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Modified Synthesis and Supramolecular Polymerization of Rim-to-Rim Connected Bisresorcinarenes

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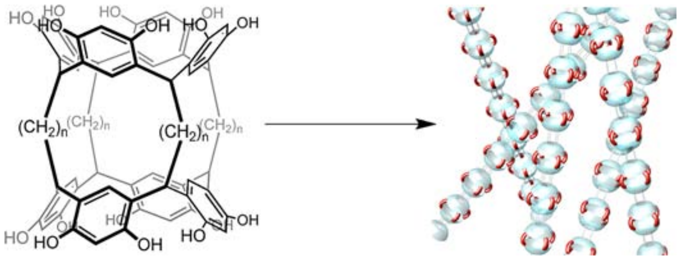
ABSTRACT



The acid-catalyzed condensation reaction of resorcinol and bisdimethoxyacetals gave rise to rim-to-rim connected bisresorcinarenes in good yields. In the presence of ethanol, the homoditopic bisresorcinarenes assembled to form supramolecular polymers via hydrogen bonding interactions. The fibrous morphologies of the supramolecular polymers were confirmed by atomic force microscopy and scanning electron microscopy.

Resorcinarenes are cyclic tetramers that are readily prepared by the condensation of resorcinol and alkyl aldehydes under acidic conditions.[1] The most stable conformer holds a bowl-shaped cavity formed by interaromatic hydrogen bonding. A great deal of effort has been devoted to the use of resorcinarenes as scaffolds in the synthesis of cavitands,[2] carcerands,[3] and self-assembled capsules[4] that contain enforced concave cavities that are sufficiently large to accommodate a variety of guest molecules.

Bisresorcinarenes have been prepared by connecting monofunctionalized resorcinarenes[5] in a back-to-back fashion.[6] The homoditopic nature of these bisresorcinarenes is potentially useful for the successful synthesis of supramolecular polymers[7] and bifunctional hosts.[8] Rim-to-rim connected bisresorcinarenes **1a**–**d** are more attractive and beneficial scaffolds for building bifunctional hosts because they are capable of participating in cooperative binding with guests in the two conformationally coupled resorcinarene cavities. Originally, Kudo, Nishikubo, and

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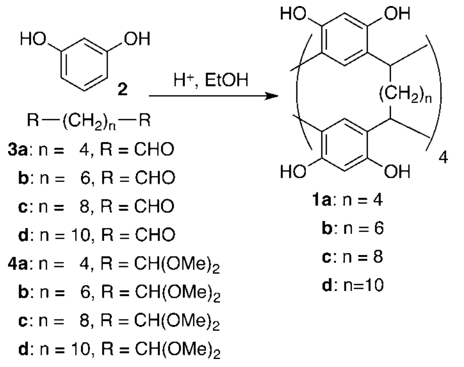
co-workers discovered rim-to-rim connected bisresorcinarene **1a**[9] during the synthesis of a double-cyclic ladder-type oligomer, named "noria."[10] We used the same reaction conditions with resorcinol and 1,6-hexandial to obtain crude mixtures containing predominantly **1a**, which required further purification. In general, the aldehyde functionality is very reactive under acidic conditions. A competitive aldol reaction might reduce the product yield. Employing dialdehydes masked with dimethylacetals can suppress the undesired side reactions to improve the yield of bisresorcinarenes. Here, we report a modified synthetic method for rim-to-rim connected bisresorcinarenes **1a**–**d** through the acid-catalyzed condensation of resorcinol **2** and bisdimethoxyacetals **4a**–**d**. We also report the crystal structure of **1a** and the supramolecular polymeric network formed by the self-assemblies of **1a**–**d** in the solid state.

Table 1. Acid-Catalyzed Condensations[a] of Bisresorcinarenes



entry	R–(CH$_2$)$_n$–R	product	yields (%)[b]
1	**3a**	**1a**	44[c]
2	**3b**	**1b**	27
3	**3c**	**1c**	19
4	**3d**	**1d**	29
5	**4a**	**1a**	45
6	**4b**	**1b**	62
7	**4c**	**1c**	57
8	**4d**	**1d**	33

[a] Reaction conditions: **2** (3.2 mol L^{-1}) and **3** or **4** (0.8 mol L^{-1}) in $^{\text{concd}}$HCl and EtOH (1:3) at 80 °C for three days. [b] Isolated yield. [c] The value reported in ref 9.

The macrocyclization reactions of **2** with dialdehydes **3** or bisdimethoxyacetals **4** were carried out in acidic ethanol at 80 °C for three days (Table 1), (entries 1–8). Every combination of reactants produced precipitates that contained predominantly the desired compounds, with no need for further purification except for the reactants in entry 1. When aldehydes **3** were reacted with **2**, the isolated yields of bisresorcinarenes **1a**–**d** were less than 50%. By contrast, the reactions of bisacetals **4a**–**d** and **2** under the same conditions gave obviously improved yields of the bisresorcinarenes. **1b**,**c** were obtained in quite good yields (entries 6 and 7). These conditions were apparently convenient for gram-scale synthesis.

Bisresorcinarenes **1a**–**d** were characterized using high-resolution mass spectrometry, ^{1}H NMR spectrometry, and ^{13}C NMR spectrometry. The high-resolution mass spectra of **1a**–**d** included peaks attributed to the molecular ions, the isotopic distributions of which perfectly matched the calculated distributions. The ^{1}H NMR and ^{13}C NMR spectra of **1a**–**d** indicated the highly symmetric natures of these compounds.

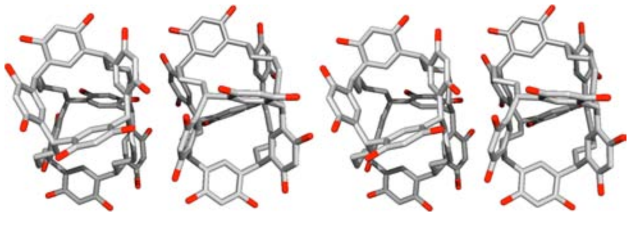


Figure 1. Stereoplot of the crystal structure of **1a**. Solvent molecules and hydrogen atoms are omitted for clarity.

Fortunately, **1a** crystallized in the triclinic unit cell $P\bar{1}$ from a DMF solution (Figure 1).[11] The crystal structure confirms that the lower rims of the two resorcinarene moieties are connected by the four alkyl chains. Two bisresorcinarene molecules are contained in the asymmetric unit, and each of the resorcinarenes adopts a cone conformation due to the interaromatic hydrogen bonds. One resorcinarene core was slightly twisted toward the other, resulting in a D_4-symmetric helical conformation. The *P* and *M* conformations combine into a racemic pair. The DMF molecules found in the crystal were hydrogen-bonded to the phenolic hydroxyl groups, and some were present in the resorcinarene cavities to fill the residual space (Figure S1d–g).

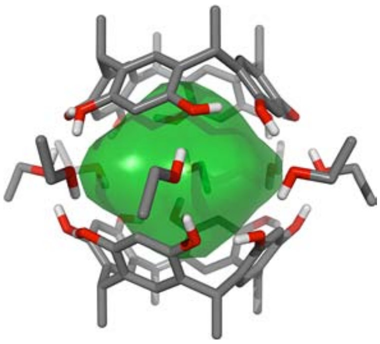


Figure 2. Calculated structure of the supramolecular capsule generated by MacroModel V.9.1.[12] The empty cavity is shown in green.

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Recently, the development of supramolecular polymers has been intensively studied in a noncovalent manner.[13] In this study, resorcinarenes in the solid state easily assembled into homodimeric capsules involving multiple hydrogen bonding networks with eight protic solvent molecules that were indirectly associated in a rim-to-rim fashion (Figure 2).[14] This structural motif can connect the bisresorcinarenes in a head-to-head manner to generate supramolecular polymeric structures.

Bisresorcinarenes **1a**–**d** were soluble in ethanol. The solutions of **1a**–**d** were drop-casted on glass and mica plates to obtain morphological information on the cast films using scanning electron microscopy and atomic force microscopy. The supramolecular polymerization of **1a**–**d** was only observed in the presence of toluene as a cosolvent (Figures S2 and S3). Figure 3a,b show the fibrous morphologies prepared from a solution of **1b** in the presence of toluene, clearly indicating the anisotropic growth of the polymeric assembly of **1b**. The height of 12 ± 5 nm was obtained from the topographical image. The molecular diameter of the dimeric capsule was ca. 1.6 nm, suggesting that the supramolecular polymer formed fibrils of approximately 12 nm in diameter. By contrast, chloroform enhanced the growth of the microcrystals (Figure 3c), whereas the absence of cosolvents gave rise to particles with an amorphous morphology (Figure 3d). A cast film of **1b** prepared in the presence of DMF contained particle-like aggregates (Figure 3e), suggesting that the competitive hydrogen bonding of the DMF molecules to the phenolic hydroxyl groups most likely disrupted the dimeric structures, leading to the random aggregation of the bisresorcinarenes.

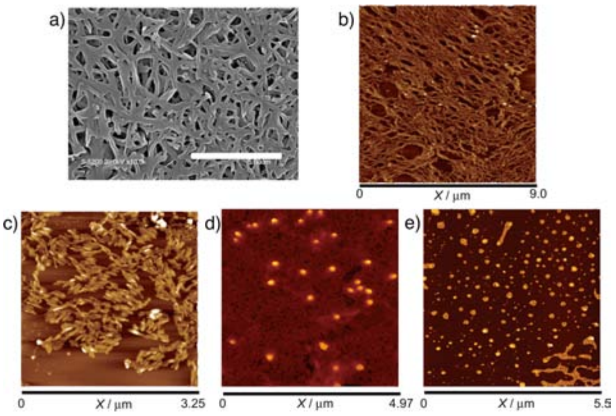

Figure 3. (a) SEM and (b–e) AFM images of cast films prepared from ethanol solutions of **1b** with (a–b) toluene, (c) chloroform, (d) no cosolvent, and (e) dimethylformamide. The white scale bar in (a) denotes 5 μm.

The presence of the cosolvents highly influenced the supramolecular polymerization. The contribution of cosolvents to supramolecular polymerization can be explained by assuming that the cosolvents are encapsulated within the cavity of the capsular structure. The volume of the inner cavity was calculated to be ca. 237 Å^3 (Figure 2).[15] Judging from the molecular volumes of toluene and chloroform molecules (100 and 70 Å^3, respectively), toluene is a better guest for the dimeric capsule.[16] The guest encapsulation could provide the additional stabilization that enhances the supramolecular polymerization; in fact, the uniform fibers disappeared without a cosolvent (Figure 3d).[17]

In summary, we developed an efficient method for the synthesis of rim-to-rim connected bisresorcinarenes and for their self-assembly to produce the supramolecular polymers. The modified reaction conditions greatly improved the purification procedures as well as the compound yields.

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(11) Crystallographic data (CCDC 890145) for **1a**: $C_{175.5}H_{227.5}N_{10.5}O_{47.5}$, M = 3244.18; crystal dimensions (mm^3) 0.2 × 0.1 × 0.1; triclinic space group $P\bar{1}$; a = 17.196(3) Å, b = 20.217(4) Å, c = 27.804(5) Å; α = 75.126(3)°, β = 86.009(3)°, γ = 66.856(2)°; V = 8585(3) Å^3; ρ_{calcd} = 1.255 g cm^{-3}; T = 173 K; Z = 2; Mo Kα radiation, λ = 0.7107 Å; 2θ = 50°; total data collected = 29151; R = 0.1268 [26507 observed reflections with $F_o^2 \geq 2\sigma(F_o^2)$]; wR_2 = 0.2652 for 2057 variables, 29151 unique reflections; GOF = 1.127.

(12) Molecular Mechanics calculation was carried out by MacroModel V.9.1 using the OPLS2005 force field.

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(15) The cavity volume was calculated by Swiss-Pdb Viewer.

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(17) The effect of tetraalkylammonium salts ($Me_4N^+Cl^-$, $Et_4N^+I^-$, n-$Pr_4N^+Br^-$, and n-$Bu_4N^+I^-$) was examined on the self-assembly of **1b** using AFM measurements. The microcrystals were formed in the presence of $Me_4N^+Cl^-$ and $Et_4N^+I^-$. n-$Pr_4N^+Br^-$ and n-$Bu_4N^+I^-$ slightly influenced the aggregation of **1b** to produce the particle-like aggregates (Figure S4).

We anticipate that this facile process will be of high value to the supramolecular community. Further modification of the bisresorcinarene platform as part of the development of new supramolecular polymeric assemblies is now underway.

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Supporting Information Available. Experimental details, characterization data, copies of NMR and HRMS spectra, crystallographic data (CIF) for **1a**, and SEM and AFM images of cast films of **1a**–**d**. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.