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COMMUNICATION

Lateral Functionalized Pillar[5]arene: A New Building Block for Covalent Self-assembly

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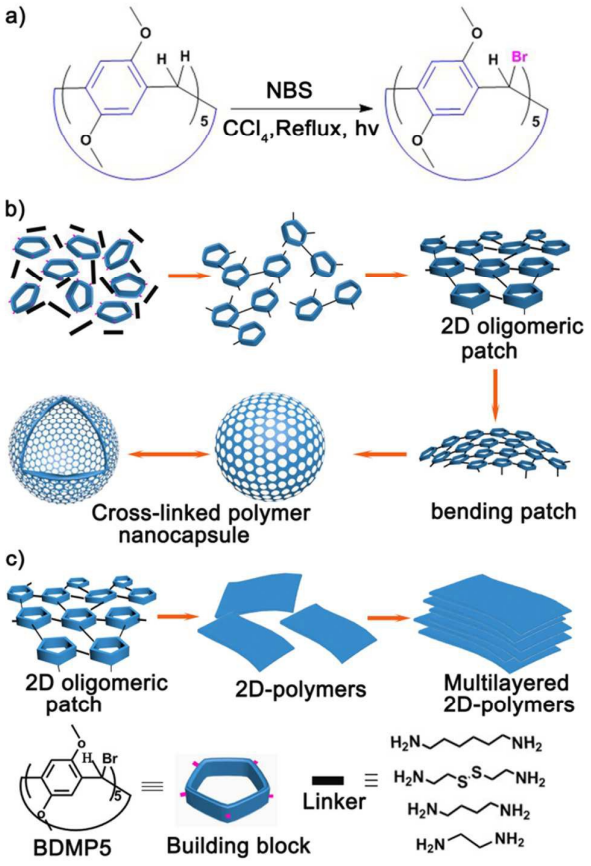
Shuang Fu, Guo An, Hongcheng Sun, Quan Luo, Chunxi Hou, Jiayun Xu, Zeyuan Dong and Junqiu Liu*

A lateral functionalized pillar[5]arene is synthesized for the first time through bromination reaction at methylene bridge of the dimethoxypillar[5]arene. The lateral functionalized pillar[5]arene has been developed as a new building block to construct polymer nanocapsules and 2D-polymer films by covalent self-assembly.

Pillar[n]arenes, linked by methylene bridges at parapositions of 2, 5-dialkoxybenzene rings, are a new type of macrocylic hosts.[1] They have highly symmetrical and rigid pillar architectures and present the binding behavior of electron accepting molecules such as viologen, pyridinium derivatives and imidazolium cations.[2] Recently, besides of host-guest chemistry based on pillararenes, contemporary chemical researchers and material scientists have focused their research interests on designing and fabricating robust materials with unique functions or structures such as supramolecular polymers,[3] transmembrane channels[4] and smart containers[5] by using their various functionalized derivatives. In previous work, almost all the reports were about exploitation of vertical functionalized pillararenes derivatives, which are macrocylic host molecules derivatives designed with functional groups through appropriate derivatization at the upper rim or the lower rim of the molecular architecture. While, lateral functionalized pillararenes derivatives, functionalized with functional groups at "equator", have not been reported so far. Lateral functionalization of pillararenes is a daunting goal because of highly symmetrical and rigid pillar architectures. On the other hand, high reactive of the methylene bridge, at the benzyl position, may cause the break of the macrocycles in some extreme reaction. For example, 1, 4-dimethoxypillar[5]arene reacted with nitric acid generated the decomposed products.[6]

Lateral functionalization of macrocylic host molecules is an important goal because of their unique physicochemical properties and interesting structures.[7] Moreover, this kind of macrocylic host molecules can be used to fabricate high-performance functional materials. For example, lateral functionalized derivatives of cucurbit[n]urils,[7a] disk-like molecules, have high symmetric flat and rigid core and



Scheme 1. a) Scheme of synthesis of BDMP5; b) and c) The mechanism of the generation of 2D-polymers nanocapsules and 2D-polymer films.

State Key Laboratory of Supramolecular Structure and Materials, College of Chemistry, Jilin University, Changchun 130012, People's Republic of China
[a] E-mail:junqiuliu@jlu.edu.cn (Prof. J. Q. Liu)
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multiple functional groups dispersed at the lateral periphery, have been successfully used to fabricate various nanomaterials, such as 2D-polymer films[8] and polymer nanocapsules.[9] Therefore, appending functional groups, particularly reactive ones, on the lateral position of the pillararenes is a challenging goal for developing novel functional nanostructures and nanomaterials.

Herein, we report a facile synthesis of lateral modificated pillar[5]arene derivatives through bromination reaction at the methylene bridge of the dimethoxypillar[5]arene to generate methylene-bridge brominated pillar[5]arenes (Scheme 1a). By using this novel lateral functionalized pillararene derivatives as building block, polymer nanocapsules and 2D-polymer films have been constructed successfully (Scheme 1b and 1c).

Considering the characteristic of the pillararenes and previous failure of lateral functionalization, we use NBS reaction in optimizing conditions to prepare methylene bridge substituted pillararenes. The lateral bromo-pillar[5]arenes (BDMP5) is synthesized through radical bromination at the methylene bridge of the dimethoxypillar[5]arene (Scheme 1a and supporting information). The detail of the synthesis is shown in the supporting information. The mass spectrum shows a main strong molecular ion peaks at 1144.3 (Figure S2) accordance with the expected m/z ratio for the fivefold BDMP5. Additionally, there are other small molecular ion peaks accordance with the fourfold BDMP5 (the peak of 1065.0 is accordance with fourfold BDMP5) and threefold BDMP5 (the peak of 983.0 is accordance with threefold BDMP5) (Figure S2). The BDMP5 can also be distinguished by ^{13}C-NMR (Figure S3) data by the main chemical shifts: δ (ppm) 148, 130, 112 (C of phenyl), 58 (C of methoxy group), 42 ppm (C of methylene bridge). Compared with the ^{13}C-NMR of DMP5 that Tomoki Ogoshi reported,[1a] it can found that the peak of the C of methylene bridge have shifted from 29.5 to 42. While, the peak of C of other posits has no change, thus also indicating the methylene bridge of the pillar[5]arenes have been modified with bromine. The FTIR analyses (Figure S4) further confirm the BDMP5, as the peak 676 cm^{-1} corresponding to C-Br stretching vibrations occurs.

The lateral distribution of bromine at periphery makes it possible for the BDMP5 as new building block to lateral cross-react with diamine to form some high-performance 2D-polymer under appropriate conditions. When stirring of a mixture of 30.0 mg BDMP5 (mixed BDMP5 without seperating them) and 15.7 mg hexanediamine in 30 mL MeCN in the presence of N_2 at 70 ^{o}C for 5 h, well-defined nanospheres generate. The FTIR spectrum of nanocapsules (Figure S4-c) shows that the wavenumber of 676 cm^{-1} corresponding to C-Br stretching has disappear and the peak of 3300-3500 cm^{-1} corresponding to N-H stretching occurs, indicating the BDMP5 has covalently cross-linked with diamine. SEM images (Figure 1a) show that these nanospheres have well-defined morphologies with a narrow size distribution. TEM images reveal that these nanospheres are hollow interior structures (Figure 1b) and surrounded by a thin shell with thickness estimating at 1.2±0.2 nm (the shell is indicated by red arrows) (Figure 1c and 1d), which indicates that the polymer

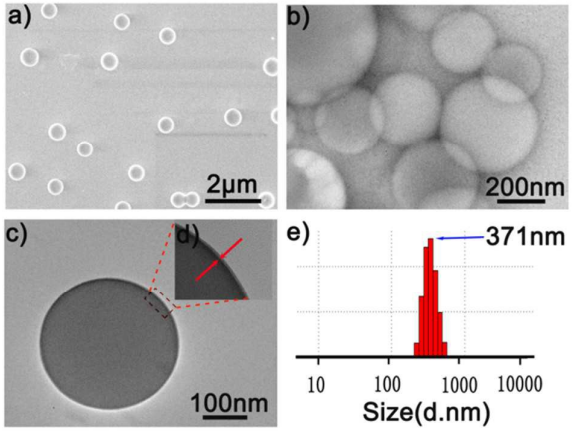

Figure 1. a) SEM image. b) and c) and d) TEM images (the red arrows indicate the thickness of the shell of capsules and the thickness is estimated for 1.2 nm). e) DLS data (size distribution by number).

nanocapsules are consist of single molecular layer through lateral covalently cross-linking pillar[5]arenes (for reason that the height of DMP5 is about 1 nm). Dynamic light scattering (DLS) studies reveal that the polymer nanocapsules have an average diameter of 371 nm (Figure 1e). All the results demonstrate that the thin shell polymer nanocapsules have been successfully synthesized by covalent self-assembly of BDMP5 with hexanediamine. To further demonstrate that these nanospheres have cavity in the interior. Covalent self-assembly of of BDMP5 with hexanediamine in the presence of Rhodamine B (RHB) followed by dialysis produced a polymer nanocapsule encapsulating RHB (RHB-Nanocap) with an average diameter of 380 nm as confirmed by fluorescence microscope (Figure S7-a) and DLS (Figure S7-b).

Some factors have effects on the formation of polymer nanocapsules. For example, the size of the polymer nanocapsule is controlled by the length of the linkers. Covalent self-assembly of of BDMP5 with cystamine dihydrochloride ($NH_2CH_2CH_2S$-$SCH_2CH_2NH_2$) (about as same length as hexanediamine) in MeCN generates nanocapsules with diameter size about 365 nm (Figure 2a and S8a). When the linker is 1, 4-diaminobutane that is shorter than hexanediamine, the covalent self-assembled nanocapsules have diameter size about 298 nm (Figure 2b and Figure S8b). While, when the linker is ethanediamine, no polymer nanocapsule generates in MeCN. Solvent medium also plays an important role in the formation of the polymer nanocapsules. For instance, polymerization of BDMP5 and hexanediamine in MeOH produces polymer nanocapsules with good morphologies and the size of diameter reaches about 447 nm that much bigger than prepared in MeCN (Figure 2c and Figure S8c). Additionally, the ratio of reactants can also affect the capsules formation. Uniform polymer capsules with large size of diameter can generate if slightly excessive ratio of hexanediamine is added (Figure 2d and Figure S8d). While, no polymer nanocapsules has been found on the condition of large excess of hexanediamine.

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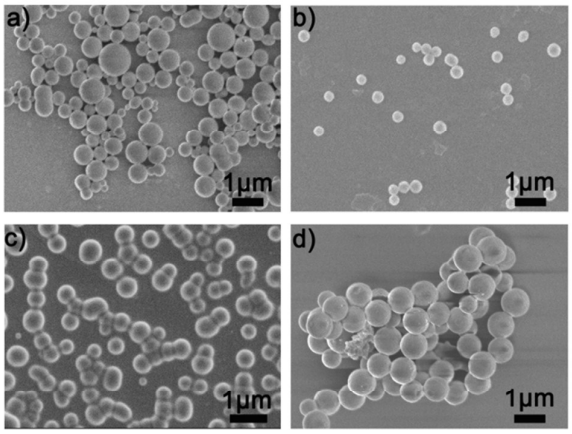

Figure 2. SEM image; a) Polymerization of BDMP5 reaction with cystamine dihydrochloride in MeCN. b) Polymerization of BDMP5 reaction with butanediamine in MeCN. c) Polymeriztion of BDMP5 reaction with hexanediamine in MeOH. d) Polymerization of BDMP5 and hexanediamine in MeOH (excess mole ratio).

In order to explore the mechanism of the formation of polymer nanocapsules thoroughly, DLS is used to monitor the covalent self-assembly process (Figure S9). Originally, no sign of the polymerization is found before heating. After stirring at 70 ^{o}C for 30 min, particles with an average size of 150 nm appear and quickly reach to 370 nm within 150 min. After 270 min, the size of these particles remains around 370 nm. After 300 min, the reaction stop and the size of these polymer nanocapsules still remains around 370 nm. SEM analysis is also used to investigate the morphology and characterization of the covalent self-assembly. There are a lot of ill-defined clusters before heating (Figure S10a). Then heating for about 1.5 h, sphere particles and some patches are observed at the same time (Figure 9Sb). Then after 2.5 h, the morphologies of these sphere particles become very well and at the same time no patches was observed (Figure S10c). Ultimately, these sphere particles remains with high uniform morphologies (Figure S10d). Considering the observation by SEM and DLS studies is similar to that produced by irreversible covalent bond formation reported in Kim group,[8a, b] we suggest that the polymer nanocapsules are formed by following mechanism (Scheme 1b): (1) At early stage, BDMP5 and linkers react to form dimers and other oligomers. (2) These dimers continue to react with each other to form 2D-oligomeric patches. (3) These patches start to bend to reduce their total energy and further reacted to each other to generate polymer nanocapsules.

We wonder that if the solvent is suitable, and linker is shorter, whether besides of polymer nanocapsules, 2D polymer films could be also formed by covalent self-assembly of BDMP5. Here by covalent assembly of BDMP5 with ethyldiamine (the mole ratio of BDMP5 and linker was 1:10) in the solvent of (1:1 volume) mixture of MeCN and CH_2Cl_2 at 50 ^{o}C for 5h, the micrometer lateral size are synthesized. The SEM image (Figure S11-a) shows that microscale films with partially folded and stacked together are formed. TEM images also

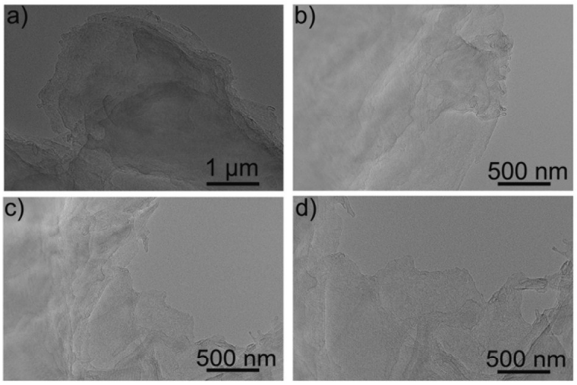

Figure 3. TEM images of multilayer polymer sheets generated from BDMP5 reacted with ethanediamine.

revealed some details. From Figure 3 and Figure S11-b and S11-c, it finds that they are multilayer films with much thin 2D-polymer films stacked over each other. Considering that the formation of 2D-polymer films is similar to that reported by Kim and coworkers[8a, 9e] for example we all use rigid and disk-shaped building blocks, short liker and appropriate solvents, we suggest a similar mechanism, that is, when the 2D-oligomeric patchs generate, they do not bend since we use rigid and disk-shaped building blocks having laterally disposed reactive groups at periphery and short linkers for high bending rigidity and appropriate solvents, which would lead to rigid intermediates and allow them to remain flat. Then they continue to grow in the lateral direction to produce huge dimension 2D-polymer films. Finally, the resulting 2d-polymers may stack together due to the reduced solubility of polymeric patches (Scheme 1c).

The capacity of encapsulating guest molecules makes these polymer nanocapsules potentially useful in many applications such as drug encapsulating and drug delivery. While, the drawback that the large amount of hydrophobic pillararenes at the shell caused these nanocapsules poor water-solubility might limit their application in biological systems. As the the new designed system installs a new kind of host pillararene molecule that can endow with multi-functions with host–guest chemistry, thus allowing facile tailoring of its surface in a noncovalent way. we wonder that if we could decorate the surface with hydrophilic groups by host-guest interaction. It is known that hyamine can bind into the cavity of the pillar[5]arenes,[2d] when the surface is decorated with hexanediamine, these nanocapsules show good water-solubility. Additionally, the water solubility can also be improved by sequential deposition of hydrophilic polymers at the surface of their shell by amination reaction. This method easily improves the water-solubility and has no damage of the polymer nanocapsules. Here, 2-(2-(2-(2-bromoethoxy)ethoxy)ethoxy)-ethan-1-ol, a hydrophilic molecular, is chosen to deposit at the surface of the nanocapsules by reacting with the secondary amine at the surface of the capsules according to the scheme S3. The polymer nanocapsules are decorated about 50% hydrophilic groups and show very good water-solubility. SEM image

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indicate this decorated polymer nanocapsules still have well-defined morphology (Figure S12a). TEM image shows that the shell of these decorated polymer nanocapsules are still thin (about 5 nm) (Figure S12b and S12c).

Conclusions

In summary, the challenge of lateral functionalized pillararenes has been solved through the first functionalization of methylene bridge of DMpillar[5]arene leading to methylene bridge brominated DMpillar[5]arene (BDMP5). It has multiple reactive groups (bromine) disposing in all directions at the lateral periphery. To demonstrate the utilities of BDMP5, we have used BDMP5 as building block to covalently self-assemble into polymer nanocapsules and 2D-polymer films. The 2D-polymer films are very huge and consist of thin polymer multi-layer films. The novel polymer nanocapsules have many advantages compared with those traditional ones for example that they are easily prepared without any template, besides, the shell is very thin and composed of multiple lateral covalent cross-linked pillararenes which can capture guest molecules by host-guest property. Additionally, the water-solubility of the polymer nanocapsules has been improved which stages their application in biological system. After all, this new lateral functionalized pillararene derivative can be applied to construct some new high-performance functional materials and have enormous potential in various applications such as drug encapsulating.

Acknowledgements

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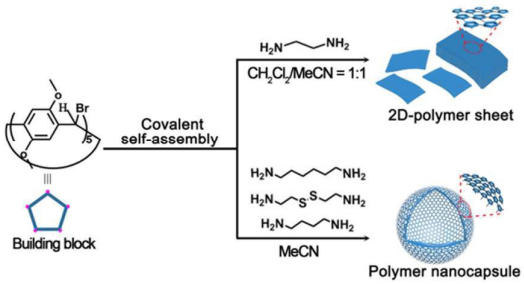

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