oxidation of alkenes using pillar[5]arene as a catalyst (Figure 34a).

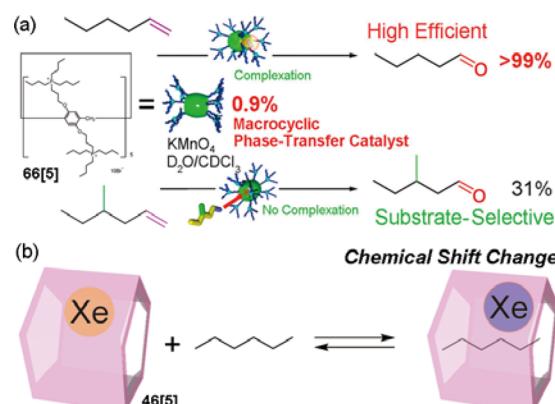


Figure 34. (a) The highly efficient and substrate-selective phase transfer catalyst 66[5]. Reproduced with permission from ref 105. Copyright 2013 American Chemical Society. (b) Detection of the inclusion of *n*-hexane based on the change in the chemical shift of the ¹²⁹Xe signal in the cavity of pillar[5]arene 46[5].

The amphiphilic pillar[5]arene 66[5] bearing 10 tetra-alkyl phosphonium cations was found to be soluble in aqueous and organic media depending on the nature of the counteranions. Counter anion exchange from Br⁻ to MnO₄⁻ led to the phase-transfer of the pillar[5]arene from the aqueous to the chloroform phase. In the organic phase, the MnO₄⁻ anions can react with the alkene molecules. At this stage, 1-hexene was fixed in close

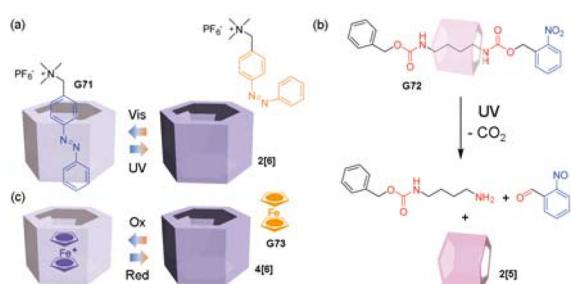


Figure 33. (a,b) Photo- and (c) redox-responsive host–guest complexation processes.

enough proximity to the MnO_4^- anions to allow for its efficient oxidation because of the host–guest complexation between pillar[5]arene and 1-hexene. The oxidation reaction of 1-hexene proceeded completely (conversion >99%). In contrast, the oxidation of the branched alkene 4-methyl-1-hexene was low conversion (conversion 31%) because of the inability of the branched structure to form complexes with pillar[5]arene.

Cohen and co-workers investigated application of water-soluble pillar[5]arene **46[5]** for ^{129}X NMR biosensors (Figure 34b).¹⁸⁰ Xenon is hydrophobic, and thus has low solubility in water. However, encapsulation of xenon into the cavity of water-soluble pillar[5]arene contributed to solubilization of xenon in aqueous media. The NMR chemical shift of xenon is highly sensitive to the microenvironment. A downfield shift of peak from xenon was observed by addition of hydrophobic *n*-hexane, indicating inclusion of *n*-hexane into the pillar[5]arene cavity changed the microenvironment around xenon in the cavity of pillar[5]arene.

Yu et al. reported the complexation of acetylcholine **G74** with the water-soluble pillar[5]arene **46[5]** under aqueous conditions. The association constant for this complex was high [$K = (1.97 \pm 0.55) \times 10^4 \text{ M}^{-1}$] (Figure 35).¹⁸¹

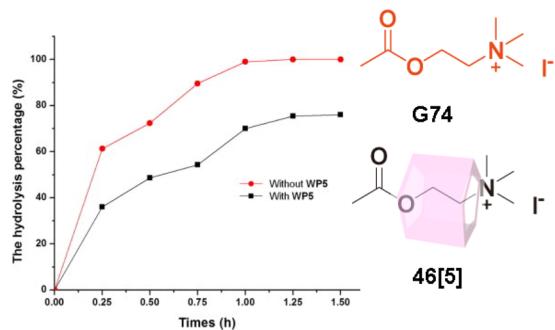


Figure 35. Percentage hydrolyses of **G74** in the absence and presence of **46[5]** with acetylcholinesterase. Reproduced with permission from ref 181. Copyright 2015 Elsevier Ltd.

The hydrolysis of **G74** is facilitated by acetylcholinesterase. The mixing of **G74** (30 mM) with acetylcholinesterase (1 U/mL) in aqueous media led to the complete hydrolysis of **G74** in 1 h (Figure 35a, red line). In contrast, the hydrolysis of **G74** proceeded at a much slower rate in the presence of the water-soluble pillar[5]arene **46[5]** (30 mM), with only 70% hydrolysis after 1 h (Figure 35b, black line). These results indicated that the hydrolysis of **G74** was being inhibited by the complexation of **G74** with the **46[5]**.

Yuan and co-workers investigated the extraction of metal ions using pillar[5]arene **117[5]** bearing 10 phosphine oxide chelating groups. The results revealed that pillar[5]arene **117[5]** selectively recognized f-block elements (Figure 36a).^{182,183}

The selectivity of this system for f-block elements was extremely high as compared to the unit model and the classic extractant tri-*n*-octylphosphine oxide. Pillar[5]arene **117[5]** showed high selectivity for thorium(IV) and uranyl(VI) cations. In contrast, per-methylated pillar[5]arene **1[5]** bearing no chelating groups did not show any extraction ability for these cations. These results therefore demonstrated that the 10 phosphine oxide moieties on the pillar[5]arene rims were contributing to the metal cation extraction process. Pillar[5]-arene **117[5]** also captured heavy-metal ions such as Co^{2+} , Cu^{2+} ,

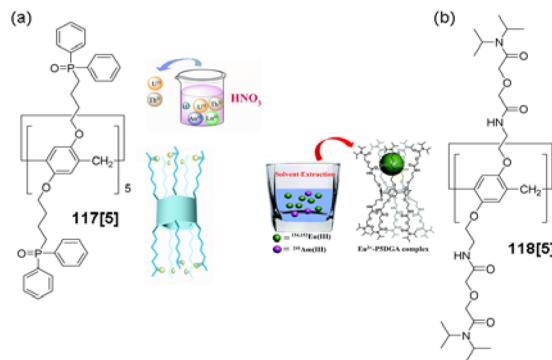


Figure 36. Selective extraction of metal cations. (a) Pillar[5]arene with 10 phosphine oxide **117[5]**. Reproduced with permission from ref 182. Copyright 2013 Royal Society of Chemistry. (b) Pillar[5]arene with 10 diglycolamide arms **118[5]**. Reproduced with permission from ref 184. Copyright 2014 Royal Society of Chemistry.

Ni^{2+} , Zn^{2+} , Cd^{2+} , Pb^{2+} , Ag^{2+} , and Hg^{2+} . Pillar[5]arenes with other chelating agents bearing 10 diglycolamide moieties on its rims **118[5]** showed excellent extraction efficiency toward americium(III) and europium(III) cations (Figure 36b).^{184,185} A characteristic emission was detected when europium(III) cation was extracted with **118[5]** because the europium(III)–diglycolamide complex shows a strong fluorescence signal.

6. SUPRAMOLECULAR ASSEMBLY OF PILLAR[n]ARENES

6.1. Supramolecular Assemblies from Pillar[n]arennes in Solution

6.1.1. Self-Inclusion Complexes, Cyclic Dimers, and Supramolecular Polymers Based on Host–Guest Complexation Processes. Supramolecular polymers are polymeric arrays of monomeric units that are brought together by physical interactions including host–guest interactions and that show chain-like behaviors in solution and in bulk.^{186,187} Pillar[5]arenes form host–guest complexes with cationic molecules and neutral molecules bearing electron-withdrawing groups. Pillar[5]arene-based heteroditopic monomers and host–guest conjugates can therefore form a variety of different supramolecular structures such as self-inclusion complexes, cyclic dimers, and supramolecular polymers. We reported the synthesis of a host–guest conjugate between pillar[5]arene and the trimethylammonium guest moiety **54[5]** (Figure 37a).⁶⁵

Compound **54[5]** formed a self-inclusion complex in CDCl_3 . The driving force for this complexation process was the formation of cationic/ π interactions. These interactions were weakened when the conjugate was treated with a polar solvent such as acetone- d_6 , which led to the dethreading of the guest molecule from the host. Hu and co-workers reported the conversion of a host–guest conjugate to a mixture of three isomers, including the uncomplexed material **119[5]a** and the two self-inclusion complexes **119[5]b** and **119[5]c**, under equilibrium conditions.¹⁸⁸ Following the addition of fluoride ions, the self-inclusion complex **119[5]b** was converted to the other self-inclusion complex **119[5]c** because of the formation of a binding interaction between the amide group of **119[5]** and the fluoride ions (Figure 37b). Huang et al. and Meier and Cao et al. also reported the formation of supramolecular dimers from host–guest conjugates (Figure 38a).

Pillar[5]arenes **120[5]**¹⁸⁹ and **121[5]**¹⁹⁰ bearing hydroxyl and bromide groups at the end of their alkyl guests formed double-

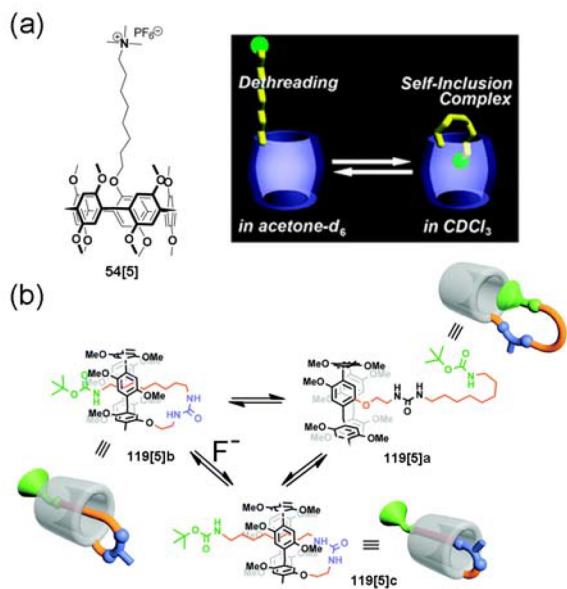


Figure 37. (a) Solvent-dependent supramolecular structural changes between the dethreaded and threaded forms of 54[5]. Reproduced with permission from ref 65. Copyright 2011 Royal Society of Chemistry. (b) Fluoride anion responsive isomerization of 119[5] between three different isomers. Reproduced with permission from ref 188. Copyright 2014 Royal Society of Chemistry.

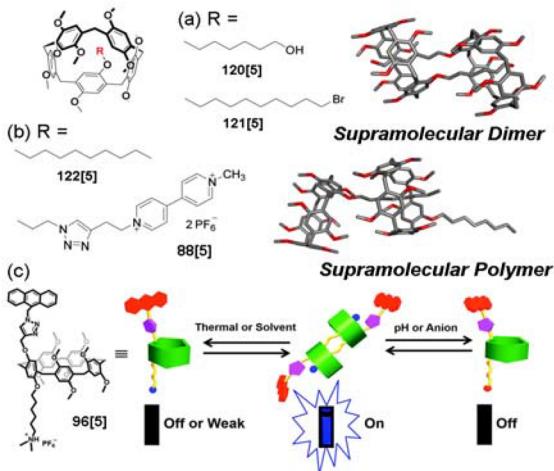


Figure 38. Formation of supramolecular (a) dimers and (b) polymers from host–guest conjugates. (c) Fluorescence on–off switching induced by supramolecular structural changes. Reproduced with permission from ref 118. Copyright 2014 Royal Society of Chemistry.

threaded supramolecular dimers (Figure 38a). Yang and co-workers reported the construction of highly emissive double-threaded supramolecular dimers from pillar[5]arenes bearing one ammonium group and the fluorescent dye 96[5] (Figure 38c).¹¹⁸ The formation of this supramolecular dimer restricted the motion of the fluorescent dye with the dimerization, therefore enhancing the fluorescence intensity. Changing the pH or adding a different anion led to the dissociation of the dimeric structure and fluorescence quenching. Huang and co-workers also synthesized pillar[5]arenes carrying the long-chain alkyl guest 122[5] without a bromide group at the end of its chain (Figure 38b).¹⁹¹ These host–guest conjugates formed supramolecular polymers under high concentration conditions,

as well as in the solid state. The driving force for the formation of supramolecular dimers and polymers are CH/π interactions. The CH/π interactions involved in the formation of host–guest complexes are weak, and high concentration conditions are required to allow for the successful formation of supramolecular polymers (ca. 500 mM). Strong host–guest interactions are therefore required for the construction of high molecular weight supramolecular polymers. Stoddart and co-workers synthesized a monofunctionalized pillar[5]arene carrying the viologen moiety 88[5] (Figure 38b).¹¹⁶ The cation/π interactions responsible for the formation of the complex between viologen and pillar[5]-arene were much stronger than the CH/π interactions formed between a linear alkyl chain and pillar[5]arene. Supramolecular daisy chain polymers therefore were formed at intermediate concentrations (ca. 20 mM), with higher concentrations (>25 mM) leading to the formation of an organogel. Pillar[5]arenes carrying ammonium groups also allowed for the efficient formation of supramolecular polymers under intermediate concentrations.^{192–196}

The installation of specific functional groups into host–guest conjugates can be used as an effective strategy for controlling and enhancing the formation of supramolecular polymers. Yang and co-workers reported the incorporation of a photoresponsive stiff stilbene between pillar[5]arene and the imidazole guest 123[5] (Figure 39).¹⁹⁷

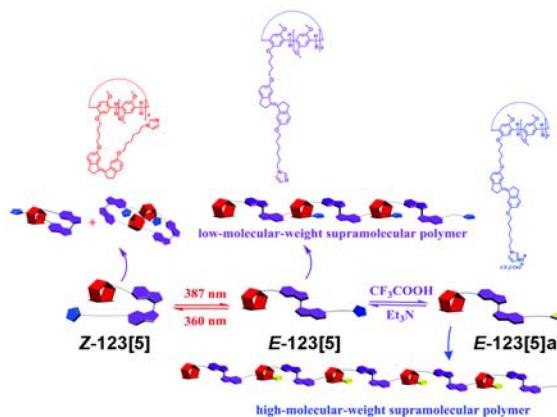


Figure 39. Photo- and pH-induced changes in the supramolecular structure of 123[5]. Reproduced with permission from ref 197. Copyright 2014 Royal Society of Chemistry.

The Z-123[5] isomer mainly formed a self-inclusion complex, as well as a double-threaded dimer. The photoirradiation of Z-123[5] resulted in its photoisomerization to E-123[5]. E-123[5] formed a low molecular weight supramolecular polymer. The addition of trifluoroacetic acid resulted in the protonation of the imidazole moiety of E-123[5]a, which led to the formation of a high molecular weight supramolecular polymer by enhancing the host–guest complexation ability of the system.

Stoddart and co-workers reported the incorporation of a porphyrin moiety between a pillar[5]arene host and a viologen guest to give conjugate 124[5] (Figure 40a).¹⁹⁸

The host–guest conjugate 124[5] formed a supramolecular polymer (Figure 40a), with intermolecular stacking interactions between the porphyrin units in the supramolecular polymers making a significant contribution to the bundle formation of the supramolecular polymers (Figure 40b). The entanglement of these bundles led to the formation of an elastic organogel. We reported the preparation of supramolecular polymers with

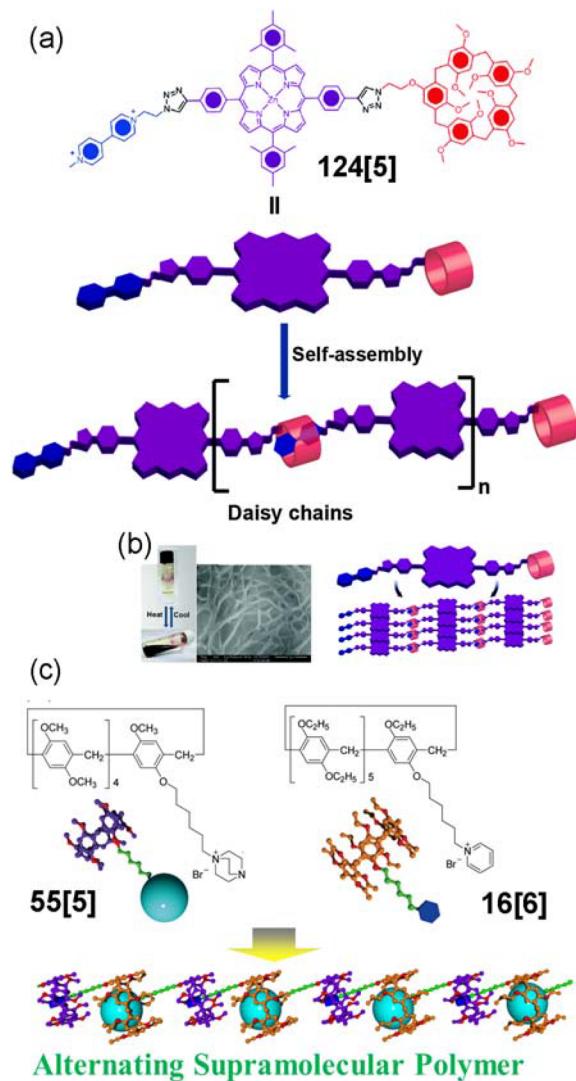


Figure 40. (a) Self-assembly of the host–guest porphyrin conjugate **124[5]**. (b) Image for the reversible formation of an organogel from **124[5]** and SEM image of the gel formed from high concentrations of **124[5]**. Reproduced with permission from ref 198. Copyright 2015 Royal Society of Chemistry. (c) Formation of a supramolecular polymer with alternating pillar[5]arene and pillar[6]arene systems by the mixing of the different host–guest conjugates **55[5]** and **16[6]**. Reproduced with permission from ref 78. Copyright 2012 Royal Society of Chemistry.

alternating pillar[5]arene and pillar[6]arene units by the mixing of the two heterotopic host–guest conjugates **55[5]** and **16[6]** (Figure 40c).⁷⁸ The mixing of monofunctionalized pillar[5]arene carrying the pillar[6]arene guest DABCQ cation **55[5]** with pillar[6]arene carrying the pillar[5]arene guest pyridinium cation **16[6]** afforded supramolecular polymers with alternating pillar[5]arene and pillar[6]arene units.

Two component mixtures of host–host and guest–guest homoditopic conjugates also afford supramolecular polymers.^{121,199} We reported that the mixing of the azobenzene-bridged pillar[5]arene dimer **101[5]** with the homoditopic bis-pyridinium guest **G75** led to a supramolecular polymerization process (Figure 41a).¹²¹

The mixing of *trans*-**101[5]** with guest dimer **G75** led to the formation of a supramolecular polymer. The subsequent irradiation of this polymer with UV light induced the

photoisomerization of the azobenzene moiety to give *cis*-**101[5]**, which contributed to the subsequent disassembly of the supramolecular polymer. These supramolecular assembly and disassembly processes were found to be completely reversible and could be readily controlled by alternating between UV and visible light irradiation. Wang and co-workers constructed a supramolecular polymer using the pillar[5]arene dimer **72[5]**, which was formed through a quadruple-hydrogen bonding interaction (Figure 41b).¹⁰⁷ The addition of the homoditopic diviologen guest **G76** led to the formation of a supramolecular polymer. Li and co-workers reported the construction of a dimer based on a 2:1 sandwich-type CT complex between pillar[5]arene and *N,N'*-bisalkylpyromellitic diimide.²⁰⁰ A 2:1:1 (mol/mol/mol) mixture of pillar[5]arene **4[5]**, *N,N'*-bisalkylpyromellitic diimide **1**, and the homoditopic guest **G77** afforded a supramolecular polymer (Figure 41c). The incorporation of fluorescent moieties between the homoditopic host–host and/or guest–guest conjugates allowed for the construction of supramolecular polymers showing a variety of different fluorescence colors.^{123,126,201} BODIPY dyes are tunable fluorescence dyes with high adsorption coefficients and fluorescence yields. Wang and co-workers reported the synthesis of the BODIPY-bridged pillar[5]arene dimer **108[5]** and two BODIPY derivative bearing two different guest moieties (**G78** and **G79**, Figure 42a).¹²⁶

The supramolecular polymerization process resulting from the mixing of the pillar[5]arene dimer **108[5]** containing BODIPY dye and the BODIPY guest dimers (**G78** and **G79**) induced a FRET process. This FRET process occurred as a consequence of the BODIPY moiety in the host dimer being positioned quite close to the BODIPY moiety in the guest dimer of the supramolecular polymer. The introduction of photo-²⁰² and γ -ray¹²⁵-responsive moieties to form pillar[5]arene dimers allowed for the formation of stimuli-responsive supramolecular polymers. The dissociation of the stimuli-responsive linker between the pillar[5]arene dimers resulted in the disassembly of the supramolecular polymers. Jiang and Wang reported the synthesis of the heteroditopic host, pillar[5]arene-fused cryptant **125[5]** (Figure 42b).²⁰³ The addition of two homoditopic guests (**G80** and **G81**) promoted the connection of the heterohost dimer, which led to the formation of a supramolecular polymer.

Li and co-workers reported the construction of supramolecular network polymers using the AB₂-type heterotritopic pillar[5]arene monomer **126[5]**.²⁰⁴ In this case, the AB₂-type monomer underwent a self-assembly process under high concentration conditions to form a supramolecular network polymer (Figure 43a).

The addition of a competitive guest to this system led to the depolymerization of the supramolecular network polymer. The other approach used for the formation of supramolecular network polymers involved the mixing of homoditopic host **97[5]** with homotritopic guest **G82** (Figure 43b, A₂/B₃-type).²⁰⁵ The combination of a homoditopic host with a homotetratropic guest (A₂/B₄-type),¹²⁹ homotritopic host **127[5]** with homoditopic guest **G83** (Figure 43c, A₃/B₂-type),²⁰⁶ a homotetratropic host with a homoditopic guest (A₄/B₂-type),^{122,127} or a homohexatopic host with a homoditopic guest (A₆/B₂-type)²⁰⁷ resulted in the formation of supramolecular polymers with network structures. Wang and co-workers reported a supramolecular polymer with vacant cavities resulting from the pillar[5]arenes **73[5]** through quadruple-hydrogen bonding interactions (Figure 43d).²⁰⁸ The addition of guest dimer **G84** to pillar[5]arene **73[5]** resulted in the formation of a

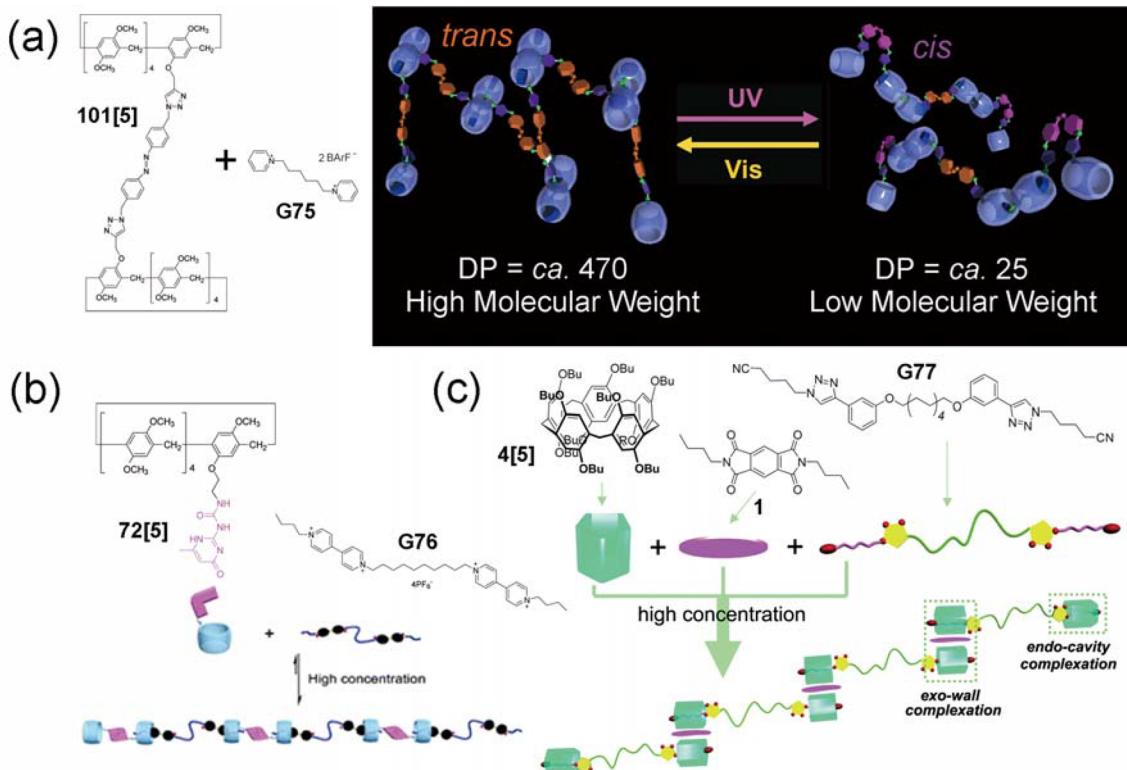


Figure 41. (a) Photoresponsive constructed of a supramolecular polymer from the photoresponsive pillar[5]arene dimer **101[5]** and the guest dimer **G75**. Reproduced with permission from ref 121. Copyright 2013 Royal Society of Chemistry. (b) Construction of a supramolecular polymer of **72[5]** via the formation of a series of orthogonal binding interactions, including quadruple-hydrogen bonding and host–guest interactions. Reproduced with permission from ref 107. Copyright 2012 Royal Society of Chemistry. (c) Supramolecular polymerization by the mixing of a host **4[5]**, guest dimer **G77**, and ditopic connector **1**. Reproduced with permission from ref 200. Copyright 2015 Royal Society of Chemistry.

supramolecular network polymer with the guest dimer acting as an intermolecular cross-linking agent between the supramolecular polymers.²⁰⁹

6.1.2. Supramolecular Assembly Using Organic Polymers with Pillar[n]arenes. The mixing of organic polymers carrying pillar[n]arenes and guest moieties is another useful method for the construction of supramolecular polymers with network structures. Wang and co-workers reported the formation of a redox-reversible supramolecular network using organic polymers consisting of pillar[6]arene **2** and ferrocene moiety **3** (Figure 44a).²¹⁰

When the ferrocene in polymer **2** existed in its reduced form, the polymer did not form a supramolecular network because the host–guest interaction between ferrocene and pillar[6]arene was weak. In contrast, the oxidation of ferrocene led to the formation of a gel-like supramolecular network because of the strong host–guest interaction between the oxidized ferrocenium ion and pillar[6]arene.

Wang and co-workers reported the synthesis of the π -conjugated polymer **4** based on a poly(phenylene ethynylene) backbone bearing molecular recognition sites for pillar[5]arenes on its side chains (Figure 44b).^{211,212} Fluorescence from the π -conjugated polymer was quenched by the addition of the *n*-octylpyrazinium cation **G85** because of an electron transfer process from the π -conjugated polymer **4** to the *n*-octylpyrazinium cation **G85**. The addition of halide anions led to fluorescence recovery in the order of $\text{Cl}^- > \text{Br}^- > \text{I}^-$. Chloride anions are small and possess a high charge density as compared to the other anions, allowing them to form a strong interaction with

the *n*-octylpyrazinium cation **G85**, thereby triggering the decomplexation of the pillar[5]arenes in polymer **4** and **G85**.

Stoddart and co-workers synthesized one-dimensional tubular arrays by the condensation reaction of pillar[5]arene with one of the A–B units in pillar[5]arene **128[5]** (Figure 44c).²¹³ The conversion of one-dimensional tubular arrays derived from pillar[5]arene dimers to pillar[5]arene 9-mers could be obtained under microwave heating conditions.

6.1.3. Formation of Micelles, Vesicles, and Tubes. On the basis of the high functionality and host–guest properties of pillar[n]arenes, it is possible to create amphiphilic pillar[n]arene hosts and amphiphilic host–guest complexes consisting of hydrophobic and hydrophilic groups. These amphiphilic hosts and complexes have the ability to form various supramolecular assemblies in hydrophobic and hydrophilic solvents. Huang and co-workers have studied the nanostructures prepared from amphiphilic pillar[n]arenes extensively. They synthesized an amphiphilic pillar[5]arene containing five amino groups on its hydrophilic head and five alkyl chains on its hydrophobic tail (Figure 45a).^{134,214}

Pillar[5]arene **129[5]** initially formed self-assembled bilayer vesicles in aqueous media, which were subsequently transformed into necklace- and sheet-like structures. These two structures were then further fused into microtubes, which exhibited a strong adsorption affinity for the famous explosive trinitrotoluene. Xue and co-workers investigated the formation of vesicles and microtubes from amphiphilic pillar[5]arenes bearing hydrophobic alkyl chains of different lengths.²¹⁵ The formation of bimolecular micelles from the amphiphilic pillar[5]arene **130[5]** bearing five hydrophilic amino groups and hydrophobic alkyl

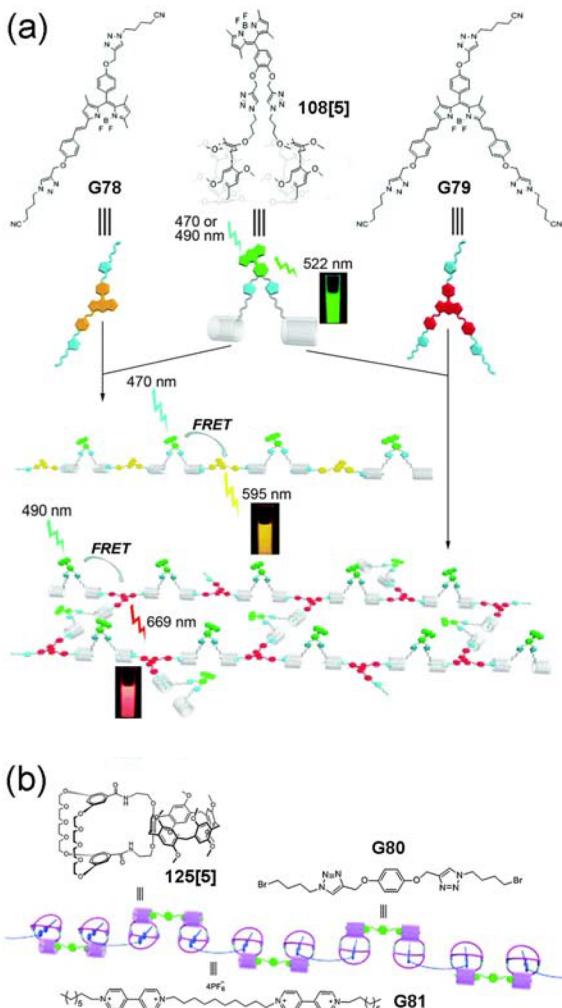


Figure 42. (a) Construction of two types of Förster resonance energy transfer (FRET)-capable functional supramolecular polymer from the pillar[5]arene dimer **108[5]** and the two guest dimers **G78** and **G79** with BODIPY moieties. Reproduced with permission from ref 126. Copyright 2015 Royal Society of Chemistry. (b) Supramolecular polymer formation using **125[5]** and two types of guest dimer (**G80** and **G81**) based on the formation of orthogonal binding interactions between the crown ether and viologen moieties, as well as the pillar[5]arene and triazole moieties. Reproduced with permission from ref 203. Copyright 2015 Royal Society of Chemistry.

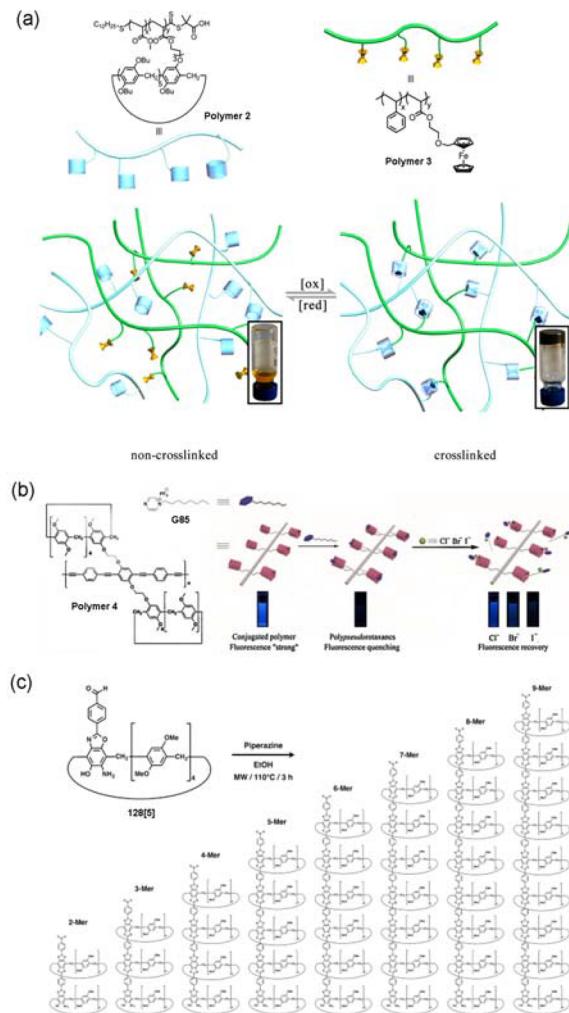


Figure 44. (a) Formation of a redox-controllable supramolecular network polymer by the mixing of polymers **2** and guest **3** moieties. Reproduced with permission from ref 210. Copyright 2015 American Chemical Society. (b) Fluorescence quenching by the complexation of the pyrazinium cation **G85** with polymer **4** and fluorescence recovery following the addition of specific anions. Reproduced with permission from ref 212. Copyright 2013 Royal Society of Chemistry. (c) Oligomerization of the AB type monomer **128[5]** under microwave-irradiation conditions to form rigid pillar[5]-arene tubular oligomers. Reproduced with permission from ref 213. Copyright 2014 Wiley-VCH Verlag GmbH & Co. KGaA.

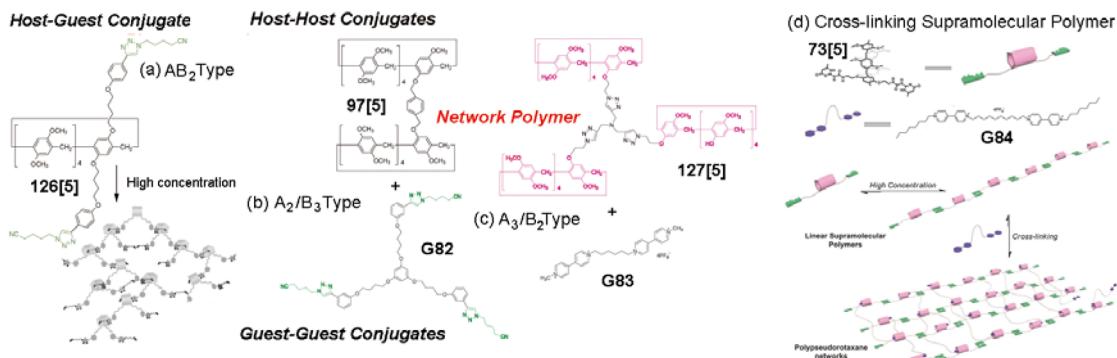


Figure 43. Formation of supramolecular network polymers from (a) AB_2 host–guest conjugate **126[5]**, (b) A_2/B_3 , (c) the A_3/B_2 -type host–host and guest–guest conjugates, and (d) cross-linking of supramolecular polymers through orthogonal host–guest interactions. Reproduced with permission from ref 209. Copyright 2013 Royal Society of Chemistry.

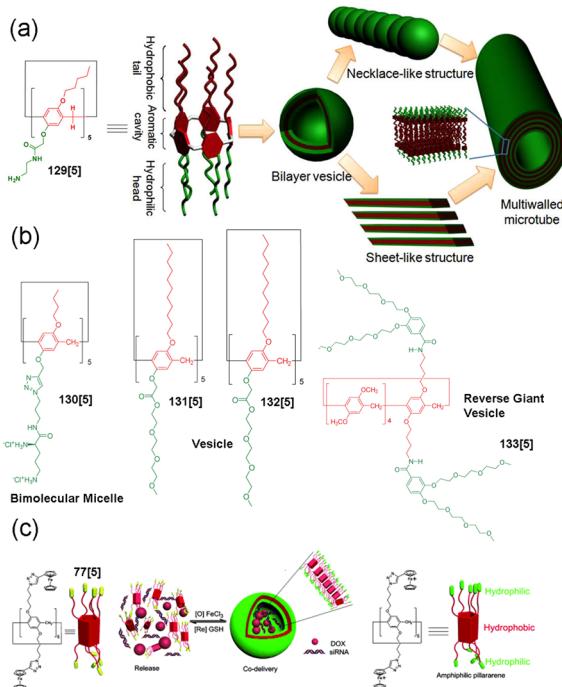


Figure 45. (a) Self-assembly pathway for the formation of microtubes from amphiphilic pillar[5]arene **129[5]**. Reproduced with permission from ref 134. Copyright 2012 American Chemical Society. (b) Chemical structures of amphiphilic pillar[5]arenes **130[5]**–**133[5]**, which formed bimolecular micelles, vesicles, and reverse giant vesicles. (c) Redox-responsive supramolecular changes between cationic vesicles and precipitates for the release of drug/siRNA materials. Reproduced with permission from ref 110. Copyright 2014 Wiley-VCH Verlag GmbH & Co. KGaA.

tails was reported by Sakurai and co-workers (Figure 45b).²¹⁶ Pillar[5]arenes **131[5]** and **132[5]** bearing five hydrophilic oligo(ethylene oxide) chains and five hydrophobic alkyl chains, respectively,^{114,217} also formed vesicles. The same occurred in copillar[5]arene **133[5]** bearing one amphiphilic oligo(ethylene oxide) chain unit,²¹⁸ as well as several monofunctionalized pillar[5]-¹¹⁷ and pillar[6]arenes.²¹⁹ Pei and co-workers reported the formation of redox-responsive cationic vesicles from the amphiphilic pillar[5]arene **77[5]** bearing five ferrocenium cations (Figure 45c).¹¹⁰ The resulting cationic vesicles exhibited redox-responsive behavior as a consequence of the redox reaction between the ferrocenium cations and the neutral ferrocenyl groups. This system allowed for the development of an ideal glutathione (GSH)-responsive drug/siRNA codelivery system for rapid drug release and gene transfection in cancer cells because cancer cells typically have a higher GSH concentration than normal cells. Another method that is often used for the formation of various nanostructures is the construction of amphiphilic molecules through host–guest complexation processes (Figure 46).

Huang and co-workers reported the construction of vesicles from the host–guest complexes formed between azobenzene guest **G71** and pillar[6]arene **2[6]**.¹³⁶ Pillar[6]arene **2[6]** formed a complex with *trans*-**G71**, and the assembled structure of this complex consisted of irregular aggregates in chloroform. The irradiation of this complex with light led to the dethreading of the azobenzene guest because it underwent a photoisomerization process from its *trans*-form to its *cis*-form. The resulting mixture of pillar[6]arene **2[6]** and *cis*-**G71** underwent

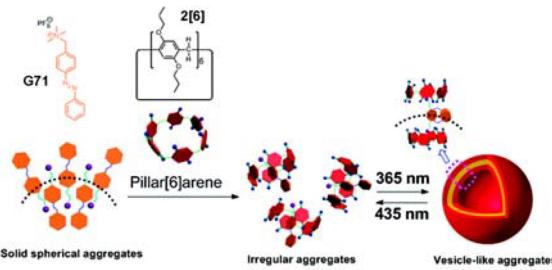


Figure 46. Photoresponsive supramolecular structural changes from irregular and vesicle-like aggregates using photoresponsive 2-[6]Dazobenzene guest **G71** complex. Reproduced with permission from ref 136. Copyright 2012 American Chemical Society.

an assembly process in chloroform to give vesicle-like aggregates. Huang et al. have also reported similar photoswitching processes for nanostructural changes between the solid nanoparticles and vesicles formed in aqueous media from a water-soluble pillar[6]arene and an amphiphilic azobenzene guest.²²⁰

The pH-,^{161,162,221–224} chemical-,^{225–232} CO₂-,^{233,234} and photoresponsive^{235,236} supramolecular vesicles consisting of water-soluble pillar[n]arene and stimuli-responsive amphiphilic molecules have also reported. Furthermore, considerable research has been directed toward the application of these stimuli-responsive supramolecular vesicles to the development of controlled drug release^{134,161,162,217,221–223,225–227,229,236,237} and bioimaging¹¹⁴ systems.

6.1.4. Lower Critical Solution Temperature Materials.

Our group reported amphiphilic pillar[5]- and pillar[6]arenes with tri(ethylene oxide) groups (**51[5]** and **15[6]**, Figure 47a), which showed lower critical solution temperatures (LCSTs) in aqueous media.^{90,97}

These pillar[5]- and pillar[6]arenes were soluble in aqueous media at 25 °C. Interestingly, these solutions became turbid when they were heated at 50 °C, but then became clear again when they were cooled to 25 °C (Figure 47a). The LCST behavior of these amphiphilic pillar[5]- and pillar[6]arenes was attributed to the combination of hydrophilic triethylene oxide chains with a hydrophobic pillar[5]- and pillar[6]arene backbone. The cloud point of the amphiphilic pillar[5]-arene **51[5]** in 2 mM aqueous solution was 41 °C, which was similar to that of the corresponding amphiphilic pillar[6]arene **15[6]** (42 °C). Pillar[5]arenes form CT host–guest complexes with viologen derivatives, which led to the addition of didecylviologen dibromide **G86**. The cloud point of the amphiphilic pillar[5]-arene **51[5]** increased from 42 to 60 °C following the addition of **G86** (Figure 47b). This increase was attributed to the existence of repulsive forces between the complexed cations following the addition of **G86**, which inhibited the aggregation of the complexes. Viologen derivatives form very stable host–guest complexes with CB[7], which led us to investigate the addition of CB[7] to an aqueous solution of the CT host–guest complex. As the concentration of CB[7] increased, the cloud point of the mixture decreased from 60 to 47 °C. This decrease in the cloud point was attributed to the decomplexation of **G86** from **51[5]** upon addition of the competitive host CB[7]. Overall, it was possible to tune the cloud point of the amphiphilic pillar[5]arene using the viologen guest **G86** and the competitive host CB[7].

Pillar[6]arenes form host–guest complexes with *trans*-state azobenzene derivatives, but not with the corresponding *cis*-state compounds. Using a photoresponsive host–guest system, we demonstrated the photoreversible switching of LCST (Figure

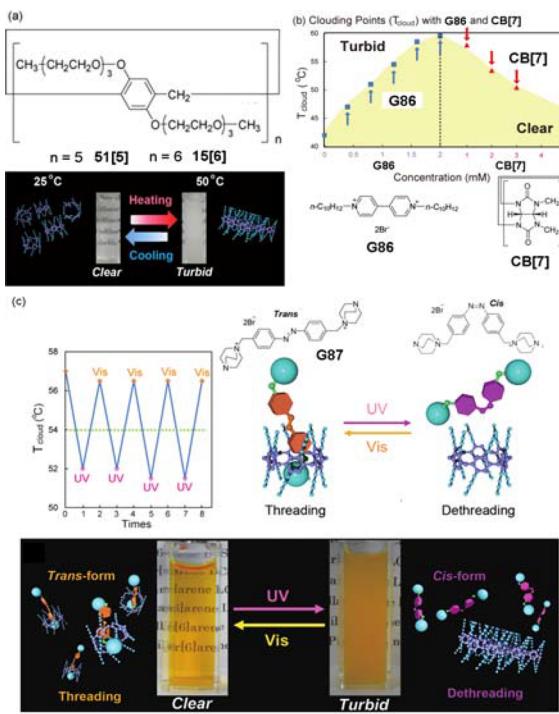


Figure 47. (a) Pillar[5]- and pillar[6]arenes with tri(ethylene oxide) chains (S1[5] and 15[6]) and photographs of an aqueous solution containing 15[6] (2 mM) at 25 and 50 °C. (b) Chemically responsive LCST changes using S1[5], viologen guest G86, and competitive host CB[7]. Reproduced with permission from ref 90. Copyright 2012 American Chemical Society. (c) Photoresponsive LCST changes using 15[6] and the photoresponsive azobenzene guest G87. Reproduced with permission from ref 97. Copyright 2012 American Chemical Society.

47c).⁹⁷ The *trans*-state azobenzene guest G87 bearing two DABCO cations formed a host–guest complex with the amphiphilic pillar[6]arene 15[6]. This complexation process led to an increase in the cloud point of the amphiphilic pillar[6]arene from 41 to 57 °C. However, the cloud point of the mixture decreased from 57 to 52 °C upon UV irradiation, which led to a change in the conformation of the azobenzene guest from its *trans*-state to its *cis*-state. This photoisomerization process led to the dissociation of the complex because the cavity size of the pillar[6]arene did not fit the *cis*-form of the azobenzene guest. Notably, the cloud point of the mixture returned to 57 °C by visible light irradiation, which led to the conversion of the *cis*-form of the guest back to the *trans*-form, which could be rethreaded through the host cavity. This photoinduced threading/dethreading sequence contributed to the photo-switching for the LCST behavior of the amphiphilic pillar[6]-arene.

We also reported dual-responsive, redox-, and host–guest complexation-responsive LCST changes following the introduction of one benzoquinone unit to the amphiphilic pillar[5]arene (quinone-H134[5], Figure 48).⁷²

The cloud point of quinone-134[5] in 2 mM aqueous solution was observed at 21 °C, which was lower than that of the amphiphilic pillar[5]arene without the benzoquinone unit (41 °C in S1[5]). This difference in the cloud points was attributed to the benzoquinone unit being more hydrophobic than the tri(ethylene oxide)-modified unit. The addition of a reducing agent resulted in the formation of the amphiphilic pillar[5]arene bearing one hydroquinone unit (2OH-134[5]). The cloud point

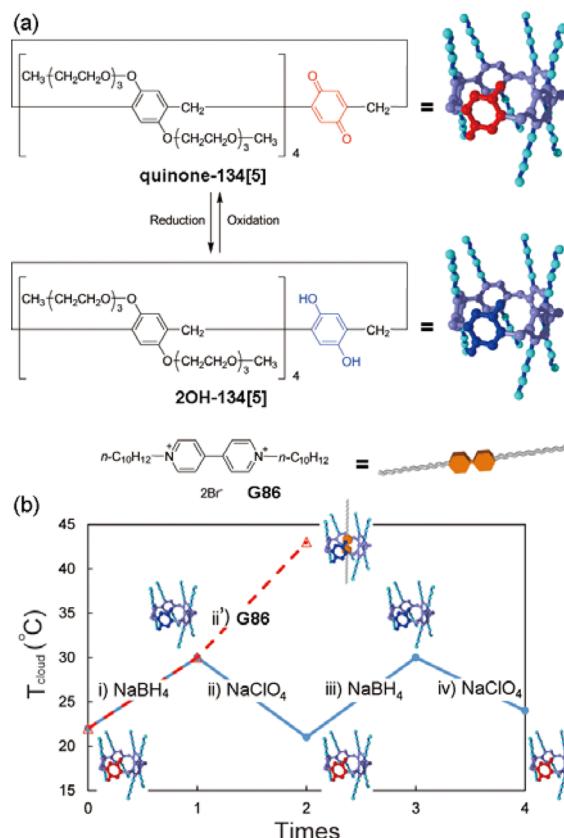


Figure 48. (a) Chemical structure of pillar[5]arene 134[5] bearing one benzoquinone unit and one hydroquinone unit and a viologen guest G86. (b) (i–iv) Reversible T_{cloud} changes for quinone-134[5] (2 mM) by the alternate addition of NaBH4 (0.5 mM) and NaClO4 (4 mM). (ii and ii') Contrasting cloud point changes upon the addition of NaClO4 (4 mM) or G86 (4 mM). Reproduced with permission from ref 72. Copyright 2015 Royal Society of Chemistry.

of this mixture was determined to be 31 °C, which was higher than that of the cloud point of quinone-134[5] (21 °C). This difference was attributed to the hydroquinone moiety being more hydrophilic than benzoquinone. The subsequent addition of an oxidizing agent led to a decrease in the cloud point from 31 to 21 °C because the hydroquinone was oxidized to a benzoquinone. The redox-switching of the cloud point was a reversible process that could be controlled by alternating the addition of reducing and oxidizing agents. Quinone-134[5] and 2OH-134[5] also showed guest-responsive LCST changes, in that the addition of a cationic viologen guest G86 to an aqueous solution of quinone-134[5] or 2OH-134[5] led to an increase in the cloud point.

Larger pillar[n]arene homologues with tri(ethylene oxide) chains also showed LCST behavior. When 2 mM aqueous solutions of pillar[7]- and pillar[10]arenes bearing tri(ethylene oxide) chains (Scheme 18, 4[7] and 4[10]) were heated at 50 °C, they became turbid.^{95,238} Huang and co-workers reported that pillar[7]arene 4[7] formed a stable host–guest complex with the *trans*-form of the azobenzene guest [$(1.97 \pm 0.24) \times 10^4 \text{ M}^{-1}$], which was more stable than the complex formed with the *cis*-form of the azobenzene guest [$(1.87 \pm 0.13) \times 10^3 \text{ M}^{-1}$]. This system could therefore be used as photoswitchable supramolecular assembly system. Xue and co-workers reported that pillar[10]arene 4[10] accommodated a bulky diazapyrenium salt [$(4.2 \pm 0.3) \times 10^4 \text{ M}^{-1}$]. The complexation of this guest led to an

increase in the cloud point from 40 to 58 °C. Notably, the complex dissociated following the addition of diethylamine, and subsequently reformed following the addition of trifluoroacetic acid. It was therefore possible to switch the cloud point of the pillar[10]arenes by alternating the addition of diethylamine and trifluoroacetic acid.

LCST is generally observed in aqueous media. Huang and co-workers reported the unique LCST behavior of the host–guest complex formed between pillar[5]arene and the ionic liquid 1,3-dimethylimidazolium iodide in chloroform (Figure 49).²³⁹

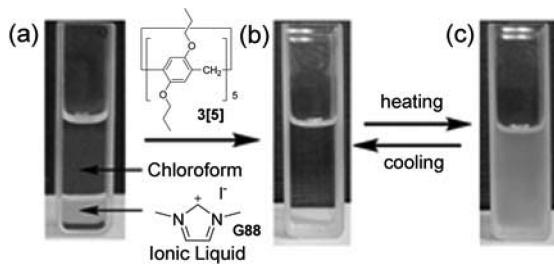


Figure 49. LCST-type phase changes induced by the host–guest complexation between pillar[5]arene 3[5] and ionic liquid G88 in chloroform. (a) Phase separation between ionic liquid G88 and chloroform. (b) The solution became transparent upon the addition of pillar[5]arene 3[5]. (c) LCST-type phase separation induced by heating. Reproduced with permission from ref 239. Copyright 2013 Wiley-VCH Verlag GmbH & Co. KGaA.

The solubility of 1,3-dimethylimidazolium iodide (G88) in chloroform is low (0.38 wt %, 25.6 mM), which resulted in the formation of a biphasic mixture at 25 °C (Figure 49a). Pillar[5]arene 3[5] formed a relatively stable host–guest complex with G88 in chloroform [$1.04 (\pm 0.15) \times 10^3 \text{ M}^{-1}$], which was highly soluble in chloroform. Therefore, the addition of pillar[5]arene 3[5] resulted in the conversion of a biphasic mixture to a homogeneous solution (Figure 49b). The complexation of G88 into the cavity of 3[5] contributed to the formation of the homogeneous solution. The solution became turbid with heating (Figure 49c), and subsequently became clear when the mixture was cooled. The detreading of G88 from the cavity of 3[5] at elevated temperatures led to the observed separation of the phases because of the reduced stability of the complex at high temperatures.

6.2. Bulk Supramolecular Assemblies Constructed from Pillar[n]arenes

The rich functionality^{37,38} and highly regular symmetrical pillar-shaped structures of pillar[n]arenes mean that they can form highly functional and well-ordered pillar[n]arene-based bulk supramolecular assemblies. In this section, we will discuss the formation and properties of bulk-state pillar[n]arene assemblies in the liquid, ionic liquid, and crystalline states.

6.2.1. Liquid Pillar[n]arenes. Macrocyclic compounds generally exist in the solid state at 25 °C. The formation of host–guest complexes involving macrocyclic compounds therefore requires a solvent. We discovered that the ionic liquid-modified pillar[5]arene 68[5] could exist in the liquid state at 25 °C based on the choice of an appropriate counteranion (Figure 50a).¹⁰²

In the case of the hexafluorophosphate anion (PF_6^-), the compound existed in the solid state, and exhibited a melting temperature of 108 °C. In contrast, the use of a bis(trifluoromethanesulfonyl)amide (TFSA) anion resulted in a compound that existed in the liquid state at 25 °C with a freezing temperature of -7 °C. The ionic liquid pillar[5]arene 68[5] bearing TFSA anions showed ionic conductivity ($8.70 \times 10^{-6} \text{ S cm}^{-1}$) and formed a host–guest complex with the electron-accepting molecule tetracyanoethylene (Figure 22, G12), even in the bulk liquid state.

The other liquid pillar[n]arenes were the tri(ethylene oxide)-modified pillar[5]- and pillar[6]arenes 51[5] and 1S[6], respectively (Figure 50b).^{97,240} These systems existed in the liquid state over a wide range of temperatures and were stable up to 250 °C. These systems could therefore be used as solvents for host–guest complexation processes and the formation of rotaxanes. Pillar[5]arenes form host–guest complexes with linear alkanes, but their complexation abilities are generally poor in solution systems ($K = 20 \text{ M}^{-1}$). However, when they are used in bulk liquid systems, their complexation abilities improve considerably because the guest molecules were surrounded by excess pillar[5]arene host molecules 51[5]. The liquid bulk system therefore represents an intelligent system for maximizing the concentrations of the host and guest molecules. Using this efficient complexation media, it was possible to investigate the formation of rotaxanes using an end-capping approach. The efficiency of the rotaxane formation process was quite high (over 92%) when the liquid pillar[5]arene 51[5] was used as a solvent for the rotaxanation because the host–guest complex was stable in this system.²⁴⁰

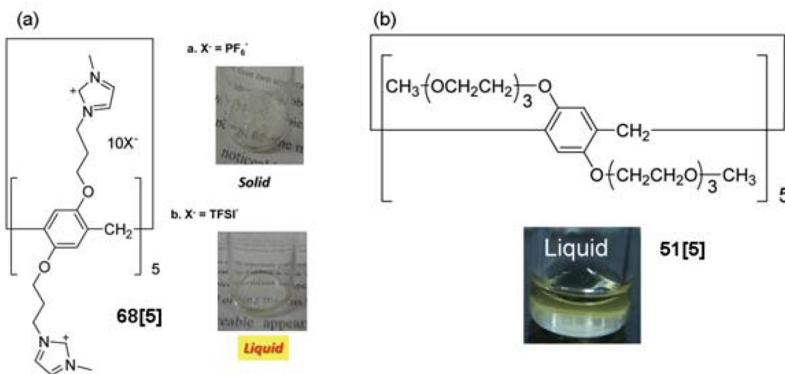


Figure 50. Liquid state pillar[5]arenes resulting from the modification of (a) ionic liquid moieties 68[5] and (b) tri(ethylene oxide) chains 51[5].

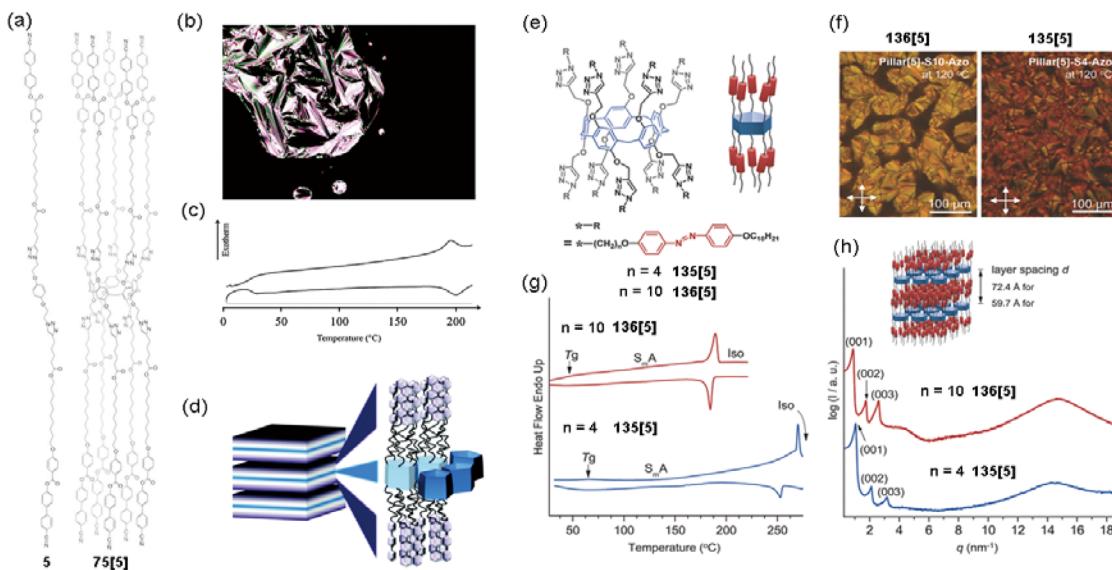


Figure 51. Liquid crystal pillar[5]arenes. (a) Pillar[5]arene with mesogenic moieties 75[5] and the unit model 5. (b) Polarized optical micrograph of the texture displayed by 75[5] in the smectic A phase at 183 °C. (c) DSC thermogram of 75[5] in the second heating–cooling cycle. (d) Proposed liquid crystal structure of 75[5] in the smectic A phase. Reproduced with permission from ref 109. Copyright 2012 Royal Society of Chemistry. (e) Chemical structures of the azobenzene-modified pillar[5]arenes with different spacers ($n = 4$, 135[5] and $n = 10$, 136[5]). (f) Polarized optical micrograph of 135[5] ($n = 4$) and 136[5] ($n = 10$) at 120 °C. (g) DSC thermograms of 135[5] ($n = 4$) and 136[5] ($n = 10$) in the heating–cooling cycle. (h) SAXS/WAXS profiles in their liquid crystalline state (80 °C). Reproduced with permission from ref 241. Copyright 2015 Wiley-VCH Verlag GmbH & Co. KGaA.

6.2.2. Liquid Crystal Pillar[n]arenes. Nierengarten and co-workers reported the development of thermotropic liquid crystals using a pillar[5]arene platform (Figure 51a).¹⁰⁹

Pillar[5]arene 75[5] bearing 10 mesogenic cyanobiphenyl moieties on both of its rims showed an enantiotropic smectic A phase (Figure 51b). The smectic A phase was observed over a wide temperature range from 32 to 201 °C by DSC measurements (Figure 51c). In contrast, the unit model 5, which consisted of two cyanobiphenyl moieties, only showed a monotropic smectic A phase during the cooling process over a narrow temperature range from 149 to 125 °C. Intermolecular π – π stacking interactions between the neighboring pillar[5]arene cores contributed to the stabilization of the smectic A phase (Figure 51d). In a manner similar to the pillar[5]arene 75[5], pillar[6]arene 20[6] bearing 12 cyanobiphenyl moieties (Scheme 23) also showed a stable smectic A phase over a wide range of temperatures.⁷⁹ Wang and co-workers synthesized pillar[5]arene-based photoresponsive liquid crystals using pillar[5]arenes bearing 10 azobenzene moieties with different spacer lengths ($n = 4$, 135[5], $n = 10$, 136[5], Figure 51e).²⁴¹ Both of these pillar[5]arenes showed smectic liquid crystalline phases over a wide range of temperatures (Figure 51f), as indicated by DSC measurements (Figure 51g). Furthermore, the lamellar periods of these systems were determined by small-/wide-angle X-ray scattering (SAXS/WAXS) analyses to be 72.4 and 59.7 Å, respectively (Figure 51h).

The lamellar distances of these systems were about 20% shorter than they were estimated to be on the basis of their molecular contour lengths, which suggested a partially interdigitated packing structure. The tubular pillar[5]arene macrocyclic platform provided sufficient free volume to allow for the reversible photoisomerization and photoalignment processes.

6.2.3. Crystalline Pillar[n]arenes for Gas and Organic Vapor Adsorption.

Pillar[n]arenes have high symmetrical pillar-shaped structures and high free volumes, making them

good candidates for the preparation of porous materials for gas and organic vapor adsorption. Yang and co-workers reported the use of pillar[5]arene crystals as gas adsorption materials (Figure 52).¹⁴⁷

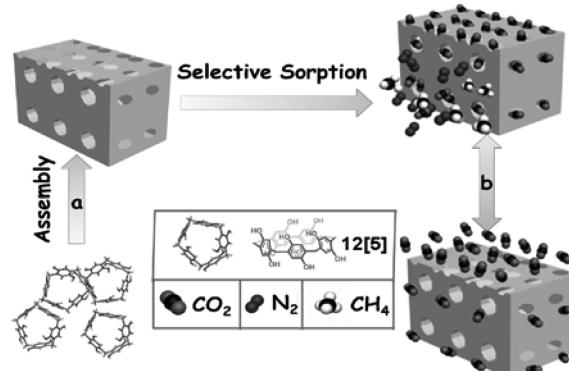


Figure 52. Schematic representation of the supramolecular organic framework constructed from per-hydroxylated pillar[5]arene 12[5] and its selective uptake of CO₂. The supramolecular organic framework can be reused for CO₂-selective adoption. Reproduced with permission from ref 147. Copyright 2014 Wiley-VCH Verlag GmbH & Co. KGaA.

Pillar[5]arene 12[5] bearing 10 phenolic moieties exhibited a 3D open network structure, which was stabilized by intermolecular hydrogen-bonding interactions. The 3D open network structure contained 0.5 acetone molecules, which were removed when the crystals were heated at 170 °C. However, the crystal structure remained unchanged even after the acetone molecules had been removed because the 3D open network structure was stabilized by intermolecular hydrogen bonds. The activated crystals absorbed CO₂ with a high sorption ability (88 mg g⁻¹, at 25 °C, 1 atm). In contrast, CH₄ and N₂ were poorly adsorbed, indicating remarkable CO₂-selectivities over CH₄.

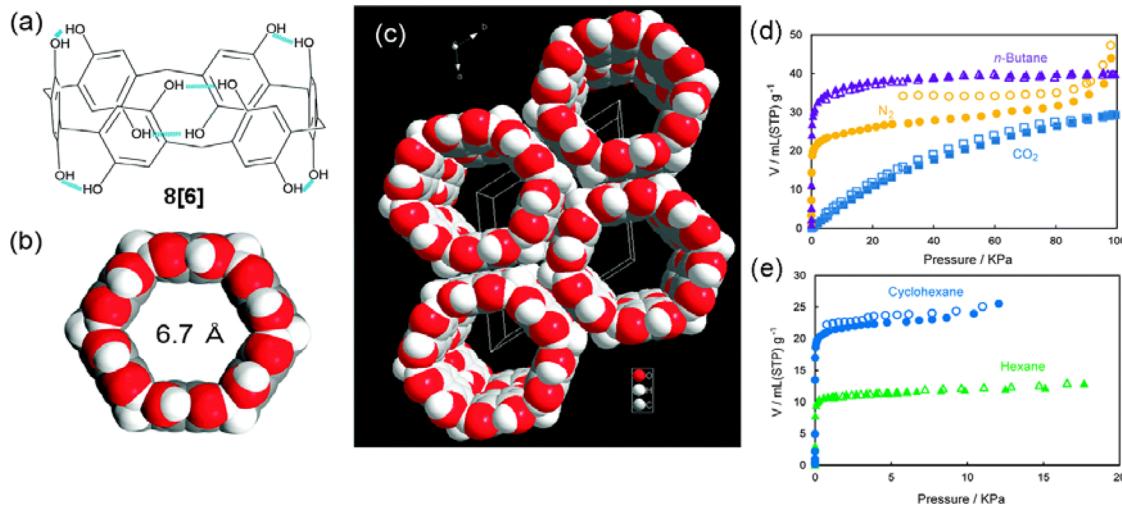


Figure 53. (a) Chemical and (b,c) X-ray crystal structures of the per-hydroxylated pillar[6]arene 8[6]. (c) View along the *c* axis. (d) Nitrogen (77 K, yellow circles), CO₂ (298 K, blue squares), and *n*-butane (298 K, purple triangles) sorption isotherms of powdered 8[6]. (e) Sorption isotherms of powdered 8[6] with pores for the vapors of *n*-hexane (green triangles) and cyclohexane (blue circles) at 298 K. Solid symbols = adsorption; open symbols = desorption. Reproduced with permission from ref 242. Copyright 2014 Royal Society of Chemistry.

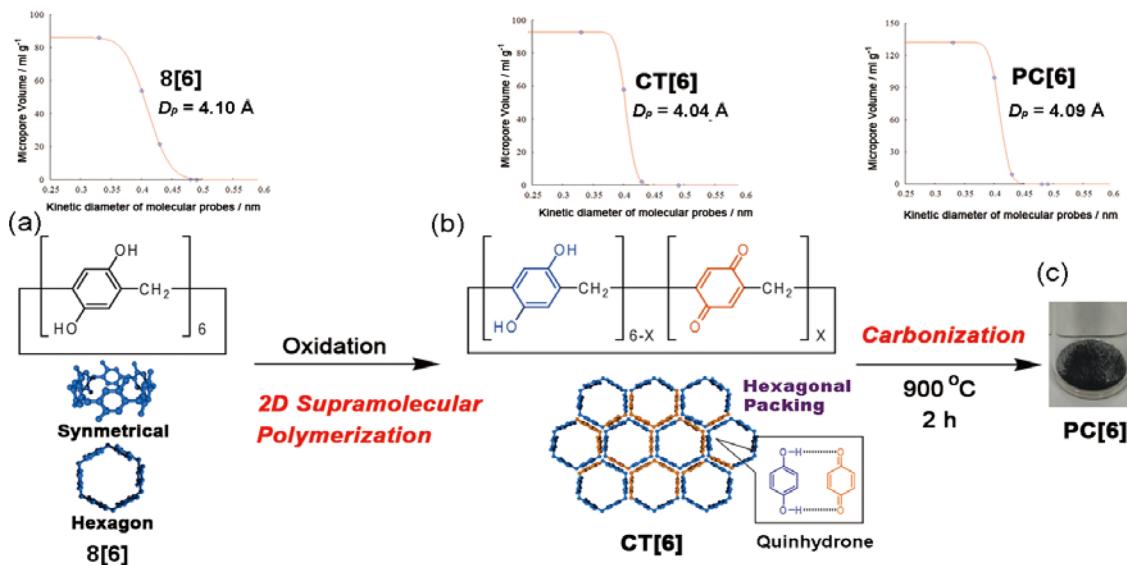


Figure 54. (a) Hexagonal structure of 8[6], (b) 2D supramolecular polymerization by the oxidation of the hydroquinone units, and (c) porous carbon PC[6], which was prepared by the carbonization of CT[6]. Reproduced with permission from ref 243. Copyright 2015 Wiley-VCH Verlag GmbH & Co. KGaA.

(375/1) and N₂ (339/1). The highly selective adsorption of CO₂ observed in this case was attributed to the porous nanostructure of the compound and the hydroxyl groups of pillar[5]arene 12[5].

Our group reported the gas and organic-vapor uptake properties of crystalline pillar[6]arene 8[6] bearing 12 hydroxyl moieties.²⁴² 8[6] assembled into a highly symmetrical one-dimensional structure in the crystalline state (Figure 53).⁷³

Pillar[6]arene 8[6] bearing 12 hydroxyl moieties and an even number of benzene rings on its rims formed multiple intramolecular hydrogen bonds in an alternating up-and-down manner, which stabilized its hexagonal structure (Figure 53a and b). The rigid hexagonal structure of this material assembled to form a 2D hexagonal sheet structure along the *a* and *b* axes, and a 1D channel structure along the *c* axis (Figure 53c). Acetone molecules were included in the channels, and the crystals were consequently heated under reduced pressure to give activated

porous crystals. The 1D channels were retained even after the removal of the acetone molecules because the structure was stabilized by multiple hydrogen-bonding interactions in the same way as the per-hydroxylated pillar[5]arene 12[5]. This crystalline material not only adsorbed various gases (Figure 53d) such as CO₂ (3.3 Å), N₂ (3.7 Å), and *n*-butane (4.3 Å), but also adsorbed organic vapors (Figure 54e) such as *n*-hexane (4.9 Å) and cyclohexane (6.7 Å). The broad adsorption characteristics of this crystalline material were attributed to the permanent one-dimensional pores with the same cavity size as pillar[6]arene 8[6] (ca. 6.7 Å), which was larger in size than the gases and organic vapors described above. The pore size of the one-dimensional channels was determined to be 4.10 Å using a molecular probe technique.

We also constructed 2D hexagonal sheets using a molecular tailing concept, where molecules with triangular, tetragonal, and hexagonal structures can be used to form densely packed

structures because of their highly symmetrical structures. It is noteworthy, however, that pentagonal molecules cannot form densely packed structures. On the basis of this concept, the 2D supramolecular polymerization of hexagonal per-hydroxylated pillar[6]arene molecules **8[6]** led to the formation of 2D hexagonal sheets.²⁴³ 2D supramolecular polymerization can be induced by the oxidation of hydroquinone to benzoquinone units because the CT complexation process between the hydroquinone and benzoquinone units of pillar[6]arenes results in the intermolecular connection of pillar[6]arene molecules (Figure 54b).

The highly ordered structure of the 2D sheets formed regular fibrous structures **CT[6]**. The 2D sheets also had pores (4.04 Å), which were derived from the original pores of the pillar[6]arene crystals (4.10 Å). The 2D sheets were converted to carbons by the calcination of the 2D sheets **PC[6]** at 900 °C for 2 h under an inert atmosphere (Figure 54c). Even after the calcination of the 2D sheets, the fibrous structures remained intact. Furthermore, the fibrous carbon had pores that were similar in size to the original starting compound pillar[6]arene assembly (4.09 Å). This method for the creation of porous carbon does not require inorganic templates, and therefore represents a simple process for the synthesis of porous carbons with angstrom-sized pores.

Our group reported the occurrence of unexpected alkane uptake behavior pronounced alkane-shape and alkene-length selectivity using activated per-ethylated pillar[5]arene **2[5]** crystals (Figure 55).¹⁴⁴

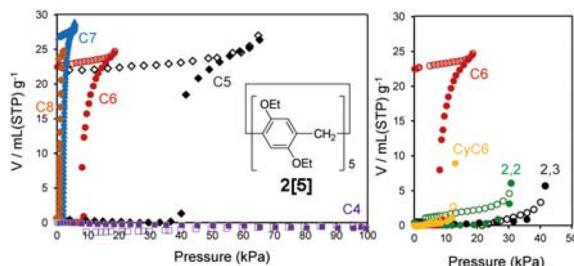


Figure 55. Sorption isotherms of activated crystals **2[5]** toward the gases and vapors of several linear alkanes, including methane (C1, pink triangle), ethane (C2, orange diamonds), *n*-butane (C4, purple squares), *n*-pentane (C5, black diamonds), *n*-hexane (C6, red circles), *n*-heptane (C7, blue triangles), and *n*-octane (C8, brown diamonds), as well as several branched alkanes, including 2,2-dimethylbutane (2,2, green circles), 2,3-dimethylbutane (2,3, black circles), and cyclohexane (CyC6, yellow circles) at 258 °C. Solid symbols = adsorption; open symbols = desorption. Reproduced with permission from ref 144. Copyright 2015 Wiley-VCH Verlag GmbH & Co. KGaA.

During the adsorption process, crystals without solvent molecules could quantitatively take up linear *n*-alkanes with gate-opening pressure. During the desorption process, the adsorbed linear *n*-alkanes were not released even under reduced pressure because they were stabilized by multiple CH/π interactions. In contrast, the cyclic and branched alkanes were not absorbed in the same way because the pillar[5]arene cavity was a poor fit for these cyclic and branched alkanes.

6.2.4. Composite Materials Based on Pillar[n]arenes. Huang and co-workers reported the preparation of composite materials from the polymerized ionic liquid polymer and the per-carboxylated pillar[5]arene **45[5]** (Figure 56a).²⁴⁴

This composite consisted of particles in the nano range (20–50 nm) that formed the sponge-like structure **6**. Furthermore, the composite material had a large pore volume (350 m²/g) and

selectively adsorbed alcohols, with an especially high affinity for 1,4-butanediol. In contrast, this composite showed a much lower affinity for monoalcohols. These foundations are derived from the host–guest ability of pillar[5]arene in the solution state. Pillar[5]arene can form more stable host–guest complexes with diols than it can with monoalcohols.

Stoddart and co-workers reported the construction of the metal organic framework (MOF) **7** bearing an active pillar[5]-arene domain (Figures 56b).⁸⁷ The pillar[5]arene-based MOF **7** was prepared by heating a mixture of Zn(NO₃)₂·6H₂O and pillar[5]arene **60[5]** carrying two carboxylic acid groups in DMF at 100 °C for 24 h. This pillar[5]arene-based MOF selectively adsorbed neutral and positively charged electron-deficient aromatic guests, including the pyridinium and viologen salts **G89** and **G90**, as well as 1,4-dinitrobenzene (**G91**). The formation of CT interactions between the guest molecules and the active domain of the pillar[5]arenes in the MOF allowed for this complexation process to be monitored on the basis of the color change of the solution. MOFs containing active enantiopure pillar[5]arene domains were also prepared by Stoddart and co-workers.¹⁴²

6.3. Assembly of Pillar[n]arenes on Inorganic Surfaces

The high functionality of pillar[*n*]arenes can contribute to improvements in their compatibility with a wide range of inorganic materials, including metal nanoparticles, nanocarbons, MOFs, and silica.

6.3.1. Metal Nanoparticles. Capping agents containing amino, carboxyl, or sulphydryl groups can be used to stabilize metal particles on the nanoscale by preventing their aggregation through the formation of coordination interaction to the metal surface. Yang and co-workers reported gold nanoparticles (AuNPs) stabilized by pillar[5]arene with 10 carboxylate moieties **46[5]** (Figure 57a).²⁴⁵

Pillar[5]arene-modified AuNPs were synthesized by reducing HAuCl₄ with NaBH₄ in the presence of the per-carboxylated pillar[5]arene **46[5]**. The resulting pillar[5]arene-stabilized AuNPs showed good dispersion characteristics in aqueous media and a narrow size distribution (3.1 ± 0.5 nm). The pillar[5]arene molecules immobilized on the AuNPs had vacant pores, allowing them to capture guest molecules. The addition of the viologen guest dimer **G92** led to a change in the color of this system, with the viologen dimer acting as a cross-linking agent between the AuNPs to induce the 1D and 3D assembly of the pillar[5]arene-stabilized AuNPs. Huang and co-workers reported the construction of various nanostructures from carboxylated pillar[6]arene **13[6]**-modified AuNPs bearing a paraquat guest with a hydrophobic chain (**G93**).²⁴⁶ These host–guest interactions resulted in the formation of numerous structures, including supramolecular micelles, onion-like disks, and vesicles (Figure 57b). The feed ratio of the paraquat guest **G93** to the pillar[6]arene **13[6]**-modified AuNPs was found to be critical to the formation of the various supramolecular assemblies. Park and co-workers reported the preparation of large AuNPs using **46[5]** as a stabilizer.²⁴⁷ HAuCl was heated at reflux in water for 10 min before being treated with the per-carboxylated pillar[5]arene **46[5]**. The diameter of the resulting AuNPs was around 17 nm. Furthermore, the AuNPs showed high stability toward a variety of salts, as well as variations in the pH. Pillar[5]arenes bearing cationic moieties are also good stabilizing agents for AuNPs. Huang and co-workers reported that pillar[5]arene **67[5]** bearing 10 imidazolium cations could be used as a stabilizer to form AuNPs (Figure 57c).¹⁰³ The use of a pillar[5]arene bearing

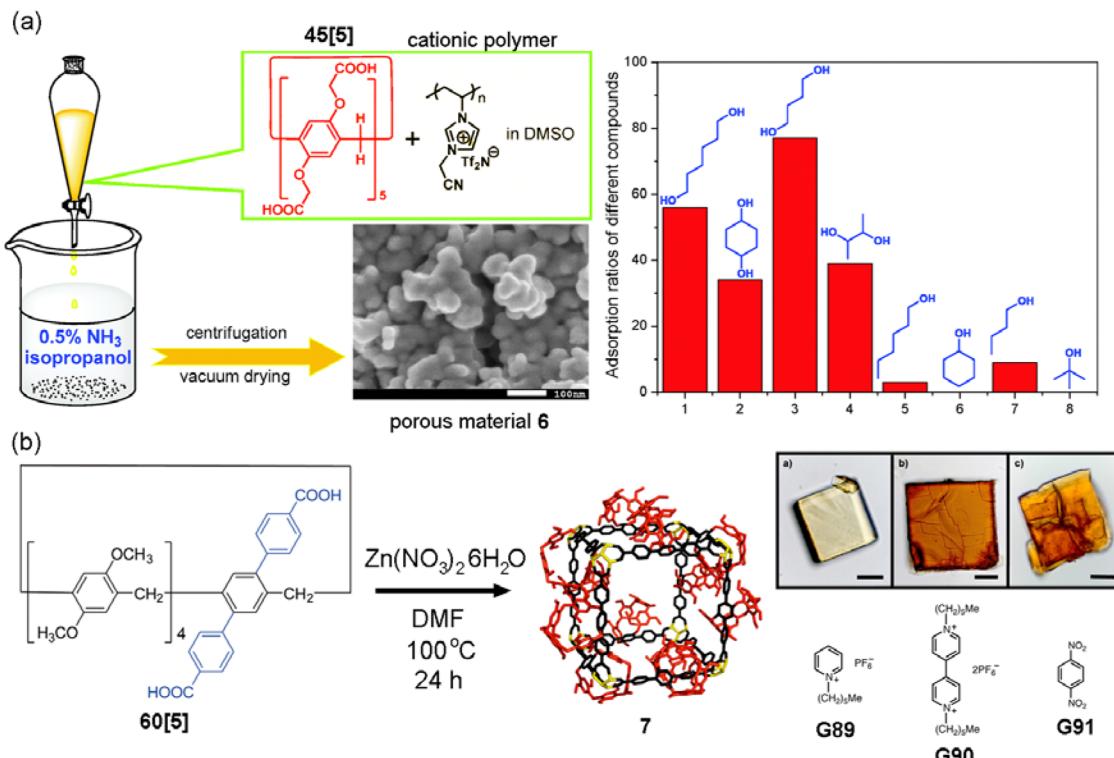


Figure 56. (a) Synthetic route to and SEM image of porous material 6 based on pillar[5]arene 45[5] bearing 10 carboxylic acid groups and cationic polymer. Adsorption ratios of different alcohols at a concentration of 1.00 mM after being treated with 1 equiv of porous material 6. Reproduced with permission from ref 244. Copyright 2014 The Royal Society of Chemistry. (b) Formation of metal organic framework 7 by the reaction of the pillar[5]arene-based structure 60[5] with Zn(NO₃)₂·6H₂O. Optical microscopy images of 7 a) with no guest (scale bar, 200 mm), b) after the uptake of G90 (scale bar, 100 mm), and c) after the uptake of G91 (scale bar, 100 mm). Reproduced with permission from ref 87. Copyright 2012 American Chemical Society.

10 imidazolium groups provided a shell of imidazolium cations around the AuNPs, which inhibited the aggregation of the AuNPs. The use of an ammonium cation-bearing pillar[5]arene also prevented the aggregation of the AuNPs and acted as a stabilizer.²⁴⁸ Zhou and co-workers reported the use of the monofunctionalized pillar[5]arene 137[5] bearing a thiol moiety as a stabilizer (Figure 58a).²⁴⁹

The surfaces of the AuNPs were covered with pillar[5]arenes, which enabled them to capture cationic guest molecules. The resulting pillar[5]arene-covered AuNPs were then treated with an ammonium derivative bearing an anthracene moiety (G94), which can undergo [4+4] cycloaddition/decycloaddition reactions when it is irradiated with UV light or heated, respectively. The AuNPs underwent reversible aggregation and dissociation processes when they were irradiated with UV light or heated in the presence of G94 because of the cycloaddition/decycloaddition of this guest molecule under these conditions. In this way, the guest molecule could be used as a switch depending on the conditions applied to the system.

Metal nanoparticles have also been synthesized using a variety of metals. For example, Xue and co-workers reported the preparation of AgNPs with narrow size distributions using the per-carboxylated pillar[5]arene 46[5] as a stabilizer (Figure 58b).²⁵⁰ The addition of spermine or its analogues to these systems led to the aggregation of the AgNPs, which resulted in a color change. This change in the color of the solution was attributed to the spermine molecules acting as cross-linking agents to connect the individual silver ions. This color change could therefore be used as a visual cue for the detection of spermine analogues in water through host–guest interactions.

Yang and co-workers synthesized per-carboxylated pillar[5]-arene 46[5]-modified quantum dots using a ligand-exchange method.²⁵¹ Quantum dots provide strong fluorescence signals with long lifetimes, and can therefore be used for biological sensing and display panels. Yang et al. also reported the synthesis of pillar[5]arene-modified Fe₃O₄ nanoparticles, which can be used as magnetic solid-phase extraction absorbents.²⁵²

6.3.2. Nanocarbons. Nanoscale carbons such as fullerenes, carbon nanotubes, nanodiamonds, and graphenes have attracted considerable interest because of their unique structural, electrical, and mechanical properties. One of the main challenges associated with the functionalization of pillar[n]arenes on nanocarbons is the development of efficient strategies for increasing the solubility of nanocarbons and introducing molecular recognition sites.

Haung and co-workers reported the dispersion of multiwalled carbon nanotubes (MWNTs) using the host–guest complex formed between the per-carboxylated pillar[6]arene 13[6] and the neutral guest molecule G95 bearing a pyrene moiety (Figure 59).¹⁶⁰

MWNTs did not disperse in aqueous media with a neutral guest, but dispersed well in the presence of the per-carboxylated pillar[6]arene 13[6]–neutral guest G95 complex under ultrasonic irradiation. This complex contained both hydrophobic and hydrophilic moieties, and was therefore capable of dispersing MWNTs in aqueous media. The MWNT dispersion was also pH responsive, in the sense that making the pH of the mixture acidic resulted in the precipitation of the MWNTs. Notably, the precipitate dispersed in aqueous media when the pH of the mixture was taken back to being neutral. Haung et al. also

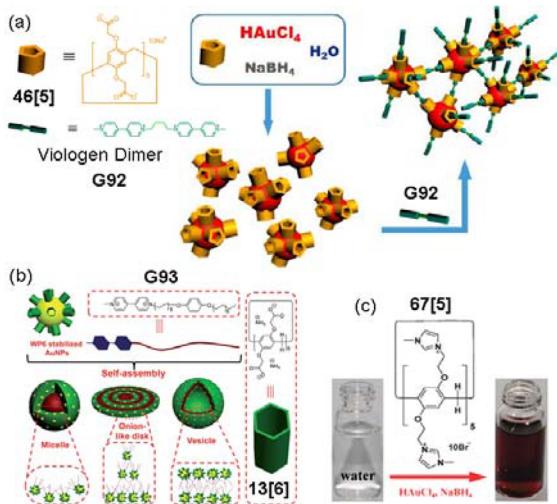


Figure 57. (a) Schematic representation of the process involved in the formation of $46[5]$ -modified AuNPs and their supramolecular self-assembly upon the addition of the guest viologen dimer $G92$. Reproduced with permission from ref 245. Copyright 2012 American Chemical Society. (b) Chemical structures of hydrophobic chain functionalized paraquat derivative $G93$ and water-soluble pillar[6]arene $13[6]$, and a schematic illustration of the self-assembly of $13[6]$ -stabilized AuNPs and $G93$ into various hybrid nanostructures such as micelles, onion-like disks, and vesicles in water. Reproduced with permission from ref 246. Copyright 2014 Royal Society of Chemistry. (c) Stabilization of AuNPs by the cationic pillar[5]arene $67[5]$. Reproduced with permission from ref 103. Copyright 2012 Royal Society of Chemistry.

reported the photoresponsive dispersion/precipitation of MWNTs using a photoresponsive host–guest complex.¹⁶³ In this case, they used a guest molecule bearing pyrene and lutidinium moieties that were connected via a photocleavable 2-nitrobenzyl ester group. The MWNTs were dispersed in an aqueous solution with a host–guest complex formed between

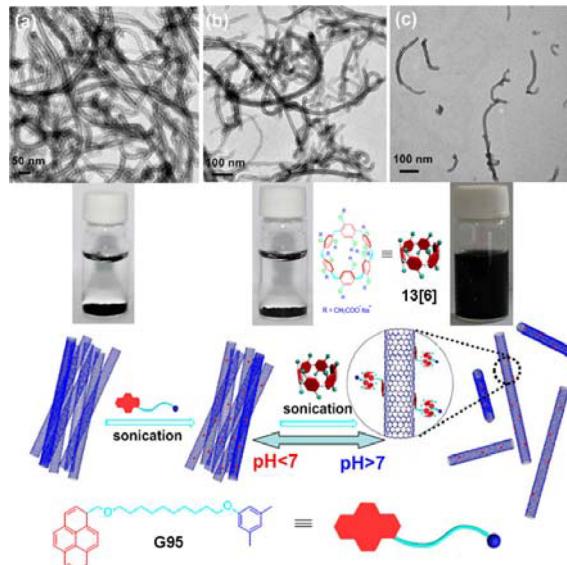


Figure 59. (a) (top) TEM images of (a) MWNTs, (b) $G95$ and MWNTs, and (c) the $13[6] \supset G95$ /MWNT complexes, as well as photographs of the corresponding mixtures with water. (bottom) Illustration of the pH-responsive solubility of the MWNTs in the presence of the $13[6] \supset G95$ complex. Reproduced with permission from ref 160. Copyright 2012 American Chemical Society.

per-carboxylated pillar[6]arene and a UV-responsive guest. The MWNTs precipitated from solution following the irradiation of the mixture with UV light because of the dissociation of the photocleavage guest.

Diao and co-workers reported the dispersion of reduced graphene oxide in aqueous media using the amphiphilic nonsymmetric pillar[5]arene $138[5]$ bearing five hydrophilic amino groups on one rim and five hydrophobic alkyl chains on the other rim (Figure 60).²⁵³

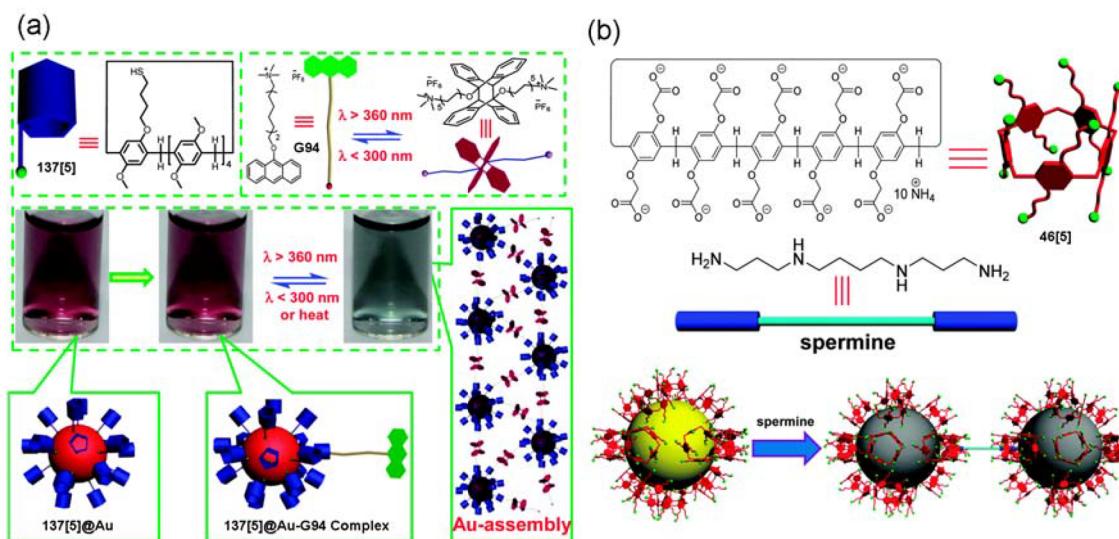


Figure 58. (a) Chemical structures and representations of the monosulphydryl functionalized pillar[5]arene $137[5]$ and quaternary ammonium salt functionalized anthracene $G94$, as well as schematic representations of the photoresponsive assembly/disassembly of $137[5]$, which was stabilized by gold nanoparticles. Reproduced with permission from ref 249. Copyright 2015 Royal Society of Chemistry. (b) Chemical structures and representations of the water-soluble pillar[5]arene $46[5]$ and spermine. Illustration of the application of the $46[5]$ -stabilized silver nanoparticles for the visual detection of spermine. Reproduced with permission from ref 250. Copyright 2014 Royal Society of Chemistry.

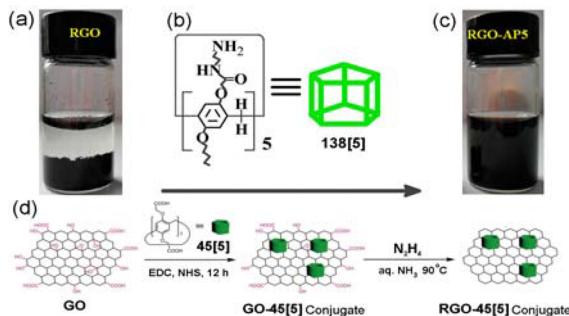


Figure 60. (a) Photo of reduced graphene oxide in aqueous media. (b) Chemical structure of the amphiphilic pillar[5]arene 138[5]. (c) Photo of reduced graphene oxide–138[5] composites in aqueous media. Reproduced with permission from ref 253. Copyright 2013 American Chemical Society. (d) Modification of the water-soluble pillar[5]arene 45[5] via the formation of covalent ester bonds to give a homogeneous dispersion of reduced graphene oxide in aqueous solution. Reproduced with permission from ref 255. Copyright 2015 Wiley-VCH Verlag GmbH & Co. KGaA.

A dispersion of graphene oxide in aqueous media was treated with 138[5], and the resulting mixture was sonicated. The mixture was then treated with hydrazine hydrate to give an aqueous dispersion of reduced graphene oxide–138[5] hybrids. It is noteworthy that this reduction process resulted in the formation of a precipitate when it was conducted without 138[5]. The self-assembly of 138[5] on the surface of the reduced graphene oxide made a considerable contribution to the formation of the water-dispersed reduced graphene oxide–138[5] hybrids. Zhao and co-workers reported the application of water-soluble pillar[n]arene-functionalized graphene oxide for *in vitro* Raman and fluorescence dual mode imaging experiments.²⁵⁴

Water-dispersed reduced graphene oxide–pillar[5]arene hybrids can be also prepared by connecting reduced graphene to pillar[5]arene 45[5] via the formation of covalent ester bonds (Figure 60d).²⁵⁵ Water-dispersed hybrids were obtained by the formation of ester bonds between the hydroxyl moieties of graphene oxide and the carboxylic acid groups on per-carboxylic acid pillar[5]arene 45[5]. The resulting solution was homogeneous even after the complete reduction of graphene oxide.

6.3.3. Metal Organic Frameworks. Yang and co-workers reported the occurrence of pH-dependent and competitive guest-responsive cargo release from nano-MOFs covered with the per-carboxylated pillar[5]arene 46[5] through a host–guest complexation process (Figure 61).²⁵⁶

The treatment of a nano-MOF material with the pyridinium guest molecule allowed for the synthesis of the corresponding nano-MOF–pyridinium guest complex. The surface of the nano-MOF–pyridinium guest complex 8 was then capped with per-carboxylic acid pillar[5]arene 46[5] after loading of the cargo. Under acidic conditions, the system released the cargo from the nano-MOF. The addition of viologen as a competitive agent also led to the release of the cargo.

6.3.4. Silica. Yang and co-workers reported the functionalization of pillar[5]- and pillar[6]-arene molecules with silica particles through the formation of a covalent bond between the two materials (Figure 62a).²⁵⁷

The silica surface was initially activated with SiCl₄, and then treated with the per-hydroxylated pillar[5]- and pillar[6]-arenes 12[5] and 8[6] to allow for the immobilization of these materials on the silica surface. These pillar[5,6]arene-modified silica

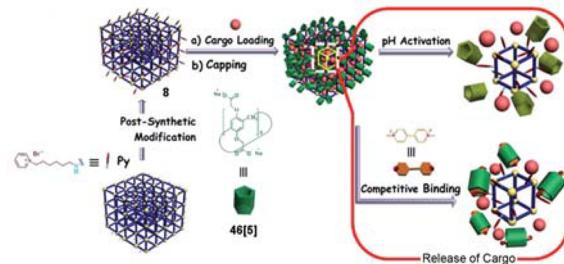


Figure 61. Schematic representation of stimuli-responsive nanocarriers based on the mechanized nano-MOFs 8, with positively charged pyridinium units as stalks encircled by pillar[5]arenes 46[5] on the surfaces. The mechanized nanovalves in 8 responded to changes in the pH or competitive binding to regulate the release of the cargo molecules. Reproduced with permission from ref 256. Copyright 2015 The Royal Society of Chemistry.

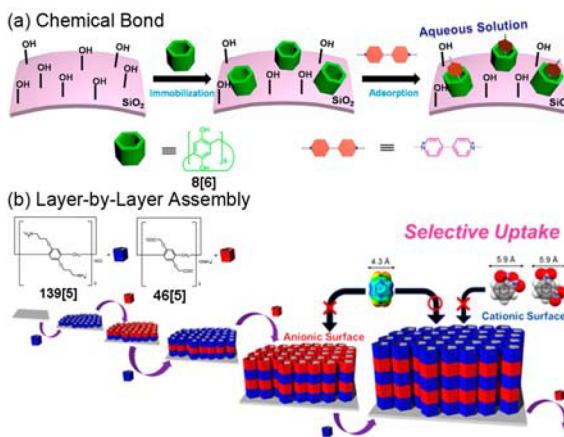


Figure 62. (a) Schematic illustration of the immobilization of per-hydroxylated pillar[6]arene 8[6] on silica and the adsorption of paraquat from an aqueous solution using the resulting hybrid materials. Reproduced with permission from ref 257. Copyright 2015 American Chemical Society. (b) Layer-by-layer assembly by the consecutive adsorption of cationic pillar[5]arene 139[5] and anionic pillar[5]arene 46[5]. The multilayered film showed size-selective and surface potential-dependent molecular recognition properties. Reproduced with permission from ref 258. Copyright 2015 American Chemical Society.

particles adsorbed paraquat in aqueous media. The pillar[6]-arene-modified silica particles adsorbed approximately twice as much paraquat as the corresponding pillar[5]arene-modified silica particles.

Our group previously reported the construction of pillar[5]-arene-based multilayer films on a silica substrate (Figure 62b).²⁵⁸ The multilayer films were obtained using a layer-by-layer assembly method, which is generally used for the construction of polymer-based thin films by the consecutive adsorption of oppositely charged polyelectrolytes on a silica surface. Pillar[5]-arene-based multilayer materials were obtained by alternating the adsorption steps with the cationic pillar[5]arene 139[5] and the anionic pillar[5]arene 46[5]. The unique pillar-shaped structures and the presence of functional groups on both rims of the pillar[5]arenes contributed to the successful formation of multilayer films using pillar[5]arenes based on a layer-by-layer assembly. The resulting films possessed the molecular recognition abilities of pillar[5]arenes, in that the films only adsorbed 1,4-dinitrobenzene and did not exhibit any adsorption

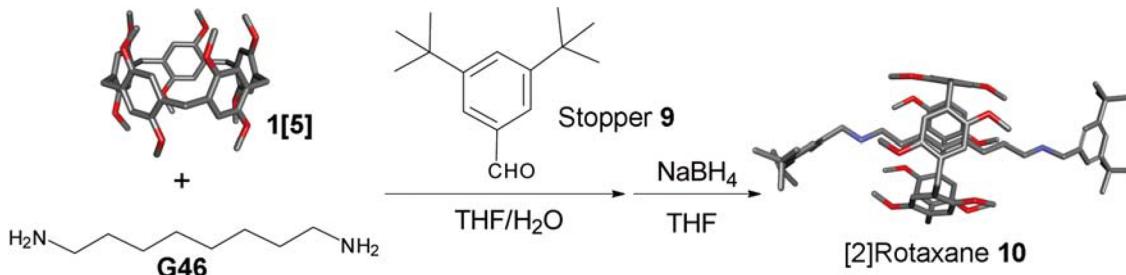


Figure 63. First pillar[5]arene-based [2]rotaxane **10** produced with end-capping by reaction between diamine axle **G46** and an aldehyde stopper **9**.

ability toward 1,2- or 1,3-dinitrobenzene. In addition, the surface electrostatic potential of these systems resulted in their molecular recognition ability. 1,4-Dinitrobenzene was adsorbed on the surfaces of films with a cationic surface, but not on the surfaces of films with an anionic surface. The amount of 1,4-dinitrobenzene adsorbed onto the surfaces of these systems could be tuned, with the amount of adsorbed 1,4-dinitrobenzene increasing with an increase in the number of deposited layers.

7. MECHANICALLY INTERLOCKED MOLECULES

7.1. Rotaxanes

Rotaxanes, using pillar[5]arene wheels, were initially investigated using simple linear alkanes as the station. The first pillar[5]arene-based rotaxane was reported by Stoddart et al.⁸² On the basis of the formation of a host–guest complex between per-methylated pillar[5]arene **1[5]** and alkanediamines, they investigated end-capping reactions of the complex between diaminoocatane **G46** and **1[5]** with an aldehyde-end stopper **9** to form [2]rotaxane **10** (Figure 63).

The subsequent reduction of the diamine with NaBH_4 afforded the [2]rotaxane **10**, but its yield was low (7%) due to the weak host–guest complexation between **G46** and **1[5]** ($K = 70 \pm 10 \text{ M}^{-1}$). Huang and co-workers synthesized [2]rotaxanes based on pillar[5]arene/alkane recognition by esterification reactions,^{259,260} in yields of 16–35%. The driving forces for the host–guest complexation are weak CH/π interactions; thus, these yields were considered to be reasonable. We reported the high yield synthesis of pillar[5]arene-based rotaxanes using a good cationic axle for pillar[5]arenes.²⁶¹ We used a pyridinium derivative as an axle and the CuAAC reaction for the end-capping reaction (Figure 64).

Pyridinium derivatives form stable host–guest complexes with pillar[5]arenes driven by cationic/ π interactions ($K > 10^4 \text{ M}^{-1}$). CuAAC reaction between the alkyne-end of pseudo[2]rotaxane, composed of axle **11**, with wheel **2[5]** and azido-stopper **12** afforded the [2]rotaxane **13** in high yield (75%). Rotation of the pillar[5]arene wheel in the [2]rotaxane was completely inhibited due to the existence of the axle in the rotaxane. From ^1H NMR measurement, the conformation of the pillar[5]arene wheel was assigned as the **a** and **a'** forms. The substituents on the pillar[5]arene rims are ethoxy moieties. There are no strong intramolecular interactions between the ethoxy moieties; thus conformers **a** and **a'** are the most stable conformers in [2]rotaxane. The ratio of **a:a'** conformers in [2]rotaxane was 50:50. A new challenge is the enantioselective synthesis of pillar[*n*]arene rotaxanes. The high yield synthesis of a [2]-rotaxane using a cationic imidazolium axle was reported by Huang and co-workers.²⁶² The [2]rotaxane showed solvent- and thermo-driven molecular motions and supramolecular gel formation.

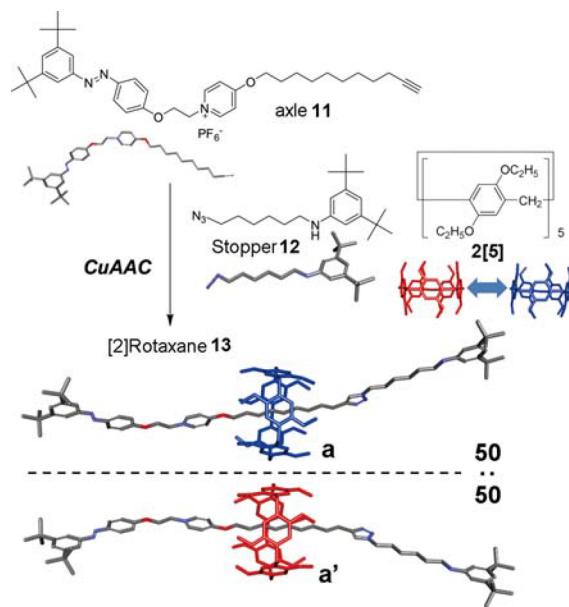


Figure 64. Planar chiral [2]rotaxanes **13** by end-capping using the CuAAC reaction.

We used the CuAAC reaction for the efficient end-capping reactions to produce the [2]rotaxane in high yield. However, the C4 linker with two 1,2,3-triazole groups, which was generated by the CuAAC reaction of alkyne and azide moieties, was a good guest station ($K > 10^4 \text{ M}^{-1}$).¹¹¹ We synthesized pillar[5]arene-based [2]rotaxanes based on multiple CuAAC reactions (Figure 65).²⁶³ The multiple CuAAC reactions generated a good station, *n*-butylene with two 1,2,3-triazole moieties at both ends.

First, the CuAAC reaction of 1,4-diazidobutane with excess 1,7-octadiene afforded an axle containing one station and two alkyne moieties at both ends of axle **14** (Figure 65a). Second, the CuAAC reaction between the axle **14** and azido-stopper **15** in the presence of pillar[5]arene **2[5]** afforded [2]rotaxane **16** in moderate yield (54%). In contrast, when 1,7-octadiene was reacted with excess 1,4-diazidobutane by the CuAAC reaction, an axle with two azide moieties **17** was afforded (Figure 65b). There were no good stations for pillar[5]arene in the axle. The CuAAC reaction between the axle **17** and alkyne-stopper **18** in the presence of pillar[5]arene **2[5]** then resulted in [2]rotaxane containing two stations with equal energy levels **19** that exhibited shuttling of the pillar[5]arene wheel between the stations. In this reaction, the first CuAAC reaction produces one good station, the butylene with two triazole ends. Thus, formation of [2]pseudorotaxane occurred. The second CuAAC reaction then achieves not only the end-capping reaction to inhibit the

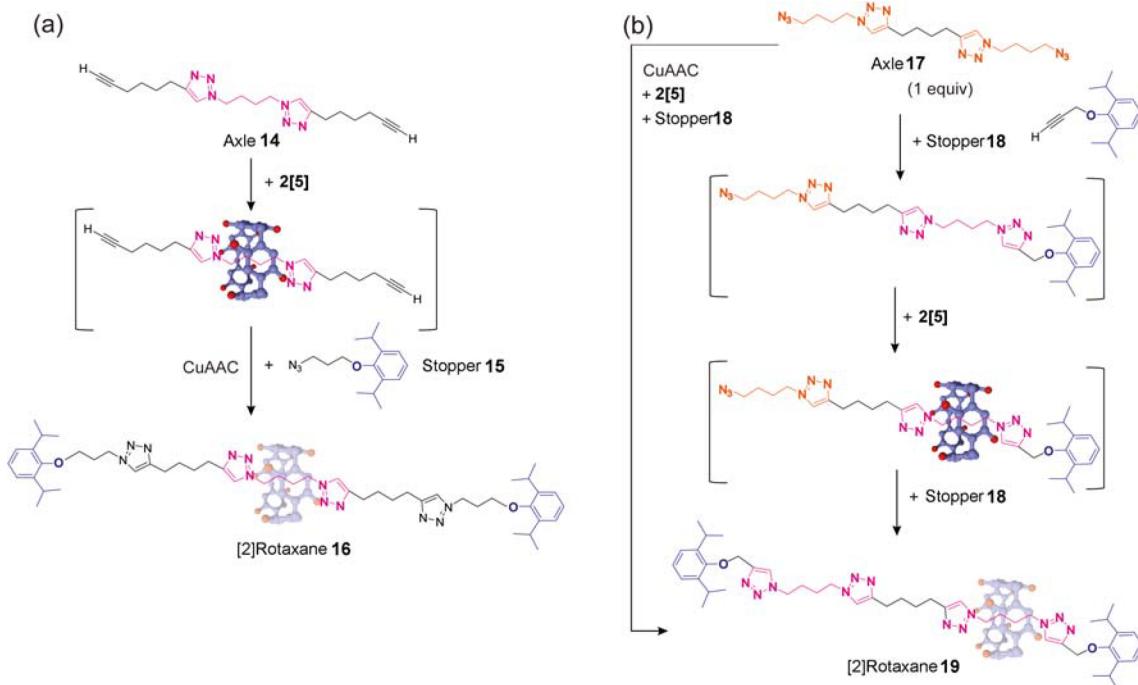


Figure 65. [2]Rotaxanes containing (a) one and (b) two stations produced by a stepwise CuAAC reaction. Reproduced with permission from ref 263. Copyright 2015 American Chemical Society.

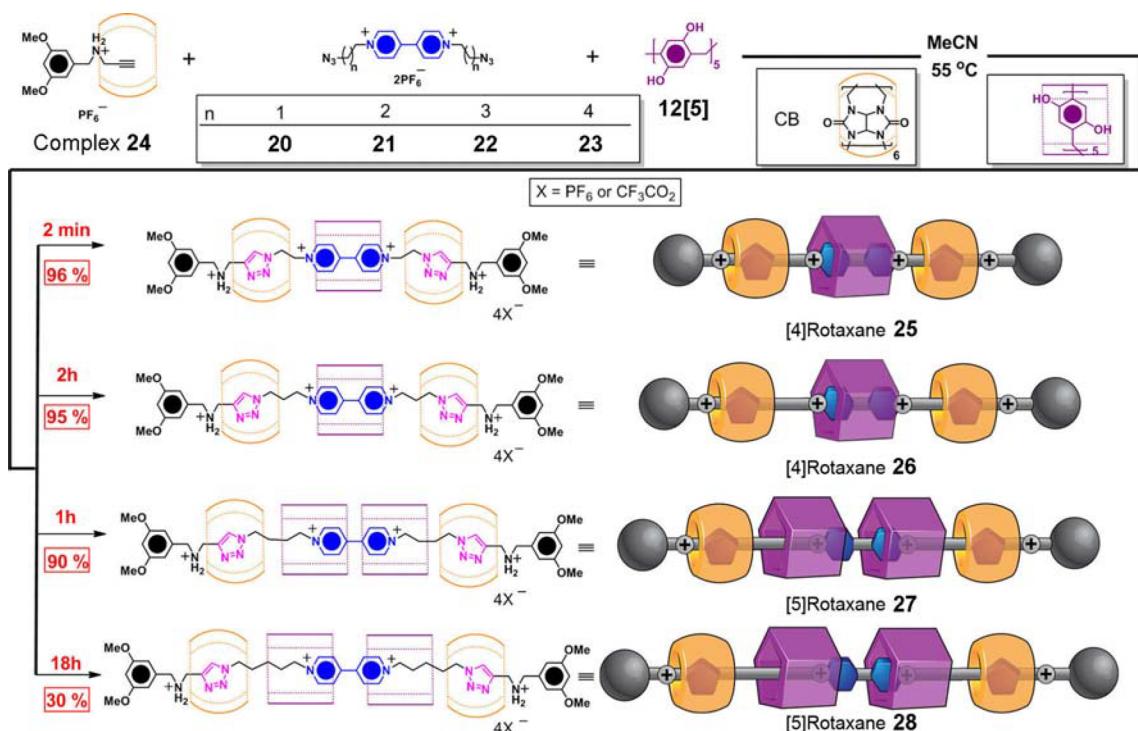


Figure 66. Synthesis of the hetero[4]- and hetero[5]rotaxanes consisting of pillar[5]arene and CB[6] wheels by the copper-free AAC reaction. Reproduced with permission from ref 264. Copyright 2013 American Chemical Society.

dethreading of the pillar[5]arene wheel, but also produces another equal energy level station.

Stoddart and co-workers synthesized [4]- and [5]-heterorotaxanes consisting of heteromacrocyclic hosts, pillar[5]-arene and CB[6] wheels, or pillar[6]arene and CB[6] wheels (Figures 66 and 67).²⁶⁴

The per-hydroxylated pillar[n]arenes have hydrogen donor OH groups at both rims. CB[6] has C=O moieties as hydrogen acceptors. Therefore, mixing these heteromacrocyclic wheels in the presence of an axle resulted in a high level of preorganization for the rotaxanation by means of the multiple hydrogen-bonding interactions between C=O moieties of CB[6] and phenol moieties of pillar[n]arenes. When per-hydroxylated pillar[5]-

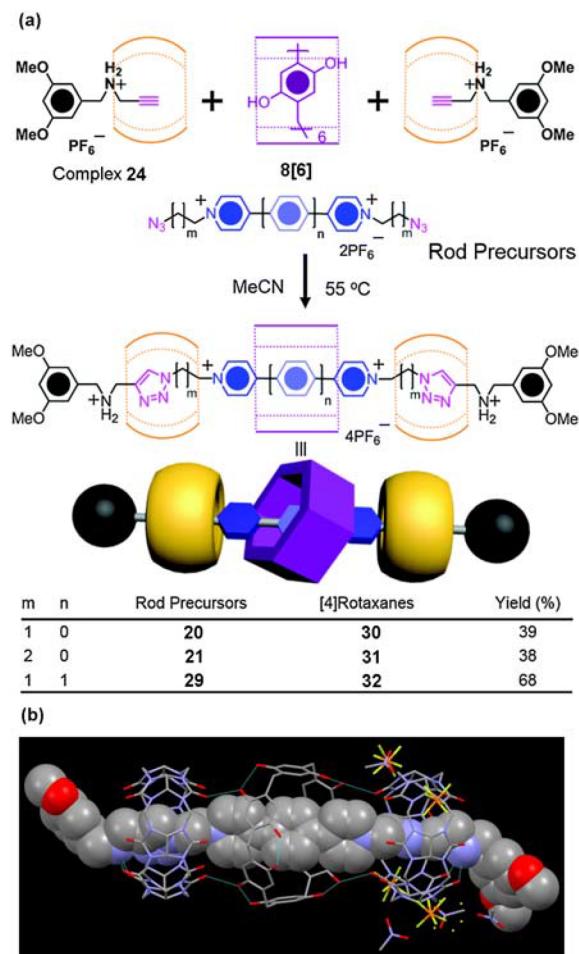


Figure 67. (a) Synthesis of the hetero[4]rotaxanes consisting of one pillar[6]arene and two CB[6] wheels by copper-free AAC reaction and (b) X-ray crystal structure of 32. Reproduced with permission from ref 265. Copyright 2014 Royal Society of Chemistry.

arene **12[5]** was used as the wheel, axles containing a viologen moiety **20–22** were suitable for the synthesis of rotaxanes. The CuAAC reaction of the preorganized pseudorotaxane structure, consisting of pillar[5]arene **12[5]**, and viologen axle with stopper-CB[6] complex **24**, yielded two [4]rotaxanes and one [5]rotaxane in >90% yields. When short spacers were used between viologen and azide moieties **20** ($n = 1$) and **21** ($n = 2$), [4]rotaxanes (**25** and **26**) containing two CB[6] and one pillar[5]arene wheels were obtained in >95% yields. In contrast, when a long spacer **22** ($n = 3$) was used, a [5]rotaxane containing two CB[6] and two pillar[5]arene wheels **27** was produced in >90% yield. These results indicate that the long alkyl spacer is sufficient to include two pillar[5]arene wheels, but the short alkyl spacer is not. In the case of a longer spacer **23** ($n = 4$), a hetero[5]rotaxane **28** containing two pillar[5]arene wheels was produced, but its yield decreased (30%) because the length of the spacer is too long to form a stable preorganized pseudorotaxane structure. Another interesting aspect of the heterorotaxane formation was that the preorganization also accelerated the reaction rate of 1,3-dipolar cycloadditions between azides and alkynes. Thus, the formation of these rotaxanes proceeded even without a Cu(1) catalyst. The conformations of the pillar[5]arene wheels in the rotaxanes were the C_5 -symmetric **a/a'** forms as the major component, but also contained **b/b'** and **c/c'** forms as minor components. Conformational isomer **d/d'**, which is the

most stable conformation in per-hydroxylated pillar[5]arene **12[5]** due to the intramolecular hydrogen bonds, was not found.²⁷ A possible reason for this is the number of the phenolic moieties without intramolecular hydrogen bonds. **a/a'**, **b/b'**, and **c/c'** forms have more than six phenolic groups, which can form intermolecular hydrogen bonds between pillar[5]arene and CB[6] wheels to stabilize the preorganized pseudorotaxane structure. However, the **d/d'** conformers only have two phenolic groups, which can participate in intermolecular hydrogen bonding with CB[6].

The same group expanded the idea for the efficient synthesis of pillar[6]arene-based hetero[4]rotaxanes consisting of one axle, two CB[6] rings, and one pillar[6]arene ring (Figure 67).²⁶⁵

In axles containing a viologen station, which were used for the synthesis of heterorotaxanes containing pillar[6]arene and CB[6] rings (Figure 67, 20 and 21), the yields of the hetero[4]rotaxanes (**30** and **31**) were not high (38–39%). However, when an axle contained a ter-phenyl moiety **29**, the yield of the hetero[4]rotaxane **32** was increased (68%). A possible explanation is that the ter-phenyl moiety should fit into the cavity of pillar[6]arene. The rotation of units of the pillar[6]arene ring in the hetero[4]rotaxanes was not inhibited at room temperature due to the large cavity of pillar[6]arene. Pillar[6]arene has 13 conformers (Figure 9c). The most stable conformation of per-hydroxylated pillar[6]arene in the hetero[4]rotaxane **32** obtained from calculation was the alternating up-to-down arrangement (**g** form), which is the most stable structure in per-hydroxylated pillar[6]arene because all 12 phenolic moieties can form intramolecular hydrogen bonds. The X-ray crystal structure of the [4]rotaxane **32** also supported the results from calculations (Figure 67b). The conformation of the pillar[6]arene ring in the hetero[4]rotaxane **32** exhibited an up-to-down arrangement. Intermolecular hydrogen bonds were also found between the pillar[6]arene and CB[6] rings to form a stable preorganized pseudorotaxane structure.

Rotaxanes having various structures and functions have been constructed using a pillar[5]arene wheel. Huang and co-workers reported a doubly threaded rotaxane dimer **33** with two stable structures by end-capping of the double-threaded dimer (Figure 68a).²⁶⁶

In chloroform, the dimer **33** formed a contracted state with a length of 31 Å because the NH/π interactions are stronger than CH/π interactions in the nonpolar chloroform solvent. However, the dimer **33** formed an extended state with a length of 37 Å in the polar solvent DMSO, because NH/π interactions are weaker than CH/π interactions in the polar DMSO solvent. Gallani and Nierengarten reported amphiphilic pillar[5]arene-containing [2]rotaxane **34** (Figure 68b).²⁶⁷ The [2]rotaxane **34** consisted of a hydrophobic axle, a pillar[5]arene wheel, and a hydrophilic stopper. Because of the good hydrophobic/hydrophilic balance, stable Langmuir films were obtained. Xue and co-workers synthesized a pillar[5]arene-based [1]rotaxane by preorganization of [2]pseudorotaxane structure by means of CH/π and cationic/anionic electrostatic interactions (Figure 68c).¹⁶⁷ Proton transfer from monocarboxylic acid pillar[5]arene **115[5]** to a linear alkane with a primary amine moiety at one end **G51** contributed to the formation of the highly preorganized [2]pseudorotaxane structure. Amidation between the primary amine group on the guest and the carboxylic acid group on the pillar[5]arene then gave [1]rotaxane **35** in high yield (73%).

We constructed an efficient FRET system based on the [2]rotaxane structure (Figure 69a).²⁶⁸

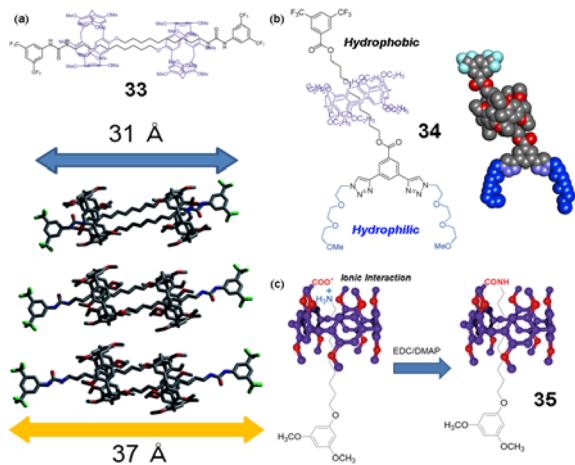


Figure 68. (a) Solvent-driven double-threaded dimer 33. Reproduced with permission from ref 266. Copyright 2012 Royal Society of Chemistry. (b) Chemical structure of amphiphilic [2]rotaxane 34, which can form Langmuir–Blodgett films. (c) High-yield synthesis of a pillar[5]arene-based [1]rotaxane 35 by preorganization using ionic interactions between the pillar[5]arene 115[5] and the guest G51.

A CuAAC reaction of an axle containing a bulky trityl moiety at one end and an alkyne at the other end 36, with an azide-perylene stopper 37 in the presence of a pillar[5]arene wheel with two pyrene moieties at the A1/A2 positions 92[5], afforded a [2]rotaxane 38 (yield 80%). The [2]rotaxane 38 exhibited a strong emission from the perylene by excitation of pyrene moieties in the wheel, indicating that FRET occurred from pyrene of the wheel to perylene in the axle. The emission intensity of [2]rotaxane 38 was approximately 26 and 20 times larger than that of the dumbbell 39 and a mixture of wheel 92[5] and dumbbell 39, respectively, due to the pyrene moiety of the wheel being fixed closely to the perylene moiety in the axle by rotaxanation.

A pillar[6]arene-based [2]rotaxane was first prepared by our group (Figure 69b).²⁶⁹ The same axle 36 to produce the pillar[5]arene-based FRET [2]rotaxane was used for the synthesis of pillar[6]arene-based [2]rotaxane 42 even though the association constant of the complex between pillar[6]arene and the axle was low ($K = 19.1 \pm 2.2 \text{ M}^{-1}$) due to the size mismatch between the pyridinium moiety and cavity size of pillar[6]arene. The AuAAC reaction between the axle 36 and bulky trityl stopper with azide moiety 40 in the presence of pillar[6]arene 1[6] afforded pillar[6]arene-based [2]rotaxane 42 in 14% yield. The axle consists of two types of alkyl linkers, short and long linkers in the axle. The association constant of the axle and pillar[6]arene was weak; thus, the pillar[6]arene wheel in the [2]rotaxane moved along the axle. As the temperature increased, the pillar[6]arene wheel moved from the short alkyl linker to the long alkyl linker due to the ΔS dominance.

7.2. Catenanes

Catenanes, which comprise two or more macrocycles, have been synthesized using pillar[5]arenes as constituent macrocycles. Our group reported a simple [2]catenane using a pillar[5]arene ring 2[5] and a pyridinium derivative bearing alkene groups at both ends 43 (Figure 70a).²⁷⁰ A ring-closing metathesis reaction of the alkene groups in the pyridinium derivative in the presence of pillar[5]arene ring 2[5] resulted in the formation of a [2]catenane 44. Pseudo[1]catenane 140[5], in which the guest alkyl cyclic chain connected to one pillar[5]arene unit, can be

produced by the CuAAC reaction between difunctionalized pillar[5]arene with alkyne moieties at the A1/A2 positions 90[5] and 1,12-diazidododecane (Figure 70b).

Pseudo[1]catenane formed a self-inclusion complex in chloroform, and had two enantiomers, the in-a and in-a' forms. The enantiomers were isolated by chiral column chromatography. Planar chiral inversion from in-a to out-a' or from in-a' to out-a occurred by the addition of competitive guests and in linear-shaped solvents such as dichloromethane and acetonitrile.²⁷¹ Liu and co-workers synthesized mechanically self-locked chiral gemini-catenanes 45 (Figure 70c). Amidation between A1/A2 difunctionalized pillar[5]arene with two carboxylic acid moieties 57[5] and 1,8-diaminoctane afforded pseudo[1]-catenane and self-locked gemini-catenanes with a/a or a'/a' forms of pillar[5]arenes (enantiomers) and a/a' form of pillar[5]arenes (meso-form).²⁷² The combination of different host molecules enables the construction of catenanes and their derivatives. Huang and co-workers reported the supramolecular structural change from pseudo[2]rotaxane to pseudo[1]-catenane (Figure 71a). They synthesized the A1/A2 difunctionalized pillar[5]arene with two crown ether units 141[5].²⁷³ A pseudo[1]catenane-like structure can be constructed by the threading followed by complexation method.

First, [2]pseudorotaxane was obtained by complexation between 141[5] and diaminoalkane. Addition of acid then led to the formation of a diammonium salt. The host–guest complex with the crown ether moieties between ammonium salts, induced upon addition of acid, was triggered to form a pseudo[1]-catenane-like structure.

Ma, Li, Jiang, Wen, and co-workers synthesized a bicyclic host consisting of a pillar[5]arene and a 1,5-dioxynaphthalene-based crown ether unit 142[5] (Figure 71b). The bicyclic host had the ability to capture two different guest molecules selectively and simultaneously.^{274,275} The pillar[5]arene ring formed a complex with an imidazolium cation, and the crown ether ring accommodated a viologen moiety. On the basis of the highly selective molecular recognition of the bicyclic compound, topologically novel mechanically interlocked molecules such as [2]rotaxane 46, [2]catenane 47, and [2]rota[2]catenane 48 can be created.²⁷⁶

7.3. Polyrotaxanes

Polyrotaxanes, in which many wheels are threaded onto a linear polymer chain, can be synthesized using pillar[5]arenes as wheels. Pillar[5]arenes form stable host–guest complexes with cationic molecules; thus, we investigated host–guest complexation between per-hydroxylated pillar[5]arene 12[5] and a viologen polymer (Figure 72a).²⁷⁷

When per-hydroxylated pillar[5]arene 12[5] was mixed with viologen polymer, formation of a polypseudorotaxane was observed (Figure 72b). By capping the chain ends with bulky adamantyl moieties through cationization, the first pillar[5]-arene-based polyrotaxane 49 was successfully prepared (Figure 72c).²⁷⁸

The emeraldine base form of polyaniline is the half-oxidized state, and thus can be oxidized upon the addition of oxidants, and reduced upon addition of reductants. Per-hydroxylated pillar[5]-arene 12[5] consists of reductant hydroquinone units, and thus can be used as a macrocyclic reductant. When reductant 12[5] was mixed with the emeraldine form of polyaniline, the blue solution color of the emeraldine form of polyaniline became colorless (Figure 73a).²⁷⁹

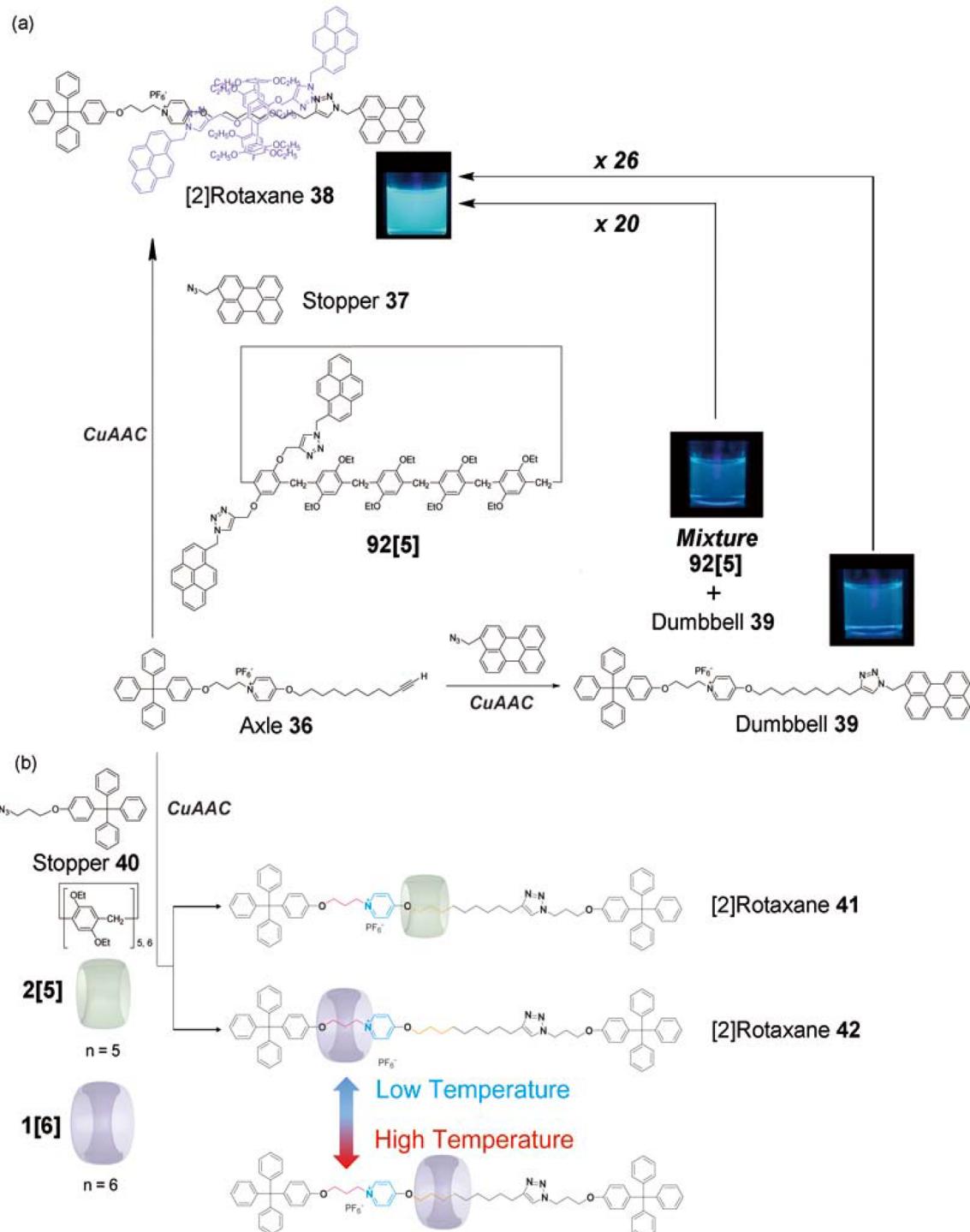


Figure 69. (a) [2]Rotaxane 38 showing FRET from the pyrene moiety in the wheel 92[5] to the perylene stopper 37 in the axle. (b) Thermoresponsive [2]rotaxane 42 constructed from the pillar[6]arene wheel 1[6].

This result indicates that the emeraldine form of polyaniline, which has a blue color, completely oxidized to a leucoemeraldine form of polyaniline, which is colorless. In contrast, a blue solution color still remained even with the same amount of reductant hydroquinone, indicating that pillar[5]arene 12[5] showed a stronger reducing ability than the unit model of hydroquinone. This arises from the formation of the polypseudorotaxane structure between polyaniline and pillar[5]arene 12[5]. Pseudorotaxanation is ideal for the reductant pillar[5]arene

12[5], which is close to the oxidized substrate of the emeraldine form of the polyaniline chain.

Pillar[5]arenes form host–guest complexes with linear alkanes; thus formation of the polypseudorotaxane structure between pillar[5]arene 5[5] and polyethylene was investigated by our group (Figure 73b).²⁸⁰ Polyethylene is hardly soluble in organic solvents; thus pillar[5]arene and polyethylene were mixed in the melted state. The formation of the polypseudorotaxane structures led to the extension of polyethylene chains, which contributed to increasing the melting point of poly-

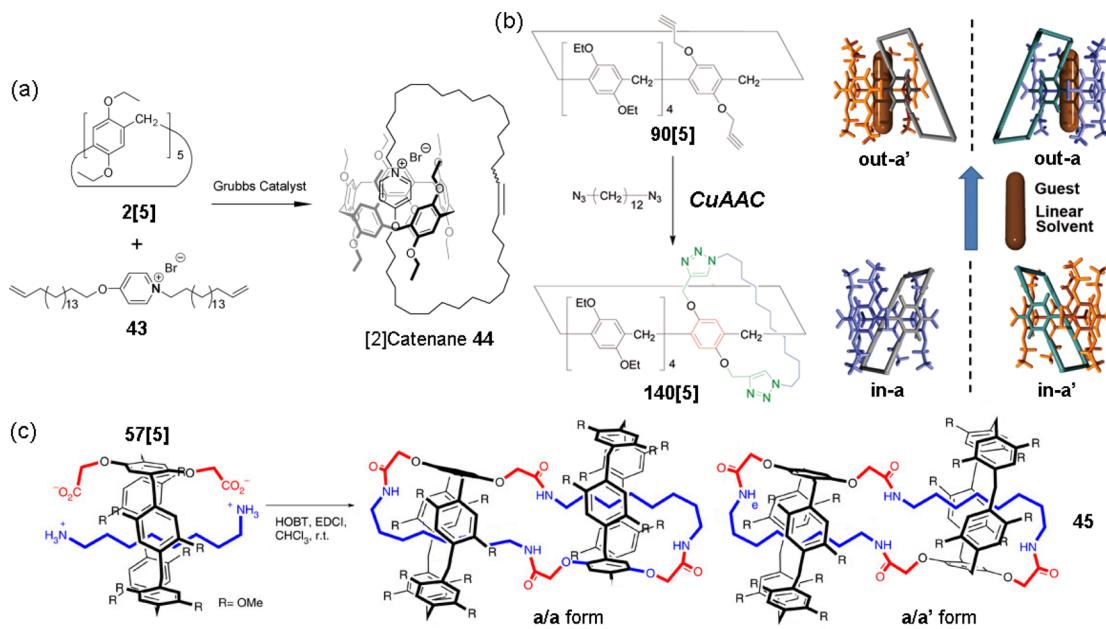


Figure 70. (a) The first pillar[n]arene-based [2]catenane **44**. (b) Guest and linear solvent-triggered planar chiral inversion of pseudo[1]catenane **140[5]**. (c) Synthesis of gemini-catenanes **45** based on pillar[5]arene. Only enantiomers in the **a/a** form are shown. Reproduced with permission from ref 272. Copyright 2015 Nature Publishing Group.

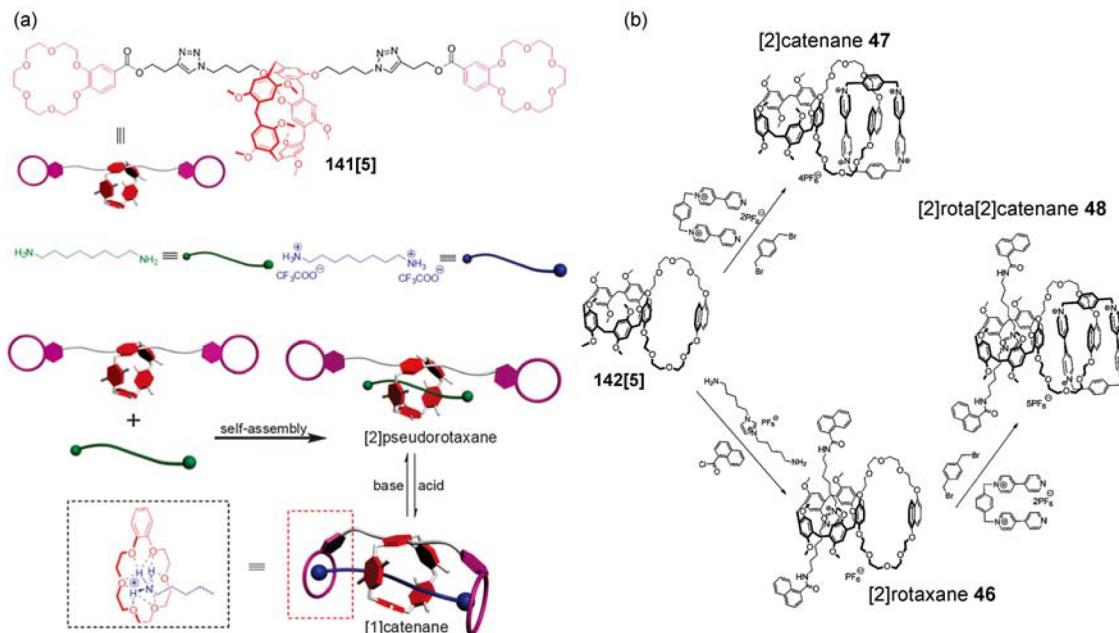


Figure 71. (a) Representation of the pH-responsive dynamic [1]catenane **141[5]**. Reproduced with permission from ref 273. Copyright 2013 Royal Society of Chemistry. (b) Synthesis of [2]rotaxane **46**, [2]catenane **47**, and [2]rota[2]catenane **48** based on the bicyclic compound **142[5]**. Reproduced with permission from ref 276. Copyright 2015 Royal Society of Chemistry.

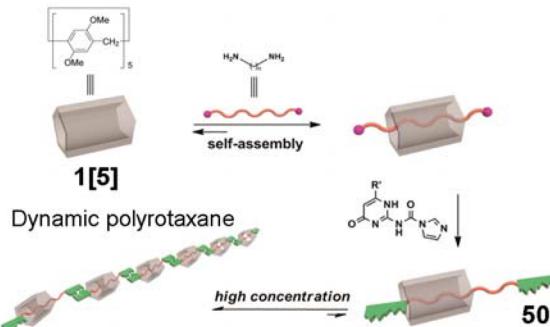
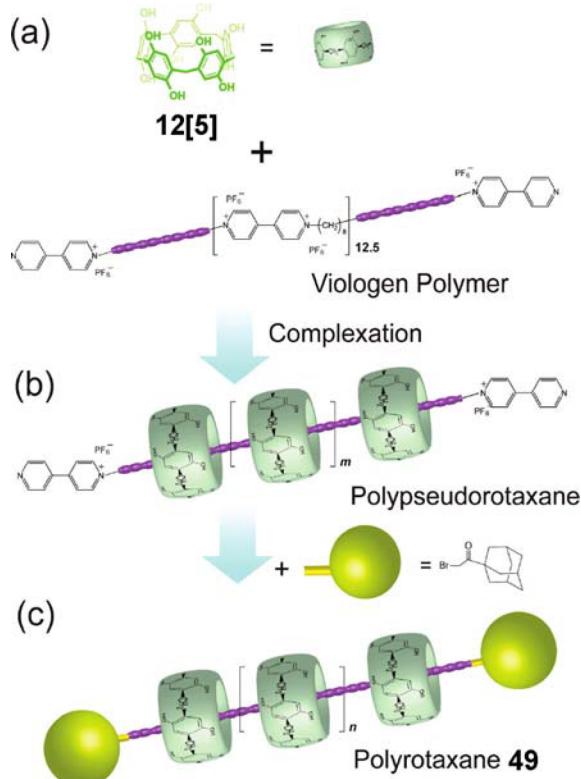
ethylene from 126 to 152 °C. The melting point change was directly observed by phase transitions from the melted state to the solid state upon addition of pillar[5]arene at 140 °C. Addition of the competitive guest, 1,4-dibromobutane, induced the phase transition from solid to melted state at 140 °C. This arises from the dethreading of the polyethylene chain from the cavity of **5[5]**. These phase transitions could be applied to the new molding and processing techniques of polyethylene.

Wang and co-workers reported dynamic polyrotaxanes using a [2]rotaxane with ureidopyrimidinone moieties that contribute

not only as an end-capping stopper but also to supramolecular polymerization of [2]rotaxane (Figure 74).²⁸¹

The [2]rotaxane **50** was prepared by end-capping of an axle with quadruple hydrogen-bonding ureidopyrimidinone in the presence of a pillar[5]arene wheel. The [2]rotaxane formed a polyrotaxane-like supramolecular polymer in high concentration by intermolecular quadruple hydrogen bonds between the ureidopyrimidinone moieties.

Pillar[5]arenes form host–guest complexes with cationic guest molecules, but are hardly formed with neutral guests. Therefore, the synthesis of polyrotaxanes consisting of nonionic



logical gel **53** was obtained by intermolecular cross-linking between polyrotaxanes by a metathesis reaction. The topological gel swelled in organic solvents with intermediate dielectric constants, but not in nonpolar or highly polar solvents.

8. MATERIAL APPLICATIONS OF PILLAR[n]ARENES

8.1. Electronic Materials

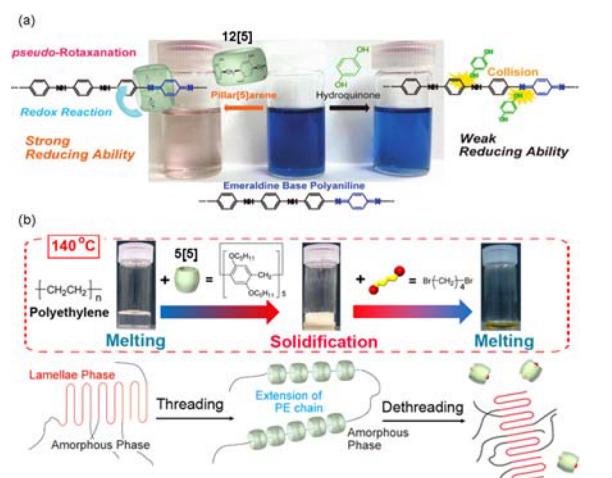
Per-hydroxylated pillar[5]arene **12[5]** has five hydroquinone units. Thus, oxidation of per-hydroxylated pillar[5]arene **12[5]** afforded pillar[5]quinone containing five benzoquinone units **144[5]** (Figure 76a).²⁸³ Hydroquinone is converted to benzoquinone by oxidation, and benzoquinone is converted back to hydroquinone by reduction. There are a total of 10 carbonyl groups with high density on both rims of pillar[5]-quinone; thus the macrocyclic structure of **144[5]** is expected to favor Li uptake. Chen and co-workers investigated **144[5]** as the cathode for lithium organic batteries.²⁸⁴ The 55 wt % pillar[5]quinone cathode showed excellent electrode properties: an average operation voltage of approximately 2.6 V, and high initial capacity (418 mAh/g) with a stable cyclability (94.7% of the initial capacity retained even after 50 cycles).

Cheng and Kaifer reported the cathodic voltammetric behavior of pillar[5]quinone **144[5]** in nonaqueous media.²⁸⁵ Four waves were observed by square wave voltammetry in the voltammetric reduction cycle of **144[5]**, which corresponded to 2, 1, 2, and 3 electrons (Figure 76a). Uptake of the first electron occurred, and then uptake of the second electron proceeded at a very similar potential as the uptake of the first electron. Therefore, the number of electrons attributed to the first waves was two. To minimize the repulsive forces, negative charges should locate in A and C benzoquinone units (Figure 76b).

Uptake of the third electron should proceed in the D benzoquinone unit to minimize the repulsive forces. In this stage, uncharged benzoquinone units were at the B and E positions; thus uptake of last two electrons proceeded at very similar potentials. Kudo et al. investigated novel resist materials using pillar[5]arene platform.²⁸⁶ A pillar[5]arene derivative with adamantly moieties connected by ester bonds showed high lithographic performance, and is thus a promising candidate for high-resolution resist materials as well as noria, calix[n]arene dimers, and CDs.

8.2. Artificial Transmembrane Channels

Hou et al. have developed various unimolecular artificial channels using the tubular-shape of pillar[5]arenes.²⁸⁷ Their chemistry started from the crystal structure of pillar[5]arene with 10 ethyl ester moieties **44[5]** (Figure 77a). The decaester molecules



polymers was difficult. To overcome this problem, we applied liquid pillar[5]arenes to synthesize nonionic polymer-based polyrotaxanes (Figure 75).²⁸²

The end-capping reaction between azido-end polytetrahydrofuran and alkyne-stopper **18** in liquid pillar[5]arenes (**51[5]** and **143[5]**) resulted in the formation of polyrotaxanes (**51** and **52**) in moderate yields. Using a new liquid pillar[5]arene with reactive vinyl moieties **143[5]**, the pillar[5]arene-based topo-

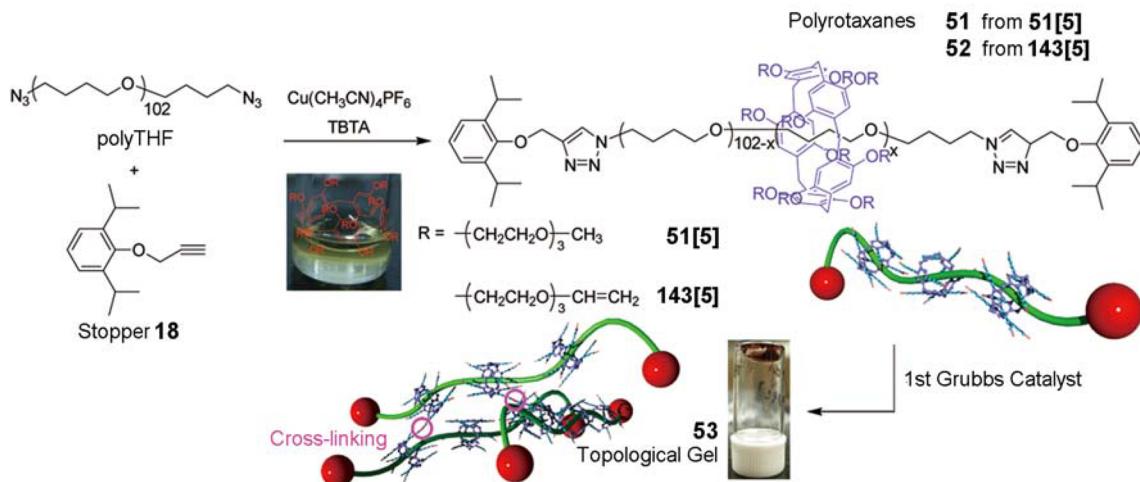


Figure 75. Nonionic polyrotaxanes (**51** and **52**) and a topological gel **53** prepared from liquid pillar[5]arenes (**51[5]** and **143[5]**). Reproduced with permission from ref 282. Copyright 2014 Royal Society of Chemistry.

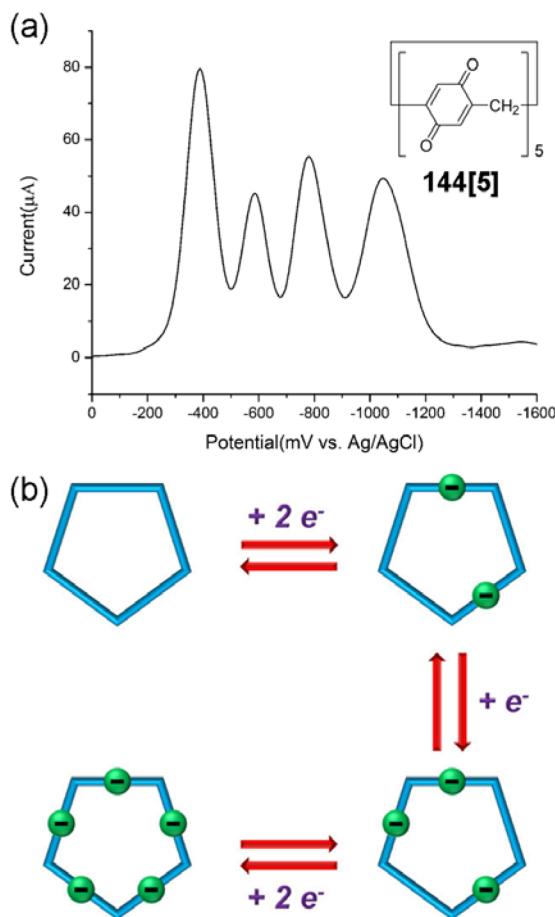


Figure 76. (a) Cathodic voltammetric behavior by square wave voltammetry on glassy carbon (0.07 cm^2) of 1.0 mM pillar[5]quinone **144[5]** in CH_2Cl_2 solution containing 0.1 M TBAPF₆ as the supporting electrolyte. (b) Steps in the five-electron reduction process of **144[5]**. Reproduced with permission from ref 285. Copyright 2015 American Chemical Society.

assembled into infinite 1D channels, and ordered water wires were observed in the 1D channels (Figure 77b).¹⁴³

Because of the assembled structure of the decaester working as proton channels, they incorporated the decaester in the lipid

bilayer to serve as proton channels.²⁸⁸ The decaester worked as proton channels even in the lipid bilayer, and the conductance using the decaester was 44 pS . However, the thickness of the lipid bilayer is approximately 3.7 nm , which is more than twice as long as the decaester pillar[5]arene (1.6 nm). Assembly of two pillar[5]arene molecules is required to act as stable proton channels (Figure 77d). The authors therefore synthesized pillar[5]arene dimers with various length linkers **145[5]**–**150[5]** (Figure 77c). The pillar[5]arene dimer with C3 linker **147[5]** was most applicable to the thickness of the lipid bilayer among pillar[5]arene dimers with various lengths. Thus, the pillar[5]arene dimer linked by the C3 linker **147[5]** exhibited similar proton conductance and high channel stability as compared to the monomeric decaester, while pillar[5]arene dimers connected by short (C1) **145[5]** and long (C6) **150[5]** linkers minimized the intramolecular stacking interactions of the two pillar[5]arene units (Figure 77e).

Water channels were also constructed by attaching hydrazide chains to pillar[5]arene rims (**151[5]** and **152[5]**, Figure 78a).²⁸⁹

In the crystal structure, the tubular structure of pillar[5]arene **151[5]** was stabilized by intramolecular hydrogen bonds of adjacent hydrazine subunits. In the cavity, hydrogen-bonded water dimers were observed. The length of the extended hydrazide-modified pillar[5]arene **152[5]** is approximately 5 nm , which is sufficient to span the lipid bilayer. **152[5]** could insert into lipid vesicles containing aqueous NaCl solution. Insertion of the tubular structure into the lipid vesicles caused water to flux into the vesicles due to the reduction of osmotic pressure difference between the outside and inside of the vesicles, and triggered swelling of the vesicles and fusion between different vesicles.

Peptide-appended pillar[6]arene **23[6]** acted as chiral selective transport channels of amino acids by insertion of **23[6]** into lipid bilayer membranes (Figure 79a).²⁹⁰

Transport of D-amino acids from the inside to outside of the lipid bilayer was faster than that of L-amino acids (Figure 79b and c). Hou et al. also synthesized per-functionalized pillar[5]arene with Arg-incorporated tripeptide chains **153[5]** (Figure 79a).²⁹¹ Under a negative potential, **153[5]** inserted into a lipid bilayer to form channels for the transport of K⁺ ions. In contrast, under a positive potential, **153[5]** left the lipid bilayer, which resulted in

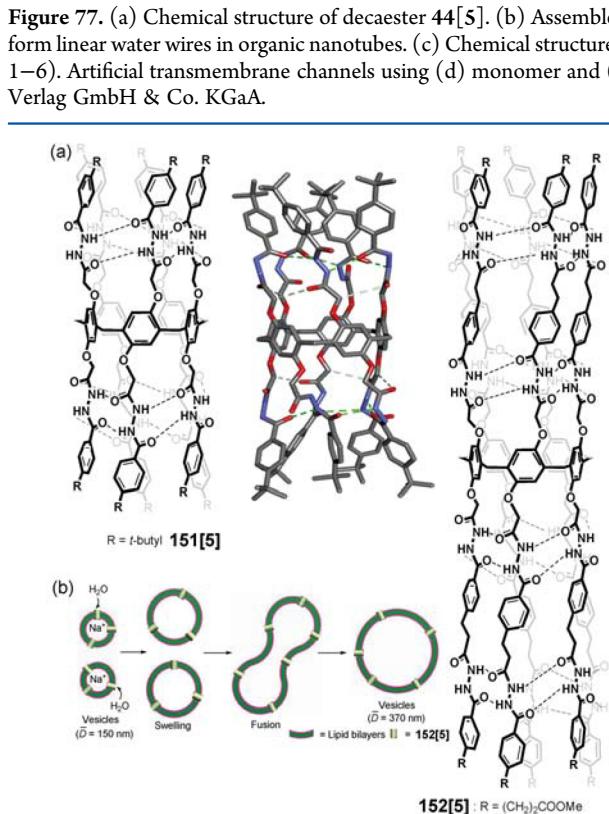
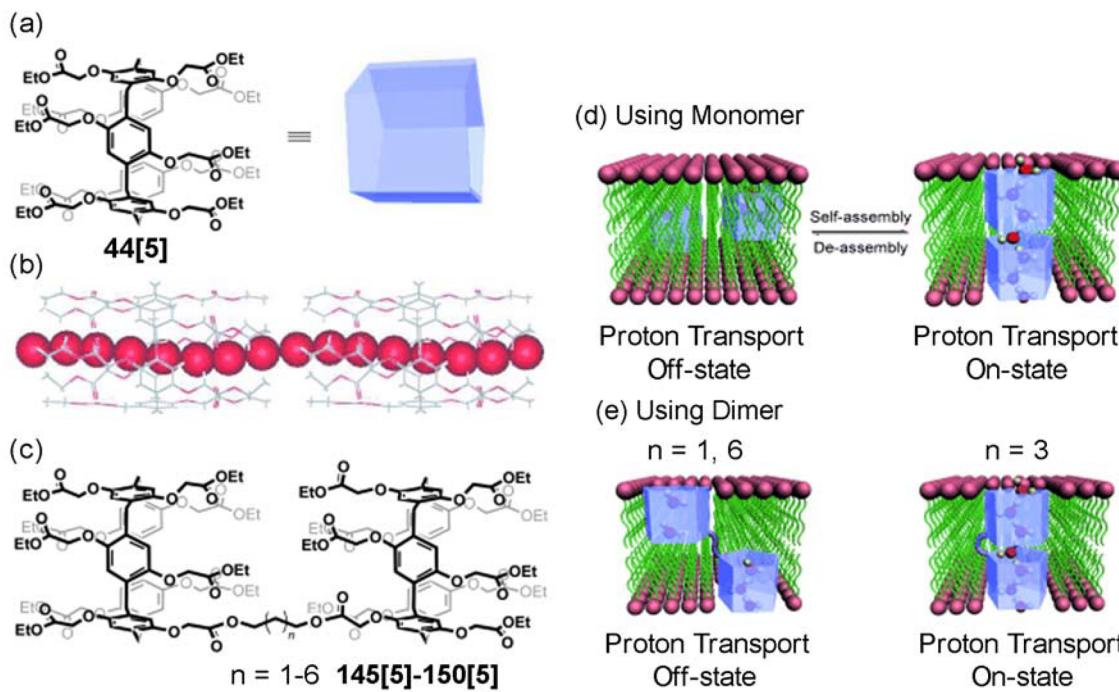


Figure 78. (a) Chemical and X-ray crystal structures of hydrazide-modified pillar[5]arenes (**151[5]** and **152[5]**). (b) The increase in vesicle size caused by the expanded hydrazide-modified pillar[5]arene **152[5]** acts as water transport from the outside to inside of vesicles, which causes an increase in vesicle size and fusion of different vesicles. Reproduced with permission from ref 289. Copyright 2012 American Chemical Society.

the nontransport of K^+ ions (Figure 79d). Therefore, transportation of K^+ ions can be switched by voltage control.

9. CONCLUDING REMARKS AND FUTURE PERSPECTIVES

Research in the field of pillar[n]arene chemistry started in 2008; thus pillar[n]arene chemistry only has a short history of 8 years. However, even in 8 years, the chemistry has developed exponentially as this field has garnered tremendous attention of many chemists. In the initial stage from 2008 to 2011, there were only a handful of researchers. However, their considerable efforts uncovered the fundamental properties of cyclic pentamers, pillar[5]arenes, such as synthesis, structure, functionality, conformational, and host–guest properties. For example, etherification of preformed pillar[5]arenes, such as per-hydroxylated pillar[5]arene, was the first approach to obtain per-functionalizing pillar[5]arenes. The first water-soluble pillar[5]arene was prepared in 2010 by the etherification approach.⁸⁸ The discovery of water-soluble pillar[5]arene was a turning point in the host–guest chemistry of pillar[5]arenes, which enabled aqueous media to be chosen as the complexation media in addition to organic media. The per-functionalization of pillar[5]arenes by the etherification approach also enabled the inhibition of the rotation of the units through the introduction of bulky substituents. Inhibition of the rotation of the units completely opened the area of planar chirality of pillar[5]arene in 2011.⁹¹ In 2010, Huang and co-workers developed a cocrystallization approach to obtain pillar[5]arene with one different unit.⁸¹ In 2011, Stoddart and co-workers synthesized monofunctionalized pillar[5]arenes based on the cocrystallization approach.⁸² The appearance of monofunctionalized pillar[5]arenes led to the construction of a wide variety of pillar[5]arene-based supramolecular polymers. From 2012, the moderate yield synthesis of cyclic hexamers, pillar[6]arenes, has expanded the fields of pillar[n]arene chemistry.⁵⁹ Photo- and redox-responsive host–guest systems using pillar[6]arenes were a major breakthrough to

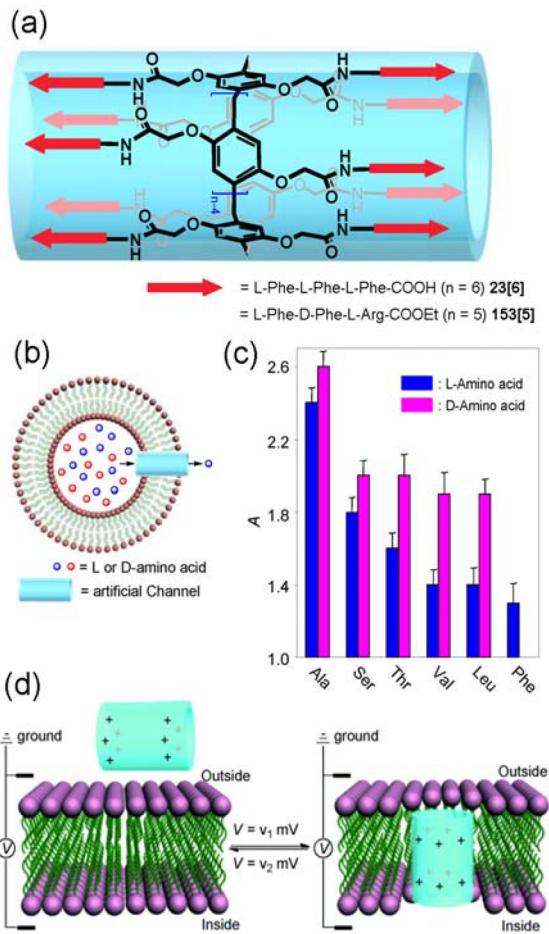


Figure 79. (a) Chemical structures of peptide-appended pillar[5]arene 153[5] and pillar[6]arene 23[6]. (b) Selective transportation of L-amino acids from the inside to outside of the lipid bilayer through pillar[n]arene one-dimensional channels. (c) Transport activities of expanded peptide-appended pillar[6]arene 23[6] for L- and D-amino acids. Reproduced with permission from ref 290. Copyright 2013 American Chemical Society. (d) The voltage-driven pillar[5]arene 153[5] inserting into and leaving the lipid bilayer. Reproduced with permission from ref 291. Copyright 2014 Wiley-VCH Verlag GmbH & Co. KGaA.

apply the host–guest chemistry of pillar[n]arene for supramolecular structural switching.^{136,179} That is, the development of pillar[n]arene chemistry was supported by a genuine team effort from pillar[n]arene chemists all over the world. Their efforts triggered the next exponential increase in the development of pillar[n]arene chemistry from 2012. Fortunately, many chemists have joined the pillar[n]arene chemistry community, and contributed to uncovering new potentials of pillar[n]arenes by applying pillar[n]arenes to different fields of chemistry, such as inorganic, polymer, biomedical, and electrical chemistry. Now, pillar[n]arenes are attracting attention from numerous researchers, and are recognized as one of the key components in supramolecular chemistry. From the history of the development of pillar[n]arene chemistry, discovery of the original pillar[n]arene features is very important for the further success of pillar[n]arene chemistry. Their beautiful pillar-shaped and regular polygonal structures should be important aspects for the construction of highly ordered original pillar[n]arene assemblies. The hydrocarbon-recognition ability of pillar[n]arenes by multiple CH/π interactions should lead to yet

unknown molecular storage and separation materials. Application of pillar[n]arenes of mechanically and thermally tough supramolecular polymers and electronic materials should be a future target. Application of the pillar[n]arenes, based on the original features of pillar[n]arenes, will lead to further breakthroughs, which might extend the field beyond the present concept of supramolecular chemistry. The structure of pillar[n]arenes is very simple; thus we believe that the pillar[n]arenes should have unlimited potential, serve as ideal platforms to construct supramolecular materials, and continue to be widely researched and loved within the ever expanding community. Pillar[n]arenes still have an infinite number of possibilities, and look forward to future discoveries in pillar[n]arene chemistry.

AUTHOR INFORMATION

Corresponding Author

*Tel.: +81-76-234-4775. Fax: +81-76-234-4800. E-mail: ogoshi@se.kanazawa-u.ac.jp.

Notes

The authors declare no competing financial interest.

Biographies

Tomoki Ogoshi received his B.S. (2000), M.S. (2002), and Ph.D. degrees (2005) from Kyoto University under the supervision of Prof. Yoshiki Chujo. He received JSPS research fellowships for young scientists (2002–2005). He was a JSPS postdoctoral research fellow (2005–2006) in the Graduate School of Science at Osaka University in the group of Prof. Akira Harada. In 2006, he moved to the Graduate School of Natural Science and Technology at Kanazawa University as an assistant professor (2006–2010). He was an associate professor (2010–2015) and was promoted to a professor at the same university at 2015. He works also as JST-PRESTO Researcher: PRESTO program “Hyper-nanospace design toward innovative functionality” since October of 2013 under the research supervisor of Prof. Kazuyuki Kuroda (Waseda University). He has received HGCS Japan Award Excellence 2010 (2011), The Chemical Society of Japan Award for Young Chemists (2012), The Cram Lehn Pedersen Prize in Supramolecular Chemistry, Royal Society of Chemistry (2013), The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology (2014), and 2014 SPSJ Award for the Outstanding Paper in Polymer Journal sponsored by ZEON (2015). His research interests include organic synthesis, and supramolecular and hybrid materials.

Tada-Aki Yamagishi received his M.S. degree (1985) in industrial chemistry from Kanazawa University and Ph.D. degree (1989) in polymer chemistry from Kyoto University. He was an assistant professor (1988–1997) at the Faculty of Engineering, Kanazawa University, and a postdoctoral fellow at Nice-Sophia-Antipolis University in France (1992–1993), an associate professor (1997–2009), and was promoted to a professor at the Graduate School of Natural Science and Technology, Kanazawa University, in 2009. He received The Japan Thermosetting Plastics Industry Association Award in 2008. His current interests include synthesis and physical chemistry for highly functional and performance polymers, designed supramolecular chemistry, and hybrid materials.

Yoshiaki Nakamoto is a honorary professor at the Graduate School of Natural Science and Technology at Kanazawa University. He received his M.S. degree (1969) in industrial chemistry from Kanazawa University and Ph.D. degree (1980) from Tokyo Institute of Technology in enzyme engineering. He was an assistant professor (1969–1980), lecturer (1980–1983), and associate professor (1983–

1989) at the Faculty of Engineering, Kanazawa University, and a postdoctoral fellow at University of Mainz in Germany at 1988. He was promoted to a professor at the Faculty of Engineering, Kanazawa University, in 1989, a position he held until his retirement in 2010. He received The Japan Thermosetting Plastics Industry Association Award (2003) and SPSJ Award for Outstanding Achievement in Polymer Science and Technology (2011).

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