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Hydrocarbon Binding Inside a Hexameric Pyrogallol[4]arene Capsule

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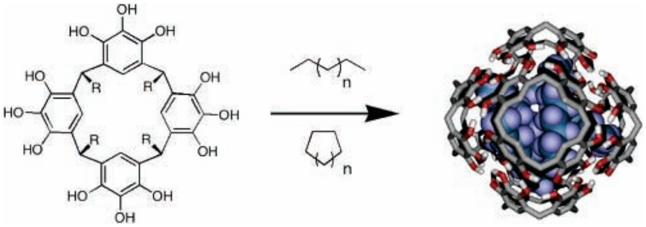
ABSTRACT



Pyrogallol[4]arene forms discrete hexameric capsules in neat normal, branched, and cyclic alkanes. These hydrocarbon guests fill the available space and show chemical exchange that is slow on the NMR time scale.

The pyrogallol[4]arene macrocycles (**1**) form hexameric capsules (**1_6**) both in the crystalline state[1,2] and even in C_6D_6 or $CDCl_3$ solutions[3,4] (Scheme 1). In the latter solvent, Avram and Cohen deduced a hexameric assembly for **1** in using DOSY NMR.[5] Unlike related resorcinarene capsules, **1_6** does not require water for assembly,[6] and we hoped that **1** would form capsules in highly apolar media. Accordingly, we investigated the behavior of **1** in aliphatic hydrocarbons and report here our experiences.

We found the amphiphilic **1** to be soluble in *n*-octane after brief heating. In the room temperature ^1H NMR spectrum (Figure 1), the phenolic protons of **1** appear as three downfield resonances (shown in blue), indicating three distinct chemical environments for these hydroxyls.[7] The remaining resonances for **1** (red) are typical of a hexameric capsule. The upfield region shows encapsulation of about

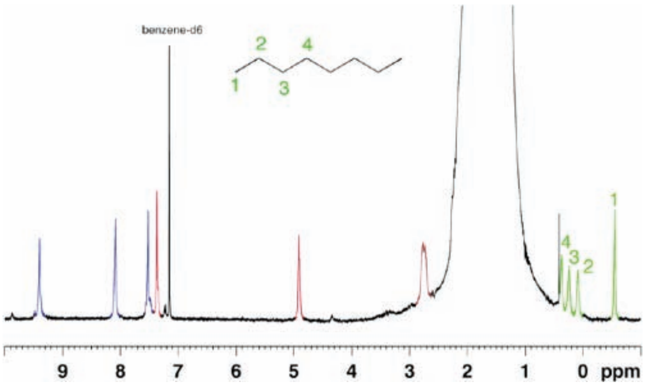


Figure 1. ^1H NMR of **1** in *n*-octane (600 MHz, 298 K). Host O−H protons are shown in blue. Other host methine protons are shown in red. Encapsulated solvent is shown in green. Benzene-d_6 was used as an external lock standard.

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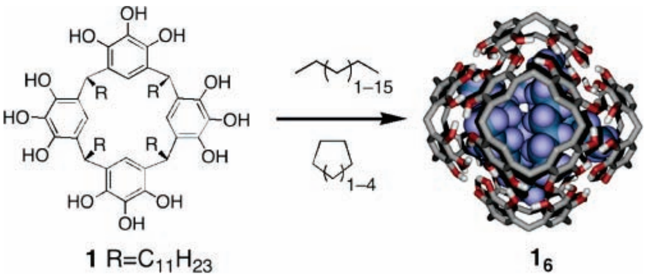
(7) All three O*H* resonances diminish when exchanged for deuterium.

10.1021/ol047673x CCC: $30.25

Scheme 1. Pyrogallol[4]arenes Assemble to Hexameric Capsules in a Variety of Nonpolar Liquid Hydrocarbons[a]



[a] Solubilizing groups (R) have been omitted from the capsule structure for clarity.

five *n*-octane molecules per hexamer.[8] Two-dimensional COSY NMR confirmed the assignment of guest resonances as shown (green). At lower field strength (400 MHz), the splitting on the encapsulated methyl resonance appeared as a triplet of triplets ($J = 7.5$ and 1.5 Hz). The observed splitting results from spin−spin coupling to the protons at both C2 and C3 and indicates some slowed C−C bond rotation for the encapsulated guest. Heating the NMR sample to 323 K caused no significant change in the peak intensities or shapes. In−out guest exchange is slow on the NMR time scale, as expected for an encapsulated species.[9]

The host **1** dissolves in *n*-octane at concentrations >60 mg/mL, higher than 8 mM in capsule. Most of the NMR samples were prepared using ca. 5 mg of **1** per 400 μL of solvent. Many of the other alkane solutions were saturated with host even at these lower concentrations.

The encapsulation appears to be general for the entire series of commercial liquid *n*-alkanes from C_5H_{12} to $C_{20}H_{42}$ (Figure 2), yet peculiarities are observed in the upfield signals of encapsulated solvents. The terminal methyls of the smaller alkanes (C_5H_{12}−C_8H_{20}) are the most upfield shifted, placing them in close proximity to the aromatic walls of the host and in an extended conformation. For longer alkanes (C_9H_{20}−$C_{12}H_{26}$), the methyls are less upfield shifted; the methylenes are nearer the aromatic walls, and the chains are folded. In the case of $C_{12}H_{26}$, the assignment of encapsulated guest protons was supported by a two-dimensional COSY experiment. The spectrum with C_9H_{20} shows two broad resonances in the upfield region, in addition to the major (sharp) peaks for guest encapsulation. Two-dimensional COSY shows that these peaks are coupled to each other but not to the other encapsulated guest protons. These peaks likely result from an impurity in the C_9H_{20}. Capsules are known to be uncanny hosts for trace impurities in solvents.[10] Typically, a 0.1% impurity in a solvent can be present at the concentrations comparable to that of the capsule (mM).

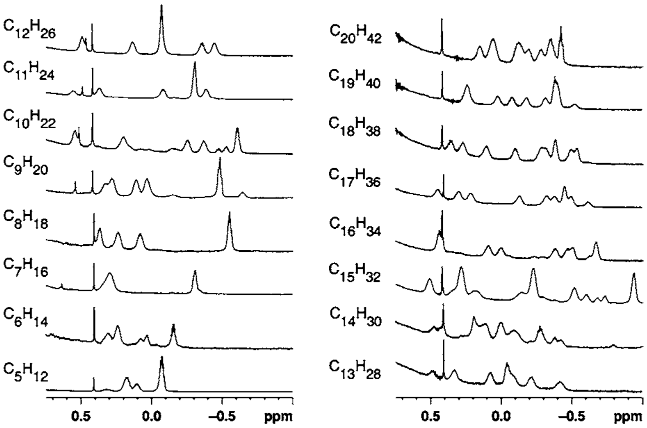


Figure 2. Upfield ^1H NMR spectra of **1** in a series of liquid *n*-alkanes (600 MHz). The higher alkanes ($C_{18}H_{38}$−$C_{20}H_{42}$) were measured at 323 K to ensure complete melting; all other spectra were acquired at 298 K.

For many capsular systems in solution, molecules occupy around 55% of the available volume, a measure of the packing coefficient (PC).[11] The observed PCs for hexameric resorcin[4]arene capsules are all lower than this value, e.g., benzene (0.45),[4b] 1,2-cyclohexanediol (0.44),[4c] and tetraalkylammonium salts (0.33−0.48).[5] X-ray crystallography has shown a range of cavity volumes from 1200 to 1520 Å^3 for the pyrogallol[4]arene and about 1375 Å^3 for the resorcin[4]arene. Even the solubilizing R groups can affect the volume.[1,2] We calculated the PCs in Table 1 using the volume of the smallest solid-state pyrogallol[4]arene capsule (1200 Å^3). For smaller guests such as C_5H_{12}, up to six molecules are encapsulated; for larger guests such as $C_{12}H_{26}$, we observe only three molecules inside (Table 1). While the number of encapsulated guests varies, the packing coefficients are within the range (0.40−0.54). Folding or coiling, particularly of the longer alkanes, could allow these guests to occupy an even greater proportion of the available space.

Table 1. Encapsulation of Nondeuterated *n*-Alkanes in Pyrogallol[4]arene Hexamer **1₆** at 298 K

guest	volume (Å^3)[a]	guest/**1₆**[b]	PC[c]
n-pentane	85	6	0.43
n-hexane	99	5	0.41
n-heptane	116	5	0.48
n-octane	130	5	0.54
n-nonane	145	4	0.48
n-decane	160	3	0.40
n-undecane	178	3	0.45
n-dodecane	190	3	0.48

[a] Size of each guest was based on the van der Waals surface of the fully extended conformation generated by WebLab Viewer Pro. [b] Integrations are based on the best-resolved encapsulated guest signal (methyl or methylene) and the methine of **1** (assumed to be 24 H per hexamer). [c] Packing coefficients based on a capsule volume of 1200 Å^3.

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(8) Presence of large nondeuterated solvent peaks and the difficulties in shimming lead to higher than normal errors in the integration (at least 20−30%).

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The spectra of the higher alkanes are more complicated and harder to interpret (Figure 2). As longer alkanes are used, the spectral baseline intensity increases and the intensity of encapsulated peaks decreases, making accurate integration even more difficult. The alkanes $C_{18}H_{38}$ and longer are solids at room temperature and must be warmed to form capsule-containing solutions. The NMR spectra of these samples were acquired at 323 K (Figure 2). Under these conditions, a single molecule appears encapsulated; some capsule "melting" was observed (i.e., monomer in equilibrium with hexamer), possibly resulting from both heating and poor host−guest complementarity.

Branched (e.g., isooctane) and cyclic alkanes (e.g., cyclopentane, cyclohexane, cyclooctane, decalin) are well encapsulated, as are Et_4Si and Bu_4Ge (see Supporting Information). Very long alkanes (e.g., $C_{21}H_{44}$) show only slight solubilization and encapsulation that may depend on the presence of trace impurities. Squalane (2,6,10,14-hexamethyltetracosane), the longest fully saturated liquid hydrocarbon that we could find commercially, shows small but detectable encapsulation at room temperature.

The ^{1}H NMR spectrum of **1** in commercial bulk hexanes (a mixture of isomers) was quite complicated, suggesting the coencapsulation of multiple species. In another experiment, the pairwise mixing of alkanes (e.g., 1:1 pentane/octane, v/v) gave new encapsulated peaks at the expense of those in the spectra of either pure hydrocarbon (Figure 3). These new resonances speak for the coencapsulation of several different guests within the large hexamer. The attractive forces (CH−π interactions[12]) are among the weakest of interactions, and hydrocarbons cannot be encapsulated in the presence of better guests. For example, no alkane encapsulation is observed in a 1:1 *n*-octane/$CDCl_3$ (v/v) solution.

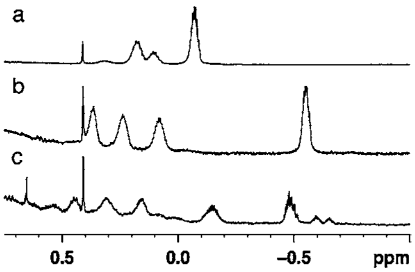

Figure 3. ^{1}H NMR of **1** in (a) *n*-pentane, (b) *n*-octane, and (c) 1:1 *n*-pentane/*n*-octane (v/v).

In summary, **1** forms a hexameric structure in neat, aliphatic hydrocarbons and encapsulates them with PCs between 40 and 55%. Coencapsulation of two different hydrocarbon guests also occurs and is likely driven by the better filling of the space by the combinations vs multiple copies of a single guest.

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Supporting Information Available: Experimental details and additional NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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