

Formation of a Cyclic Dimer Containing Two Mirror Image Monomers in the Solid State Controlled by van der Waals Forces

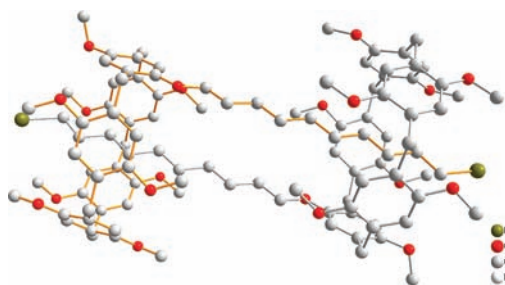
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ABSTRACT



Two new copillar[5]arenes were prepared. They are arranged in two completely different motifs, a cyclic dimer containing two monomers with two different conformations that are mirror images of each other and linear supramolecular polymers in the solid state. Not only has it been shown that to form this kind of dimer is a unique feature associated with pillar[5]arene macrocycles but also it was demonstrated that weak van der Waals forces can be used to control the self-organization of monomers during their supramolecular polymerization process.

Compared with hydrogen bonds, van der Waals interactions are neither strong nor directional in nature. Although the typical energy of van der Waals interactions is less than 5 kJ/mol, collectively these interactions can compete with hydrogen bonding interactions.¹ They have

played important roles in host–guest chemistry,² gas storage,³ biological systems,⁴ crystal packing,⁵ and self-assembly of molecules on surfaces.⁶ A mirror image cyclic dimer is a cyclic dimer containing two monomers with two different conformations that are mirror images of each other. We are interested in building mirror image cyclic dimers not only because they are beautiful structures from the view of molecular esthetics but also because they have potential applications as building blocks to generate novel controllable mechanically interlocked supramolecular

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structures, including molecular muscles, molecular actuators, and nanoswitches, that can be operated at the molecular level.⁷ There are three basic requirements to construct a mirror image cyclic dimer. First, it is necessary to build a self-complementary monomer that can self-assemble into a cyclic dimer. Second, the monomer should have the two most stable conformations that have the same stability and are mirror images of each other. Third, these two conformations can exactly hug together in unity. There are some macrocycle-derived self-complementary monomers previously reported that could form cyclic dimers based on crown ethers⁸ and cyclodextrins.⁹ However, all of these monomers have only one of the most stable conformations, which means there are two halves that are exactly the same in these reported cyclic dimers. Therefore, these previously reported self-complementary monomers cannot

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(12) The two most stable conformations are interchangeable in solution by rotation of the repeating units through the annulus of pillararenes. However, if each side of a pillararene is incorporated with large enough groups, the rotation of the repeating units is prohibited and the two most stable conformations should become enantiomers which can be separated.^{11c}

(13) There is a convenient way to verify the planar chirality of the two most stable conformations. First, stand outside of the cavity of a pillararene and choose a random repeating unit. Second, draw a line (like the green dotted line in Figure 1) through the two bridging carbon atoms. Third, draw another line in the benzene plan which should pass through the center of the benzene ring and also be perpendicular to the first one (the blue dotted line in Figure 1). Finally, the two lines cut the plan into four parts. Label them 1, 2, 3, and 4 (clockwise from the top right part). If the substituents are in parts 1 and 3, it is a *pS*-conformation. Otherwise, it is *pR*.

be used to construct mirror image cyclic dimers in a one-pot reaction. Recently, pillararenes (including pillar[5]arenes and pillar[6]arenes), a new type of macrocycles, and their interesting host–guest binding properties were reported.¹⁰ Different from traditional macrocycles, they all have the two most stable conformations (*pS* and *pR*) that are mirror images of each other (Figure 1).^{11–13} Therefore, pillararenes are good candidates for constructing mirror image cyclic dimers. In this study, we successfully prepared a copillar[5]arene¹⁴ which can form a mirror image cyclic dimer in the solid state controlled by van der Waals forces.

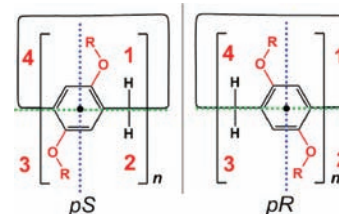


Figure 1. *pS*- and *pR*-conformations of pillar[*n*]arenes.

To increase the binding ability between the host and guest moieties, we added an electron-withdrawing bromo atom at the end of the alkyl guest part to make the adjacent methylene group a better hydrogen bond donor. Moreover, we incorporated a long alkyl chain in the target monomer to strengthen the interactions between the guest parts, which can increase the possibility to form cyclic dimers. A mixture of 4 equiv of 1,4-dimethoxybenzene, 1 equiv of 1-(10-bromodecyloxy)-4-methoxybenzene, which was prepared from 4-methoxyphenol and 1,10-dibromodecane in only one step, 5 equiv of paraformaldehyde, and 5 equiv of $[\text{BF}_3 \cdot \text{O}(\text{C}_2\text{H}_5)_2]$ was stirred at room temperature for 4 h. After purification by column chromatography using petroleum ether/ethyl acetate (30:1) as the eluent, copillar[5]arene **1** was isolated in 10% yield (Figure 2). To investigate the influence of the bromo atom, we also synthesized copillar[5]arene **2** in 23% yield as a reference compound.⁹

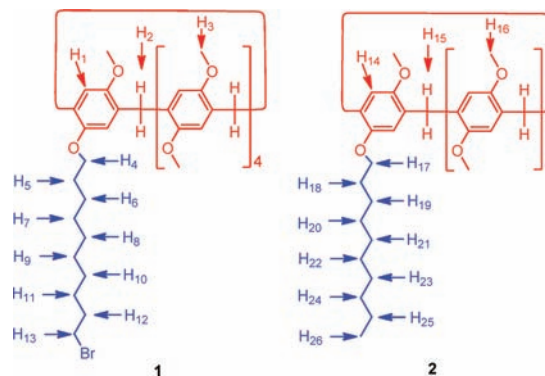


Figure 2. Structures of copillar[5]arenes **1** and **2**.

The ^1H NMR spectrum of **1** in chloroform-*d* is quite different from that of **2** at the same concentration (Figures S9 and S10). Signals from the bridging protons H_2 and methoxy protons H_3 of **1** are significantly overlapped and could not be identified clearly. Peaks from aromatic protons H_1 of **1** are located in a relatively wider range compared with **2**. Also, there are three broad peaks located at higher field than TMS. These observations indicated that the self-complexation of **1** is occurring even at very low concentrations (Figures S10 and S11). By employing 2D ^1H – ^1H COSY experiments of **1** (Figure S21) and 1-(10-bromodecyloxy)-4-methoxybenzene (Figure S12), the signals from their decyl protons can be identified clearly. From comparison of their ^1H NMR spectra (Figure S13), the chemical shift changes of the decyl protons caused by formation of copillar[5]arene can be estimated respectively. The protons H_{13} , H_{12} , H_{11} , H_{10} , and H_9 next to the bromo atom on the decyl group of **1** show much bigger upfield chemical shifts than the other protons. These phenomena indicated that these five protons are deeply located within the cavity of **1** and the other ones are positioned outside the electron-rich copillar[5]arene cavity, which was proved by its crystal structure (Figure 3a). The assignment and correlation of the peaks were further validated by a NOESY NMR spectrum of **1** (Figure S14). Strong correlations were observed between all of the decyl protons H_{5-13} and the aromatic protons H^1 as well as bridging methylene protons H_2 of the copillar[5]arene unit, also suggesting that the decyl group is deeply threaded into the copillar[5]arene cavity in solution.

The ^1H NMR spectra of **1** (chloroform-*d*, 400 MHz, 293 K) at different concentrations in the range of 0.25 to 48 mM were monitored (Figure S11). As expected, the proton NMR spectra of **1** are concentration-dependent, reflecting the involvement of fast-exchanging noncovalent interactions in solution. As the concentration increased, the proton NMR spectra revealed upfield shifts for H_{10-13} , but the other protons did not show obvious chemical shifts. Moreover, the chemical shifts for H_{10-13} changed rapidly at first (0.25–8 mM) and then slowly at relatively higher concentrations (8–48 mM). The ^1H NMR spectra of **2** are also concentration-dependent (Figure S15). The biggest difference between **1** and **2** is that as the concentrations increased, the signal of H_4 of **1** showed upfield shifts, while the signal of H_{17} of **2** showed downfield shifts (Figure S16). Combined with the crystal analysis, we can conclude that as the concentration increased and the aggregates of **1** changed from self-inclusion monomers into cyclic dimers while those of **2** changed into cyclic and linear oligomers in solution. It is well-known that, in more polar solvents, the hydrogen-bonding interactions become weaker. Therefore, we then investigated the ^1H NMR spectra of **1** in different solvents. However, the introduction of the bromo atom greatly decreased the solubility of **1** in organic solvents. It is almost insoluble in acetonitrile, DMSO, and other polar

solvents. We only recorded the proton NMR spectra in the mixtures of chloroform and acetone with different volume ratios (Figure S17). From these spectra, we found that as the portion of acetone increased, the self-complexation of **1** became weaker. In the proton NMR spectrum of **1** in a mixture of acetone-*d*₆/chloroform-*d* (4:1, v/v), no longer are there peaks located at higher field than TMS. These observations indicated that weak hydrogen bonds are the main driving forces for the self-complexation of **1**.

To investigate the average size of the assemblies in solution, two-dimensional diffusion-ordered ^1H NMR spectroscopy (DOSY) experiments were performed. We found that different aggregates of **1** and **2** are in fast exchange on both the ^1H NMR and DOSY time scales. As the concentration of **1** increased from 8 to 48 mM, the measured weight average diffusion coefficients was almost constant (Figure S22), suggesting that the average dimension of aggregates from monomer **1** did not change much. However, as the concentration of monomer **2** increased from 8 to 48 mM, the measured weight average diffusion coefficient decreased considerably from 17.2×10^{-10} to $6.7 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$ (Figure S22), suggesting that the average size of the aggregates from monomer **2** increased continuously. It is noteworthy that **1** and **2** have almost the same dimensions because of their quite similar structures. However, at the same concentrations, **1** assembled into relatively smaller aggregates with higher measured weight average diffusion coefficients than **2**. Therefore, we can conclude that copillar[5]arene **1** forms relatively smaller aggregates in chloroform-*d* in a certain range of concentration. Hence, we probably obtained a cyclic dimer based on **1** as designed. We also attempted to gain evidence for the formation of dimers from mass spectrometry. However, no peaks corresponding to the dimeric supermolecules were observed. There are three possible reasons. First, usually mass spectrometry was performed in polar solvents such as methanol and acetonitrile, but **1** is insoluble in these polar solvents. Second, even with dissolved **1** it is still hard to form a dimer in polar solvents. Finally, even if **1** molecules form cyclic dimers in solution, they still have to complex cations or anions to form charged species for detection.

Single crystals of **1** were obtained by slow evaporation of a solution of **1** in a chloroform/ethyl acetate mixture. The X-ray crystallographic analysis reveals that the two most stable conformations of **1** (Figure S18) form a mirror image cyclic dimer, in which the alkyl group of the *pS*-conformation of **1** is threaded simultaneously through the electron-rich cavity of the *pR*-conformation of **1** (Figure 3a). There are four hydrogen atoms on the included decyl group with C–H $\cdots\pi$ -plane distances of 2.81–2.93 Å, shorter than 3.05 Å, implying the existence of C–H $\cdots\pi$ interactions between the decyl guest part and the copillar[5]arene host cavity (see the blue dotted lines in Figure 3a).¹⁵ This is similar to the case for the previously reported mono-octyl-substituted copillar[5]arene in the solid state.^{14b} Moreover, there

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are two C–H···O interactions with H···O distances of 2.65 and 2.75 Å¹⁶ (see the red dotted lines in Figure 3a), which keep the bromo end of the alkyl group located in the cavity (Figure 3a). This further influenced the assembly manner (Figure S19). The energy for the formation of the cyclic dimer came from the dimerization of the uncomplexed part (carbons out of the cavity) of the decyl groups (Figure S19).^{1b} These are the main driving forces for the copillar[5]arene **1** to form a mirror image cyclic dimer instead of a linear assembly in the solid state. The distance *d* between the two 5-carbon decyl part skeletons remains constant with a value of 4.08 Å,¹⁷ implying the existence of van der Waals forces between the two different conformations.^{1b} The dimerization energy for a 5-carbon alkyl chain is about 3.3–4.3 kcal/mol.^{1b} Therefore, controlled by van der Waals forces, the self-complementary monomer **1** assembled as mirror image cyclic dimers in the solid state.

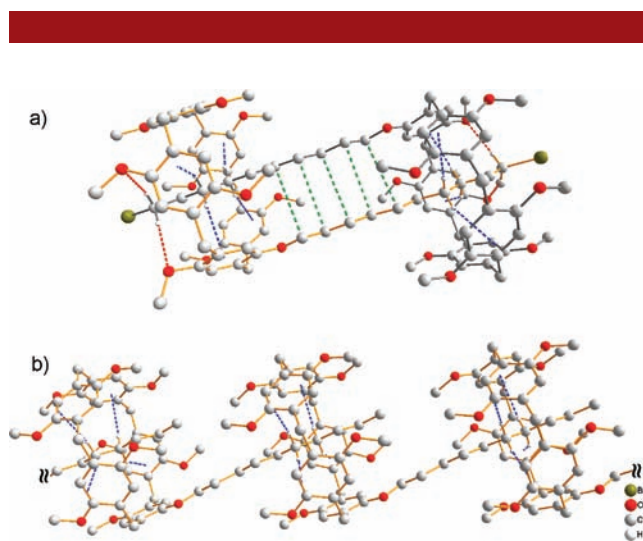


Figure 3. Ball-and-stick views of a mirror image cyclic dimer (a) from **1** and a *pS*-supramolecular polymer (b) from **2** in the solid state. Hydrogen atoms related to the C–H··· π and C–H···O interactions were preserved. The other hydrogen atoms and solvents were omitted for clarity. The blue dotted lines indicate the quadruple C–H··· π interactions. The red dotted lines indicate the C–H···O interactions. The green dotted lines indicate the van der Waals forces between the decyl groups. Atoms of *pS*-conformation are connected by orange bonds while atoms of *pR*-conformation are connected by silver bonds. For clarity, the *pR*-supramolecular polymer in the crystal structure of **2** is not shown.

Single crystals of **2** were obtained by slow evaporation of a solution of **2** in acetone. Just like the mono-octyl-substituted copillar[5]arene reported previously,^{14b} monomer **2** forms linear supramolecular polymers¹⁸ in

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(17) Here *d* is the average distance between the related five carbon atoms to the nearest C–C bond of the other conformation.^{1b}

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the solid state (Figure 3b). There are also four hydrogen atoms on the included decyl group with C–H··· π -plane distances, 2.88–3.01 Å. The main driving forces for the linear assembly are still the quadruple C–H··· π interactions. However, without the assisting C–H···O interactions, the decyl groups penetrate too deeply, leaving shorter alkyl parts out of the cavity which cannot provide sufficiently strong van der Waals interactions to form cyclic dimers. Copillar[5]arene **2** is arranged in a different manner from the mono-octyl-substituted copillar[5]arene reported before (Figure S20).^{14b} The mono-octyl-substituted copillar[5]arene is arranged in linear $-(pS-pR)-$ alternated arrays. Copillar[5]arene **2** forms two linear arrays, $-(pS)-$ and $-(pR)-$, that are mirror images of each other. We can speculate that there are two other possible types of cyclic dimers, $(pS-pS)$ and $(pR-pR)$, for copillar[5]arene **1**; however, only the mirror image $(pS-pR)$ dimer was observed in the solid state. This is probably due to the fact that the mirror image $(pS-pR)$ dimer has the lowest energy.

In conclusion, here we successfully prepared two similar monomers that self-assemble in two completely different manners, mirror image cyclic dimers and linear supramolecular polymers, in the solid state. By combination of various techniques, such as ¹H NMR, COSY, NOSEY, and DOSY, it was demonstrated that monomer **1** forms a smaller interlocked assembly in a certain concentration range in chloroform-*d* than **2**. From X-ray single crystal analysis, we found that **1** forms a mirror image cyclic dimer in the solid state, which is the very first cyclic dimer composed of two conformations of a monomer. The dimerization of **1** is caused by van der Waals forces between the *exo* cavity parts of the decyl groups. However, monomer **2** formed linear suprastructures, *pS* and *pR* separated arrays, in the solid state. This research provides a facile approach to control the self-assembly manner of self-complementary copillar[5]arene monomers between cyclic dimers and linear supramolecular polymers. In the future, we want to investigate the application of different noncovalent interactions (like $\pi\cdots\pi$ interactions) to control the assembly motifs by introducing other functional groups onto the guest moieties of copillar[5]arenes. To further use these copillar[5]arene monomers in the construction of stimuli-responsive mechanically interlocked polymers, molecular actuators and molecular nanovalves stand as another goal.

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Supporting Information Available. Synthetic procedures, characterizations, crystal data, and other materials. This material is available free of charge via the Internet at <http://pubs.acs.org>.