

Short Communication

Stable Hydrogen-bonded Spherical Capsules formed from Self-assembly of Pyrogallol[4]arenes

QIAN-FENG ZHANG^{1,2,*}, RICHARD D. ADAMS², and DIETER FENSKE³

¹Department of Chemistry and Chemical Engineering, Anhui University of Technology, Maanshan, Anhui, 243002, P.R. China; ²Department of Chemistry and Biochemistry and the USC Nanocenter, University of South Carolina, Columbia, SC, 29208, USA; ³Institut für Anorganische Chemie, Universität Karlsruhe, 76128, Karlsruhe, Germany

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Abstract

The self-assemblies of two pyrogallol[4]arenes held together by 48 intermolecular hydrogen bonds stably associate in the form of spherical hexameric capsules. The molecular structures of two hexameric capsules with large interior space were analyzed by single crystal X-ray crystallography.

Introduction

Self-assembling molecular capsules are known to encapsulate a variety of neutral and charged guests in the solid state as well as in solution, and in the gas phase [1]. In recent years, Atwood and Rebek have successfully developed series of organic molecular capsules based upon modified resorcin[4]arenes and calix[4]arenes [2–4]. The formation of molecular capsules has followed two main methods: covalent synthesis and synthesis via self-assembly. From this viewpoint, the hydrogen-bonding interaction plays an important role during the process of self-assembly in some highly polar solvents, such as alcohols and water, which can provide essential parts of multicomponent capsule assemblies [5]. For example, water and methanol molecules act as hydrogen-bonding links between hemispherical resorcin[4]arene modules in the solid state [6, 7]. With this help, both dimeric and hexameric capsules can be assembled in the presence of small polar solvent molecules [8, 9].

In many cases, dimeric capsules were usually formed as inclusion complexes with the embedded organic cations inside the cavity [7–11]. The resorcin[4]arene molecules in the dimeric capsules adopt a perfect cone conformation stabilized by intra- and inter-molecular hydrogen bonds. However, few large hexameric aggregates formed as spherical capsules have also been found both in the solid state and in solution [12]. Up to date, three hexameric capsules structurally characterized by X-ray crystallography have been reported by Atwood and Mattay [9, 13–15]. The macrocycle *C*-methyl-

resorcin[4]arene was crystallized from nitrobenzene to form the hexameric capsule [(*C*-methyl-resorcin[4]arene)₆(H₂O)₈] which possesses an excess of four hydrogen bond donors from water molecules, but these donors are positioned such that they project outward from the surface of the enclosure [8]. The macrocycle *C*-*iso*-butyl-pyrogallol[4]arene self-assembles to form a hexameric capsule [(*C*-*iso*-butyl-pyrogallol[4]arene)₆] crystallized in the triclinic space group *P*-1 in acetonitrile [13] or in the rhombohedral space group *R*-3 in methanol [14]. Similarly, *C*-*n*-propyl-pyrogallol[4]arene hexamer may be obtained in methanol solution in the absence of nitrobenzene, and its crystal system is the triclinic space group *P*-1 [15]. As a part of our interests on symmetry substituted resorcin[4]arenes possessing the increased numbers of potential hydrogen-bonding functionalities for more extended self-assembled structures [16], we herein report a reproducible method for the crystallization of the stable hexameric capsules formed by self-assemblies of pyrogallol[4]arenes and crystal structures of [(*C*-methyl-pyrogallol[4]arene)₆] and [(*C*-*iso*-butyl-pyrogallol[4]arene)₆]. The present report would be expected to extent Atwood's previous relevant work for the supramolecular chemistry of the molecular capsules [2, 17].

Experimental

General

All reagents, unless otherwise stated, were purchased as analysis grade and were used without further purification.

* Author for correspondence. E-mail: zhangqf@ahut.edu.cn

C-methyl-pyrogallol[4]arene (**1**) and *C*-*iso*-butyl-pyrogallol[4]arene (**2**) were synthesized according to a procedure described in the literatures [13, 18]. ¹H-NMR spectra were recorded on a Bruker DPX-300 Fourier-transform spectrometer with reference to SiMe₄.

Crystal growth

[(*C*-methyl-pyrogallol[4]arene)₆].3PhNO₂.4MeOH.2H₂O: 100 mg *C*-methyl-pyrogallol[4]arene was dissolved in 95% methanol (15 ml) and 1 ml nitrobenzene was added. The mixture was stirred 5 min with heating, and light yellow solution was thus obtained. The solution was then allowed to evaporate slowly at room temperature. Light yellow hexagonal crystals formed in two weeks. ¹H-NMR (300 MHz, DMSO-*d*₆, ppm): δ 1.32–1.40 (m, 12H, CH₃), 1.51 (bs, H₂O), 4.11–4.85 (t, 4H, Ar₂C HCH₃), 7.12 (s, 4H, ArH, ortho to OH), 7.21–7.36 (m, C₆ H₅NO₂), 7.47 (s, 4H, ArH, meta to OH), 8.19, 8.35, 8.62 (br. s, 6H, ArOH), 8.81 (br. s, 2H, ArOH).

[(*C*-*iso*-butyl-pyrogallol[4]arene)₆].C₆H₆.H₂O: 100 mg *C*-*iso*-butyl-pyrogallol[4]arene was dissolved in 95% methanol (10 ml) and 2 ml benzene was added. The mixture was stirred 10 min with heating, and a light yellow solution was thus obtained. The solvent was then allowed to evaporate slowly at 4 °C. Light yellow hexagonal crystals formed in 10 days. ¹H-NMR (300 MHz, DMSO-*d*₆, ppm): δ 0.92–1.34 (br. m, 24H, CH₃), 1.51 (bs, H₂O), 1.62–1.94 (m, 4H, CH(CH₃)₂), 2.11–2.65 (m, 8H, CH₂), 4.25–4.92 (t, 4H, Ar₂CHCH₂), 7.08 (s, 4H, ArH, ortho to OH), 7.20 (s, C₆H₆), 7.29 (s, 4H, ArH, meta to OH),

8.14, 8.21, 8.33 (br. s, 6H, ArOH), 8.63 (br. s, 2H, ArOH).

Single crystal x-ray analysis

Crystallographic data were collected on a Bruker SMART diffractometer equipped with a CCD area detector, using a graphite-monochromated Mo-*K*α radiation (λ = 0.71073 Å) at room temperature. Data in the frames corresponding to an arbitrary hemisphere of data were integrated with SAINT [19]. Data were corrected for Lorentz and polarization effects and were further analyzed by using XPREP. An empirical absorption correction based on the measurement of redundant and equivalent reflections and an ellipsoidal model for the absorption surface was applied with use of SADABS [20]. The structure solution and refinement were performed with SHELXTL (refining on *F*²) program [21]. All non-hydrogen atoms were refined anisotropically. The positions of all hydrogen atoms attached on carbon were generated geometrically with the C–H bond fixed at 0.96 Å, assigned by isotropic thermal parameters, and allowed to ride on their respective parent carbon atoms before the final cycle of refinement. The O–H hydrogen atoms were located by a difference Fourier map and refined isotropically. The NO₂ moiety of one of nitrobenzenes in [(**1**)₆].3PhNO₂.4MeOH.2H₂O were also refined isotropically due to disorder. The crystallographic data and structure refinement are given in Table 1.

Crystal data (excluding structure factors) for the structures in this paper have been deposited with the

Table 1. Crystal data and structure refinement for 2(**1**).3PhNO₂.4MeOH.2H₂O and 2.C₆H₆.H₂O

Compound	2(1).3PhNO ₂ .4MeOH.2H ₂ O	2.C ₆ H ₆ .H ₂ O
Empirical formula	C ₈₆ H ₉₉ N ₃ O ₃₆	C ₅₀ H ₆₄ O ₁₃
Formula weight	1750.76	873.01
Crystal system	Rhombohedral	Rhombohedral
Space group	<i>R</i> -3	<i>R</i> -3
<i>a</i> , Å	35.4943(14)	34.9792(10)
<i>c</i> , Å	36.024(3)	24.4459(15)
Volume, Å ³	39304(4)	25903(2)
<i>Z</i>	18	18
<i>T</i> , K	293	293
Density (calcd), g/cm ³	1.363	1.007
Absorption coefficient, mm ⁻¹	0.106	0.072
<i>F</i> (000)	17064	8424
θ range for data collection, deg	0.87–22.98	1.07–22.72
Reflections collected	65780	25747
Independent reflections	12116	7735
<i>R</i> (int)	0.1290	0.0615
Data/restraints/parameters	12116/12/1110	7735/58/527
Goodness of fit on <i>F</i> ²	1.144	1.101
Final <i>R</i> ¹ , <i>wR</i> ² ^b [<i>I</i> > 2σ(<i>I</i>)] (all data)	0.1039, 0.2471	0.1215, 0.2405
	0.1740, 0.3378	0.1871, 0.2998
Final diff. features, e/Å ³	0.767, -0.402	0.871, -0.524

^a $R1 = \sum ||F_o| - |F_c|| / \sum |F_o|$ ^b $wR2 = [\sum w(|F_o|^2 - |F_c|^2)|^2 / \sum w|F_o|^2]^{1/2}$.

Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-254331/254332. These data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/conts/retrieving.html> (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

Results and discussion

Pyrogallol[4]arenes were prepared by using the same procedure for resorcin[4]arenes [22]. By comparison of resorcinol, pyrogallol was easily oxidized by the air, it is accordingly necessary to exclude the oxygen in the reaction system. The C_{4v} symmetrical isomer can be mostly isolated both under mild and reflux conditions, which may be reflected from the simple $^1\text{H-NMR}$ spectra, as reported [13]. *C*-methyl-pyrogallol[4]arene **1** and *C*-*iso*-butyl-pyrogallol[4]arene **2** are of typical C_{4v} symmetry which may provide the highest ability of supramolecular assembly. Treatment of a methanol solution of **1** with nitrobenzene under heating condition gave a clearly light yellow solution which was slowly diffused to yield large hexagonal crystals. Similarly, hexagonal crystals were also harvested from a methanol solution of **2** treated by benzene instead; the relatively high solubility of **2** is due to *iso*-butyl groups. The stable hexagonal-shaped crystals can be reproducibly obtained in a polar/non-polar mixture solvent system. Thus, far Atwood has reported hexameric molecular capsules of pyrogallol[4]arenes for $R = n$ -propyl, *n*-butyl, *iso*-butyl and *n*-pentyl [2], of which part hexameric molecules were crystallographically characterized [14, 15]. But the present hexameric molecular capsule of **1** ($R = \text{methyl}$) reported here is the first *C*-methyl to date. Although the hexameric capsule of **2** ($R = \textit{iso}$ -butyl) was previously prepared from the crystallization solutions of acetonitrile and methanol/nitrobenzene, respectively; accordingly, the hexameric structure was twice reported on space groups triclinic $P-1$ and rhombohedral $R-3$, respectively [13, 14]; it can be readily isolated from the methanol/benzene crystallization solution in an excellent yield and its structure reported here was refined without any solvent disorder.

Both hexameric molecular capsules of **1** and **2** crystallize in the rhombohedral space group $R-3$. The structures of the *C*-methyl-pyrogallol[4]arene and *C*-*iso*-butyl-pyrogallol[4]arene hexameric capsules are shown in Figures 1 and 2, respectively. As known, the macrocyclic rings of pyrogallol[4]arenes are more π -basic than those of resorcin[4]arenes, which should cause stronger interactions among each of six pyrogallol[4]arenes. The formation of capsule hexamers of **1** and **2** is further facilitated by direct hydrogen bonding between hydroxyl groups as shown in the crystalline state. A detailed inspection of Figures 1 and 2 shows that the hexamer, comprised of six molecular building blocks, is held together by 48 intermolecular hydrogen bonds, or by eight hydrogen bonds per

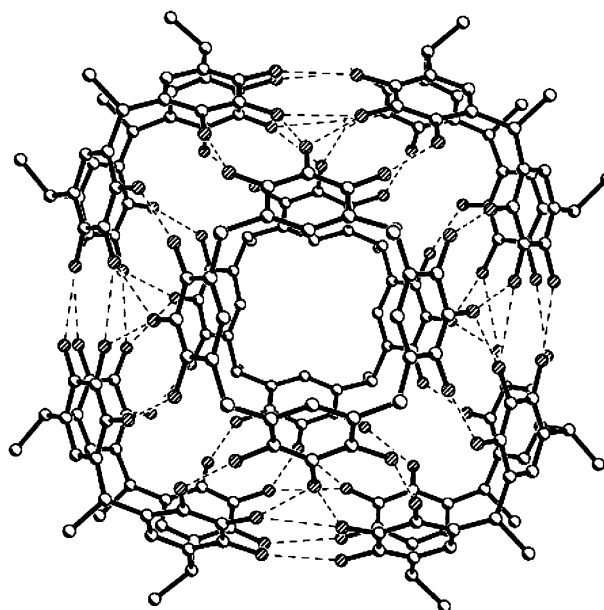


Figure 1. Crystal structure of the [(*C*-methyl-pyrogallol[4]arene)₆] hexamer (top view).

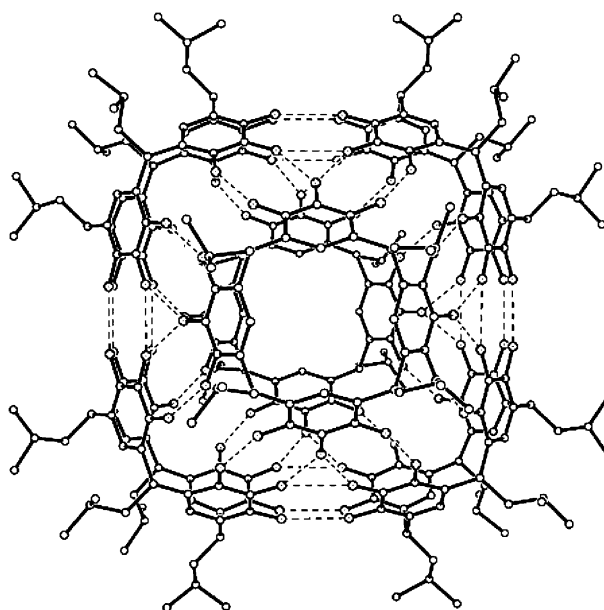


Figure 2. Crystal structure of the [(*C*-*iso*-butyl-pyrogallol[4]arene)₆] hexamer (top view).

molecule. The proximate hydroxyl $\text{O}\cdots\text{O}$ contacts within each pyrogallol[4]arene are in the range of 2.61–2.70 Å, implying that those oxygen are also hydrogen bonded to one another to form 24 intramolecular hydrogen bonds, or six hydrogen bonds per molecule. The $\text{O}\cdots\text{O}$ distances for the intermolecular hydrogen bonds range from 2.63 to 2.79 Å. The effective interior volumes of the hexameric capsules of **1** and **2** are ca. 1490 and 1520 Å³, respectively, calculated from the solid-state structures, which can be regarded as the total space available to the guest molecules. The volume difference between the capsules **1** and **2** is minute, partially being due to the difference of the steric bulk of the methyl and *iso*-butyl groups. The cavity volume of *C*-*n*-propyl-pyrogallol[4]arene hexameric capsule is about 1500 Å³ [15].

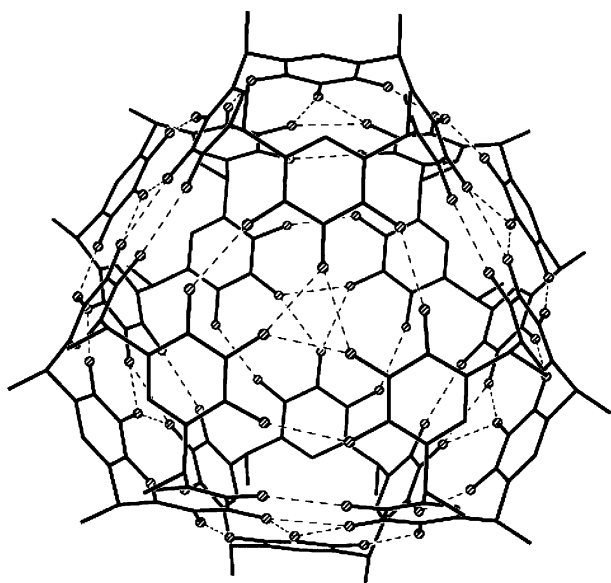


Figure 3. The spherical capsule of $[(C\text{-methyl-pyrogallol[4]arene})_6]$ hexamer is shown in the capped-stick (side view). Intermolecular H-bonds are shown in dash lines.

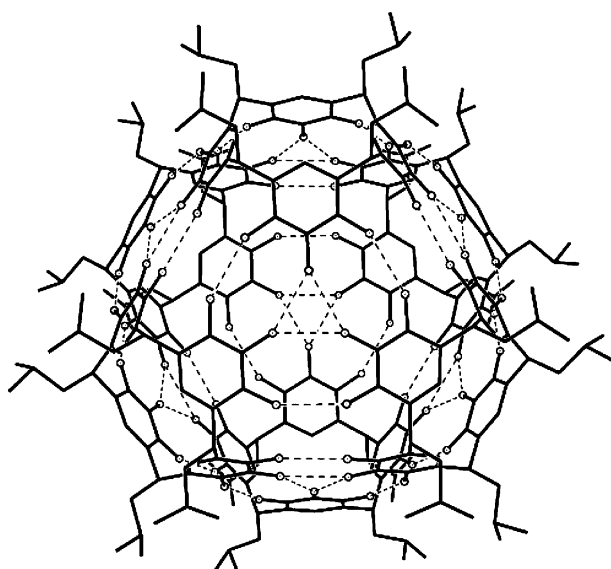


Figure 4. The spherical capsule of $[(C\text{-iso-butyl-pyrogallol[4]arene})_6]$ hexamer is shown in the capped-stick (side view). Intermolecular H-bonds are shown in dash lines.

Figures 3 and 4 present side views of capsules of **1** and **2**, respectively, with the framework in line bond representation. It is interesting to note that both capsules have similar geometry with the shape of a trigonal antiprism constructed from the centroids of the centers of the rings of mixed pyrogallol[4]arenes. In the capsule of **1**, the conformation of the pyrogallol[4]arenes is slightly distorted. A possible reason is that the equivalent distances between the centroids of the opposite pyrogallol rings range from 13.7 to 18.2 Å. Figure 5 illustrates the space-filling representation of the spherical capsule of **1** from the top view. It is clearly seen that a hole of the cavity formed by the opposite pyrogallol[4]arene rings may provide an effective entrance for the size-match guest molecules. Figure 6 displays the space-filling representation of the spherical capsule of **2**

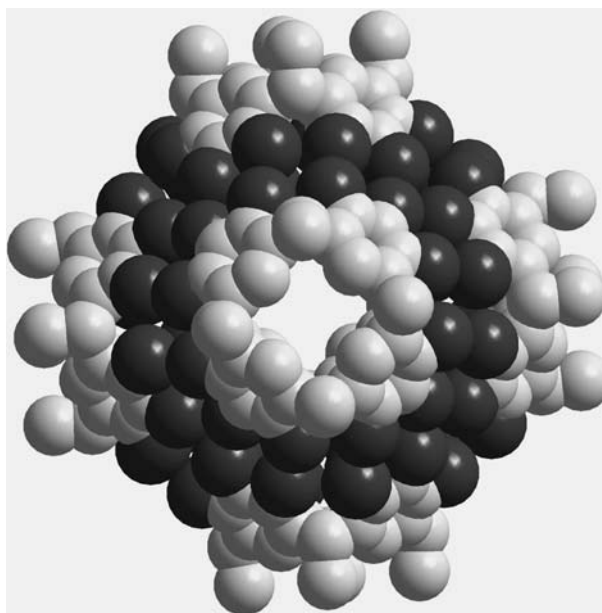


Figure 5. Space-filling representation of the spherical capsule of $[(C\text{-methyl-pyrogallol[4]arene})_6]$ (top view, black for oxygen atoms, grey for carbon atoms).

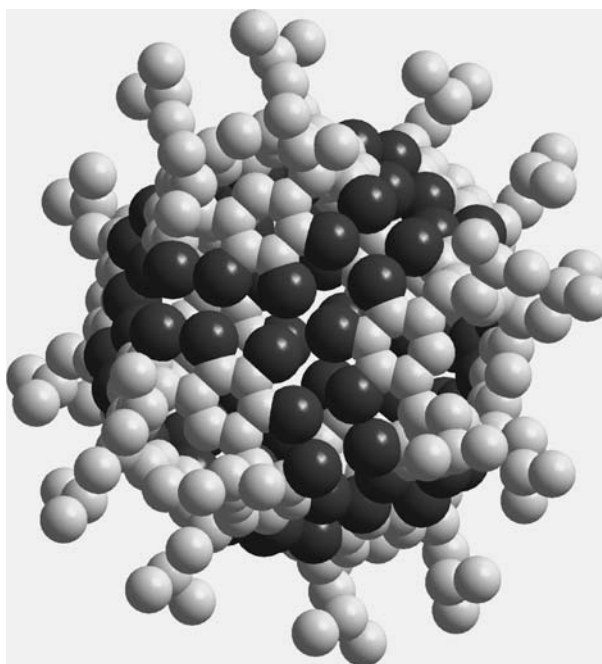


Figure 6. Space-filling representation of the spherical capsule of $[(C\text{-iso-butyl-pyrogallol[4]arene})_6]$ (side view, black for oxygen atoms, grey for carbon atoms).

from the side view. It may be seen that the oxygen atoms (black ball) form hydrogen-bonded bands to stabilize the capsule. In a view of structural characterization of the molecular capsule, the crystallization solvents were not found entrapped in the cavities of molecular capsules in the crystalline states. There are the bulk solvents (nitrobenzene in **1** and benzene in **2**) on the outside of the hexameric capsules, as shown in the packing diagrams of Figures 7 and 8. In conclusions, two spherically hexameric capsules of pyrogallol[4]arenes in highly polar media have been reproducibly synthesized and structurally characterized.

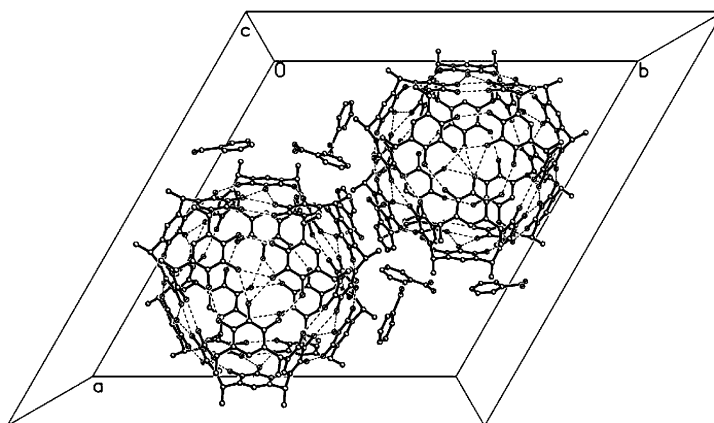


Figure 7. Unit cell packing of [(C-methyl-pyrogallol[4]arene)₆] with nitrobenzene molecules outside the spherical capsules.

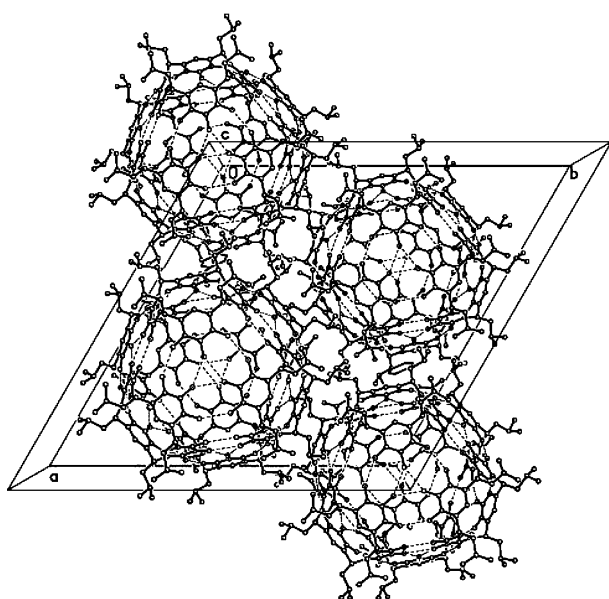


Figure 8. Unit cell packing of [(C-iso-butyl-pyrogallol[4]arene)₆] with benzene molecules outside the spherical capsules.

The spherical capsules exhibit very good stability with strong intermolecular hydrogen bonds, a possible explanation for the small variation in ¹HNMR spectra at different temperatures [14]. Therefore, since the capsules are readily assembled by dissolving the pyrogallol[4]arenes in suitable polar solvents, followed by crystallization by slow evaporation of the solvents, the interior volume of the capsule is large enough to accommodate molecular compounds as large as fullerenes as guests. This would be an interesting direction for the new host-guest chemistry.

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