

## Supporting information

### Guest Mediated Switching of the Assembly State of Water-Soluble Deep-Cavity Cavitands

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## Contents

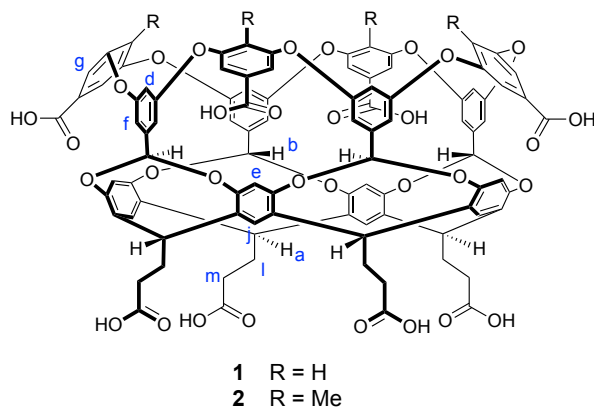
Experimental Section	p S3
Synthesis of tetrahedral template guest <b>3</b>	p S4
Steric Influences of <i>Endo</i> Methyl groups of TEMOA <b>2</b>	p S5
<sup>1</sup> H NMR data for binding between TEMOA <b>2</b> and straight-chain alkanes	p S6
<sup>1</sup> H NMR shifts ( $\delta$ ) and $\Delta\delta$ for the complexes between TEMOA <b>2</b> and straight-chain alkanes	p S10
<sup>1</sup> H NMR data for the encapsulation of tetrahedral template <b>3</b>	p S11
Pulse-gradient stimulated spin-echo NMR studies	p S12
References	p S16

## Experimental section

### General

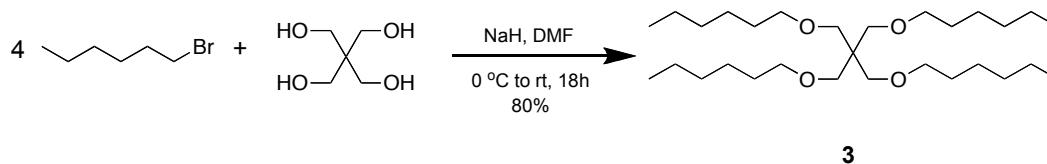
All reagents were purchased from Aldrich Chemical Company. The compounds *n*-tetradecane (C14), *n*-eicosane (C20), *n*-pentacosane (C25), and *n*-hexacosane (C26) were used as received without further purification. Compounds *n*-heneicosane (C21) through *n*-tetracosane (C24) were found to be contaminated with *n*-decane (C10). Consequently, these were purified by adding the crude guest to a 1 mM aqueous solution of host **1** in 10 mM NaOH and heating and shaking the resulting suspension for 5 minutes. (Host **1** readily forms a 2:1 capsular complex with *n*-decane.) After decanting off the aqueous solution, this process was repeated before the purified long chain alkane was washed with water. Decanting the water and drying under reduced pressure gave the pure guest.

Hosts **1** and **2** were synthesized as previously reported.<sup>1,2</sup> Column chromatography was performed using Dynamic Adsorbents Inc. 32-63 micron silica gel. NMR spectra were recorded either on a Varian Inova 400 MHz or Varian Inova 500 MHz spectrometer. Chemical shifts are reported relative to solvent (D<sub>2</sub>O at 4.80 ppm and CDCl<sub>3</sub> at 7.26ppm). Mass spectra were obtained using the GC-MS technique on Varian 300 MS (SQ Mass Spectrometer). Elemental analyses were conducted by Midwest Microlab.



### Synthesis of tetrahedral template guest **3**

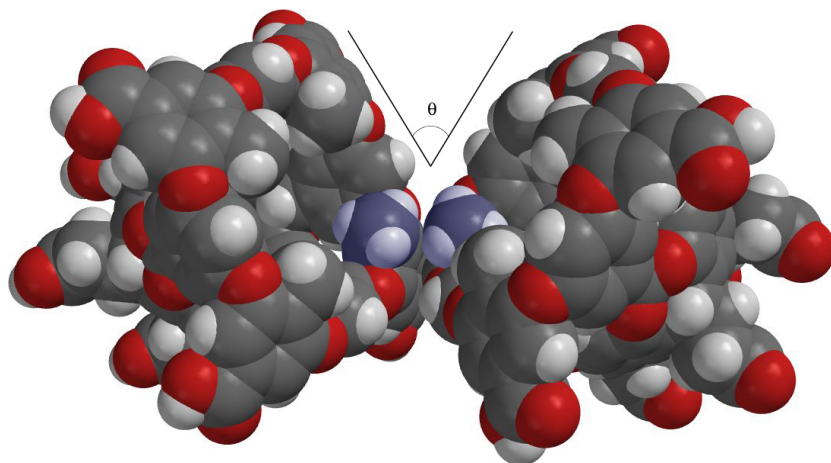
The synthesis of guest **3** is shown in Scheme S1. Pentaerythritol (200 mg, 1.47 mmol) was dissolved in anhydrous DMF and then added to a flask containing 25 mL anhydrous DMF and 1.13 g NaH (1.13 g, 29.4 mmol, 60% suspension in oil) at 0 °C. This mixture was allowed to stir at this temperature for 30 min then warm to rt for 30 min. To this flask was added 1-bromohexane (1.03 mL, 7.35 mmol), and the reaction stirred at rt for 1 d. Subsequently the solvent was removed under reduced pressure to give the crude product as a yellow solid/oil. This was then filtered through celite and washed with CHCl<sub>3</sub>. Removal of the solvent under reduced pressure gave the crude oil product that was purified by column chromatography (5% EtOAc-Hexane mobile phase). This gave pure **3** in 80% yield. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ (ppm) 0.88 (t, *J* = 6.4 Hz, 12H), 1.29 (m, 24H), 1.52 (m, 8H), 3.37 (m, 16H). GC-MS: Calcd. 473.5 [M + 1], Found: 473.4 [M + 1] Anal. Calcd. for C<sub>29</sub>H<sub>60</sub>O<sub>4</sub>: C, 73.67; H, 12.79. Found: C, 73.71; H, 12.63.



Scheme S1. Synthesis of tetrahedral template guest **3**.

### Steric Influences of Endo Methyl groups of TEMOA 2

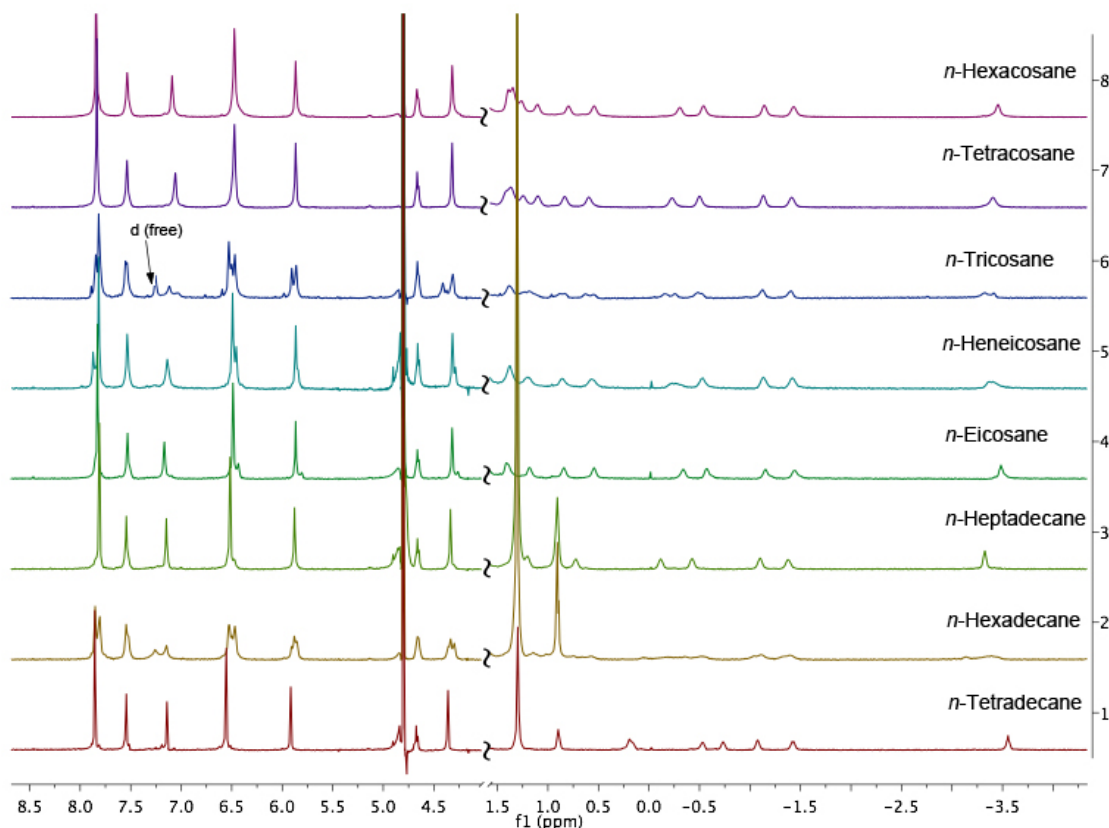
An inspection of CPK models shows that the steric hindrance imparted by the methyl groups in the dimer assembly is diminished in both a tetrameric assembly ( $D_{2d}$ /pseudo  $T_d$ ) and a hexameric ( $O_h$ ) assembly. Thus as the bite-angle  $\theta$  between two cavitand subunits (Figure S1) is opened from  $0^\circ$  (dimer) to  $70.5^\circ$  (tetrahedron) to  $90^\circ$  (cube) so steric clash between the endo-methyl group (highlighted in blue) decreases.



**Figure S1.** Bite-angle ( $\theta$ ) between two cavitand subunits. In the dimer, tetrameric  $D_{2d}$ /pseudo  $T_d$ , and hexameric ( $O_h$ ) assemblies this angle is respectively  $0^\circ$ ,  $70.5^\circ$ , and  $90^\circ$ .

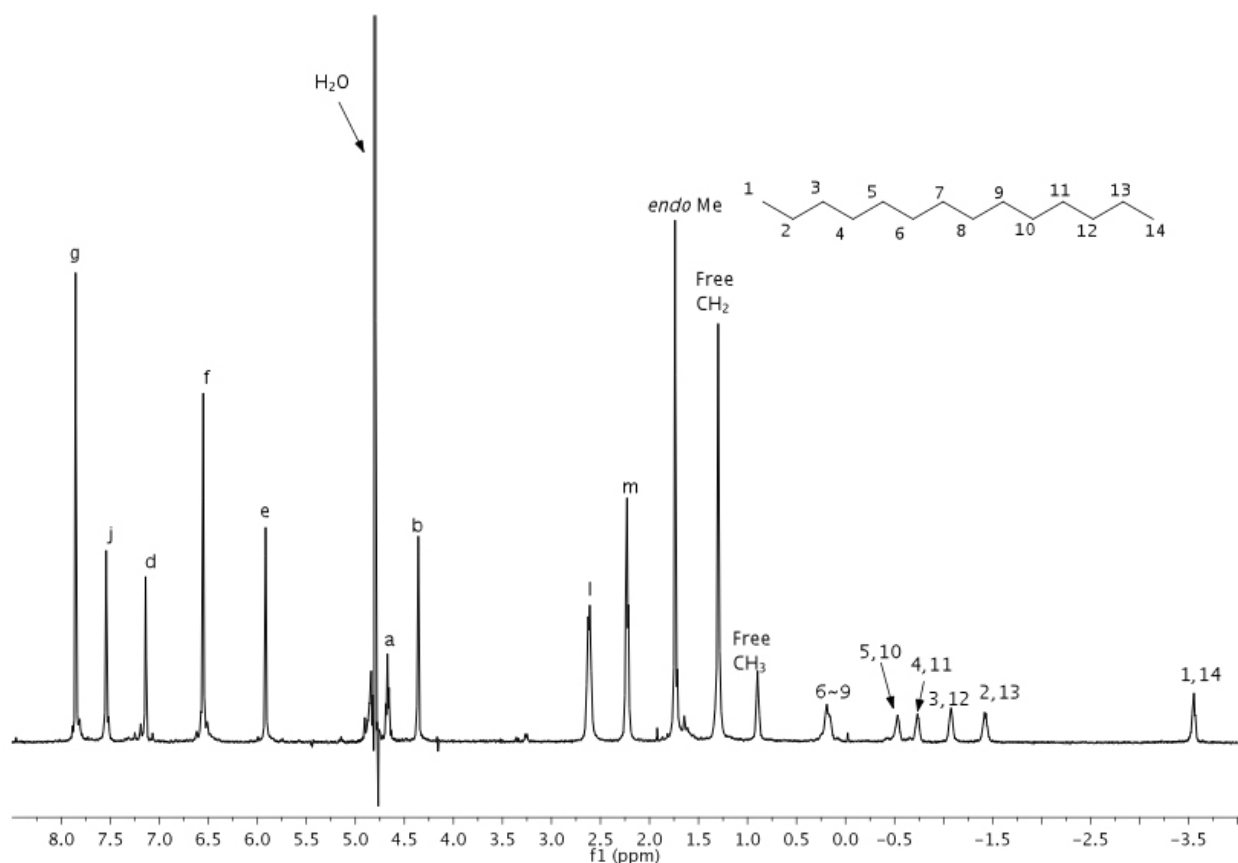
## <sup>1</sup>H NMR data for binding between TEMOA **2** and straight-chain alkanes

<sup>1</sup>H NMR spectra were recorded on an INOVA 500 MHz (Varian Inc.) instrument at 25 °C. 1 mM aqueous solutions of host **2** in 100 mM NaOH were used in the formation of assemblies involving guest *n*-tetradecane through *n*-tricosane. For the larger guests *n*-tetracosane through *n*-hexacosane 3 mM host **2** in 100 mM sodium hydroxide was used to ensure complete formation of the hexameric host assembly. In each case an excess of guest (10 μL for liquid guest, ca. 2 mg for solid guest) was added to 0.6 mL of the solution of host **2**. For the guests C14-C17, 30 minutes sonication was sufficient for complete complex formation. For the guests C18 to C26 it was necessary to heat the solution in an oil bath at 70-80 °C for periods that depended on the concentration of the host and the size of the guest. For example, C24 at 3 mM host and 100 mM NaOH required two days, whereas at a 1 (3) mM host concentration the guests C21-C23 (C25-C26) required 20 days. The NMR spectrum of each mixture was subsequently recorded. Integration for the host peaks versus the bound guest methyl peaks gave the ratio of host and guest.

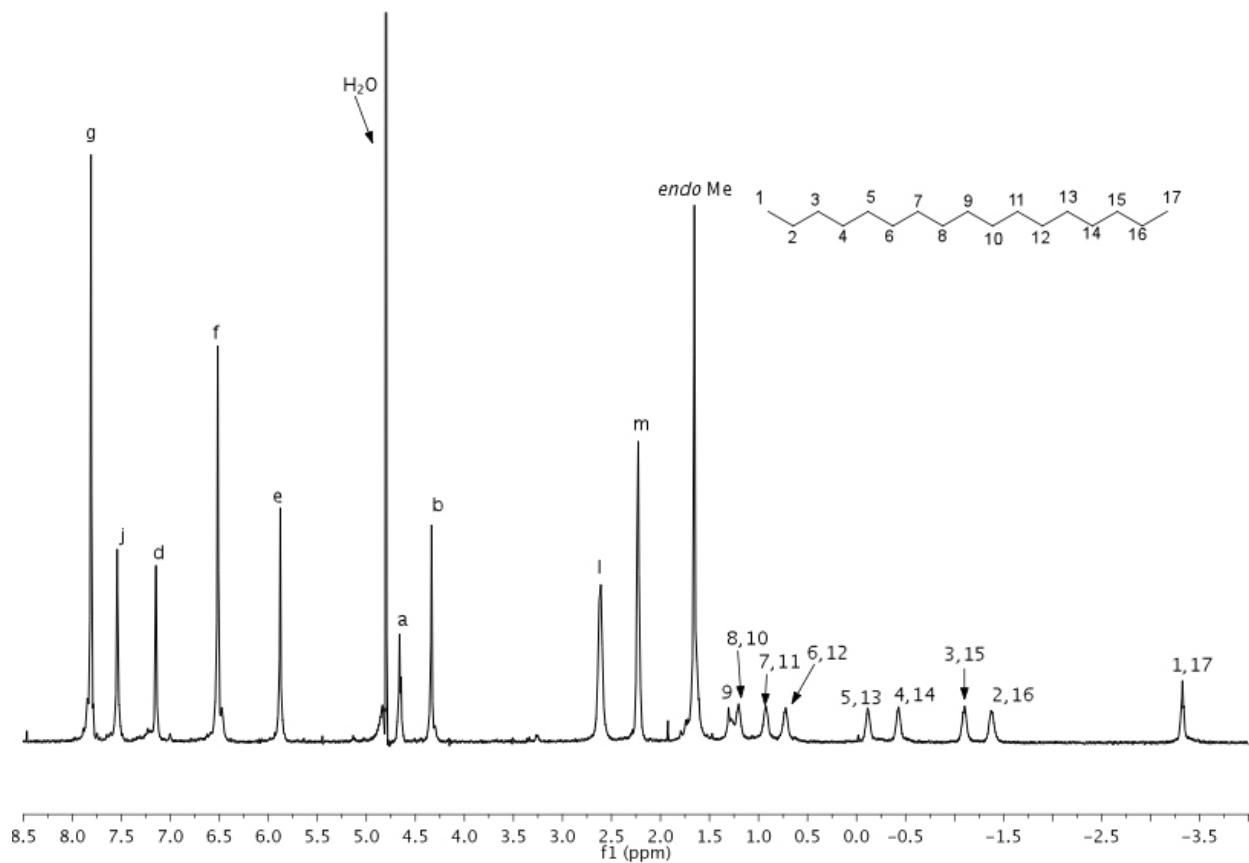


**Figure S2.** <sup>1</sup>H NMR spectra of the complexes formed between host **2** and: 1) *n*-tetradecane C14; 2) *n*-hexadecane C16; 3) *n*-heptadecane C17; 4) *n*-eicosane C20; 5) *n*-heneicosane C21; 6) *n*-tricosane C23; 7) *n*-tetracosane C24; and 8) *n*-hexacosane C26. Solutions 1 to 6 were 1 mM complex in D<sub>2</sub>O, 100 mM NaOD; solutions 7 and 8 were 3 mM complex in D<sub>2</sub>O, 100 mM NaOD.

The  $^1\text{H}$  NMR spectra of the complexes formed with *n*-tetradecane C14, *n*-hexadecane C16, *n*-heptadecane C17, *n*-eicosane C20, *n*-heneicosane C21, *n*-tricosane C23, *n*-tetracosane C24 and *n*-hexacosane C26 are stacked in Figure S2. Expanding on three of these, the  $^1\text{H}$  NMR spectra of the complexes with C14, C17, and C24 are shown respectively in Figures S3, S4 and S5. Guest signal assignments were made from COSY NMR experiments. Integration of the  $^1\text{H}$  NMR data gave a 2:1 host-guest ratio in the case of all complexes. PGSE NMR experiments (below) were necessary to confirm the 2:1 host-guest stoichiometry in the case of small guests such as C14, and the higher stoichiometries of the larger assemblies (4:2 and 6:3).

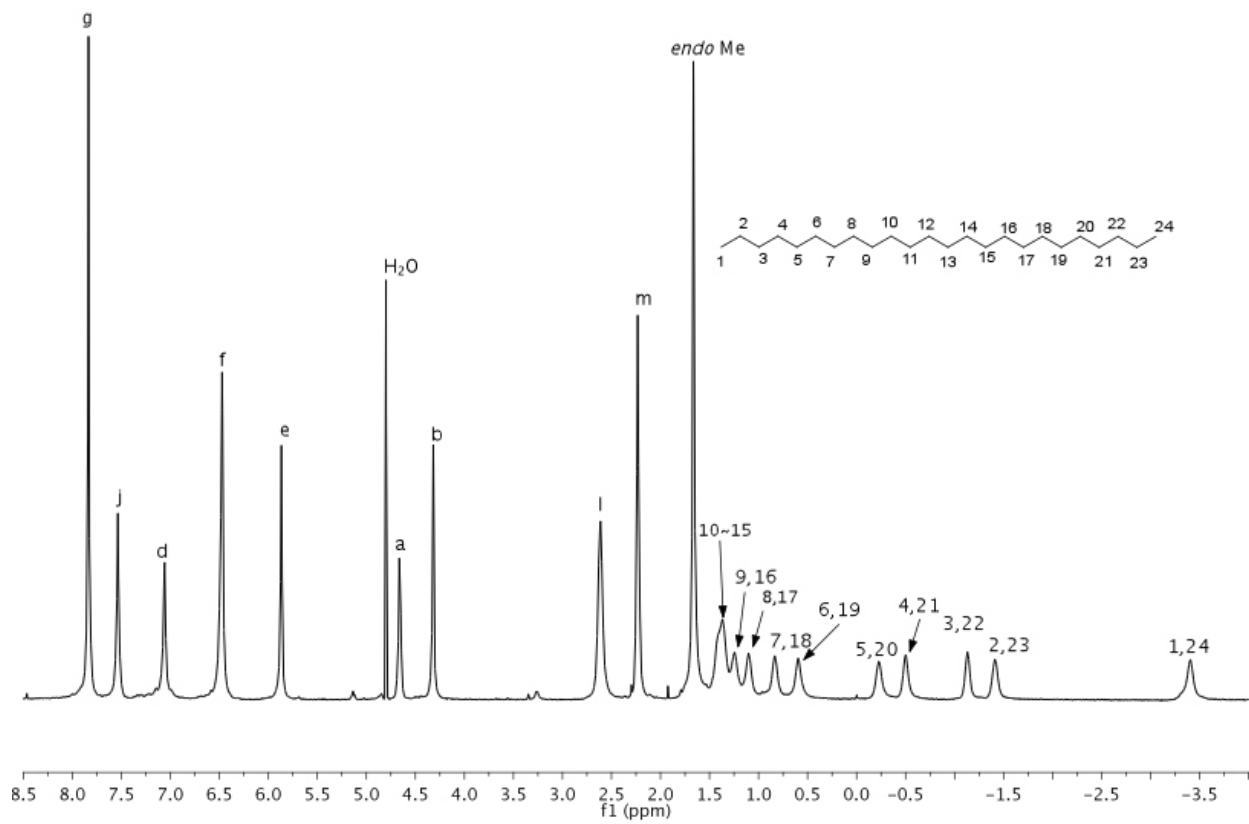


**Figure S3.**  $^1\text{H}$  NMR spectra of the complexes formed between 1 mM **2** and *n*-tetradecane in  $\text{D}_2\text{O}$ , 100 mM NaOD.



**Figure S4.**  $^1\text{H}$  NMR spectra of the complexes formed between 1 mM **2** and *n*-heptadecane in  $\text{D}_2\text{O}$ , 100 mM NaOD.





**Figure S5.**  $^1\text{H}$  NMR spectra of the complexes formed between 3 mM **2** and *n*-tetracosane in  $\text{D}_2\text{O}$ , 100 mM NaOD.

## <sup>1</sup>H NMR shifts ( $\delta$ ) and $\Delta\delta$ for the complexes between TEMOA 2 and straight-chain alkanes

The <sup>1</sup>H NMR shift values ( $\delta$ ) and  $\Delta\delta$  for four sets of host protons are shown in Table S1. Characteristic of assembly of the dimeric capsule is a small upfield shift in the H<sub>d</sub> signal, and as shown here, as the assembly increases in size so this upfield shift is seen to increase up to a maximum of  $\Delta\delta = 0.19$  ppm for the octahedral assembly. In contrast, the signal from the endo-Me group undergoes a small but characteristic downfield shift with the dimeric assembly, but this shift attenuates as the assembly product increases in size. Other signals that may be expected to shift upon complex formation (H<sub>g</sub> and H<sub>j</sub>) underwent only small changes.

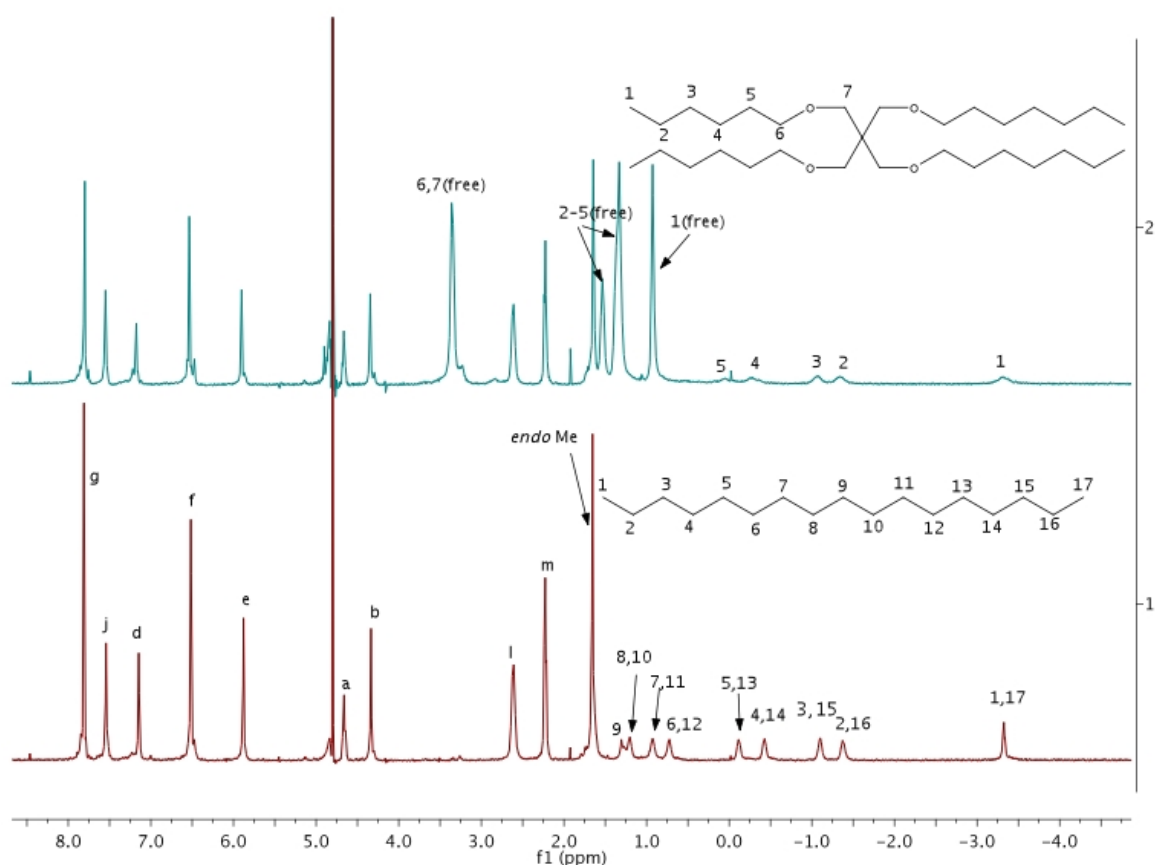
**Table S1:** <sup>1</sup>H NMR shift values ( $\delta$ ) and \* $\Delta\delta$  ( $\delta_{\text{bound}} - \delta_{\text{free}}$ ) values for the complexes formed by TEMOA 2.

System (in 100 mM NaOD)	H <sub>d</sub> $\delta$ ( $\Delta\delta$ ) values	H <sub>Endo Me</sub> $\delta$ ( $\Delta\delta$ ) values	H <sub>g</sub> $\delta$ ( $\Delta\delta$ ) values	H <sub>j</sub> $\delta$ ( $\Delta\delta$ ) values
1mM TEMOA	7.22	1.68	7.82	7.55
1mM TEMOA + C14	7.14 (-0.06)	1.74 (0.06)	7.85 (0.03)	7.54 (-0.01)
1mM TEMOA + C15	-	1.62 (-0.06)	7.86 (0.04)	7.53 (-0.02)
1mM TEMOA + C16	7.15 (-0.07)	1.61 (-0.07)	7.81 (-0.01)	7.52 (-0.03)
1mM TEMOA + C17	7.15 (-0.07)	1.65 (-0.03)	7.81 (-0.01)	7.54 (-0.01)
1mM TEMOA + C18	7.17 (-0.05)	1.65 (-0.03)	7.83 (0.01)	7.54 (-0.01)
1mM TEMOA + C19	7.16 (-0.06)	1.65 (-0.03)	7.83 (0.01)	7.54 (-0.01)
1mM TEMOA + C20	7.17 (-0.05)	1.64 (-0.04)	7.83 (0.01)	7.53 (-0.02)
1mM TEMOA + C21	7.14 (-0.08)	1.64 (-0.04)	7.87 (0.05)	7.53 (-0.02)
1mM TEMOA + C23	7.12 (-0.10) <sup>1</sup> 7.03 (-0.19) <sup>2</sup>	1.66 (-0.02) <sup>1</sup> 1.66 (-0.02) <sup>2</sup>	7.85 (0.03) <sup>1</sup> 7.89 (0.07) <sup>2</sup>	7.54 (-0.01) <sup>1</sup> 7.54 (-0.01) <sup>2</sup>
3mM TEMOA	7.20	1.65	7.82	7.56
3mM TEMOA + C24	7.06 (-0.14)	1.66 (0.01)	7.84 (0.02)	7.54 (-0.02)
3mM TEMOA + C26	7.09 (-0.11)	1.67 (0.02)	7.84 (0.02)	7.54 (-0.02)

<sup>1</sup>Tetrameric assembly. <sup>2</sup>Hexameric assembly.

### <sup>1</sup>H NMR data for the encapsulation of tetrahedral template **3**

Tetrahedral template guest **3** has eight non-hydrogen atoms on each side-chain and one center carbon. It therefore has approximately the same (methyl to methyl) length as *n*-heptadecane (C17). The broad guest signals of the <sup>1</sup>H NMR spectrum of the complex between **2** and **3** reveal that exchange between the free and the bound state is faster than that of *n*-heptadecane, C17 (Figure S6). One possible reason for this is that pinning two 'C17-chains' together leads to limited host-guest interactions in the central region of the assembly. Although kinetically less stable, the PGSE diffusion experiment confirmed a tetrameric assembly with the corresponding HV measured at 20.8 nm<sup>3</sup> (Figure S11). The slightly lower HV value than that of the *n*-heptadecane (C17) tetrameric assembly (22.5 nm<sup>3</sup>) is likely due to the presence of small amounts of free subunit or dimeric assembly.



**Figure S6.** <sup>1</sup>H NMR of 1) *n*-heptadecane; 2) tetrahedral template **3** in 1 mM host **2** (100 mM NaOD).

## Pulse-gradient stimulated spin-echo NMR studies

Diffusion measurements were performed on an INOVA 500 MHz (Varian Inc.) instrument equipped with a Performa II pulsed field gradient (PFG) module capable of producing pulses up to 52 gauss/cm. The experiments were carried out on a 5 mm PFG indirect detection probe. The STE (stimulated echo) diffusion experiment using the Varian pulse sequence “pge” (stimulated option on) were performed with pulse gradients of 2 ms in duration separated by 155 ms. All experiments were run at 25°C, at a host concentration of 1 mM and 3 mM in 100 mM sodium hydroxide. Calibration utilized D<sub>2</sub>O samples with a diffusion constant of  $1.88 \times 10^{-5}$  cm<sup>2</sup>/s. The data was analyzed using the optional Varian diffusion software.

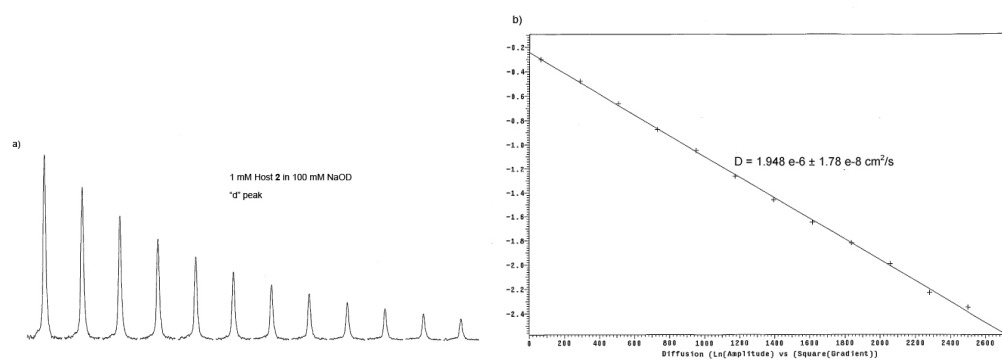
In the case of a spherical particle in a continuous medium of viscosity  $\eta$ , the hydrodynamic radius  $R_H$  can be obtained by Stokes–Einstein equation (Eq. S1)<sup>3</sup>

$$R_H = \frac{k_B T}{6\pi\eta D} \quad (\text{Eq. S1})$$

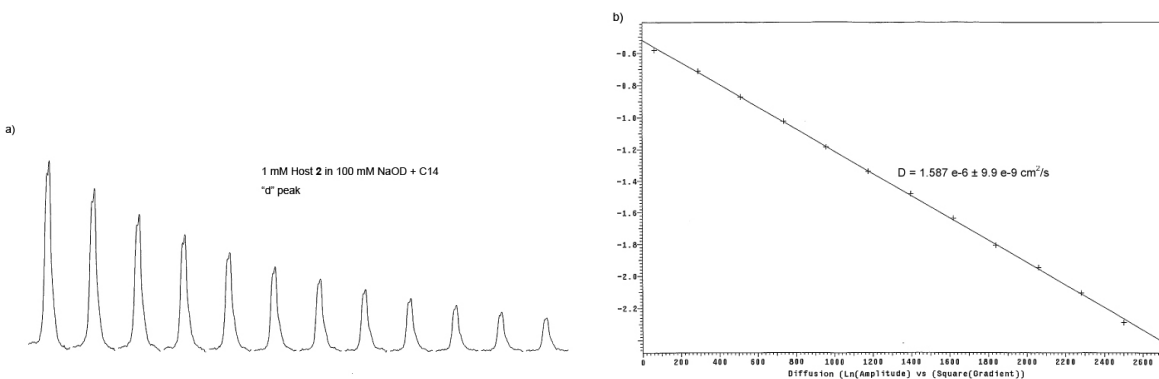
where  $k_B$  is the Boltzmann constant,  $T$  is the temperature,  $\eta$  is the viscosity, and  $D$  is the diffusion constant. In our study, we assume the particles we examined have spherical shape thus the corresponding hydrodynamic volume (HV) can be determined from equation (Eq. S2).

$$V = \frac{4}{3}\pi R_H^3 \quad (\text{Eq. S2})$$

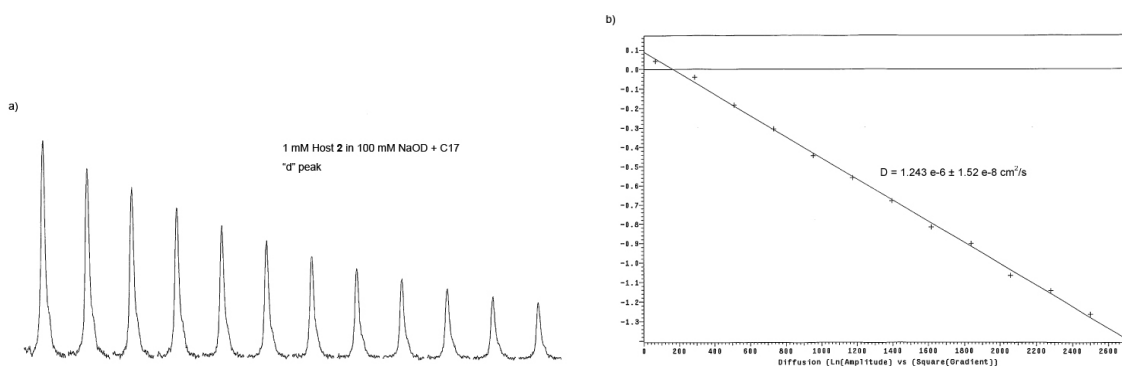
In most cases the obtained diffusion constants and the corresponding hydrodynamic volumes (Table S2) were averages of measurements from the H<sub>j</sub>, H<sub>d</sub>, and H<sub>f</sub> signals of host **2**. However for the guests C17 and C24, the aforementioned three host peaks and the corresponding bound guest methyl signals were used to determine an average diffusion coefficient. Figure S7-S14 shows illustrative examples of the obtained plots of the ln(amplitude) versus the square of the gradient strength applied for the H<sub>d</sub> and guest methyl signals. These results revealed that the assembly comprised of C14 and 1mM host **2** was the 2:1 dimeric complex (Figure S8, Table S2) with a hydrodynamic volume of 11.5 nm<sup>3</sup>. For the complex with guest C17 (Figure S3) PGSE analysis of the bound host and guest signals gave a corresponding HV value of 22.5 nm<sup>3</sup> (Figure S9, S10), which in conjunction with the 2:1 host-guest ratio identified a 4:2 complex. In the case of guest C24, the combination of <sup>1</sup>H NMR and PGSE NMR (Figure S4, S13, S14) revealed the assembly was the 6:3 hexameric complex with a HV value of 48.9 nm<sup>3</sup>, i.e., six times that of the monomer.



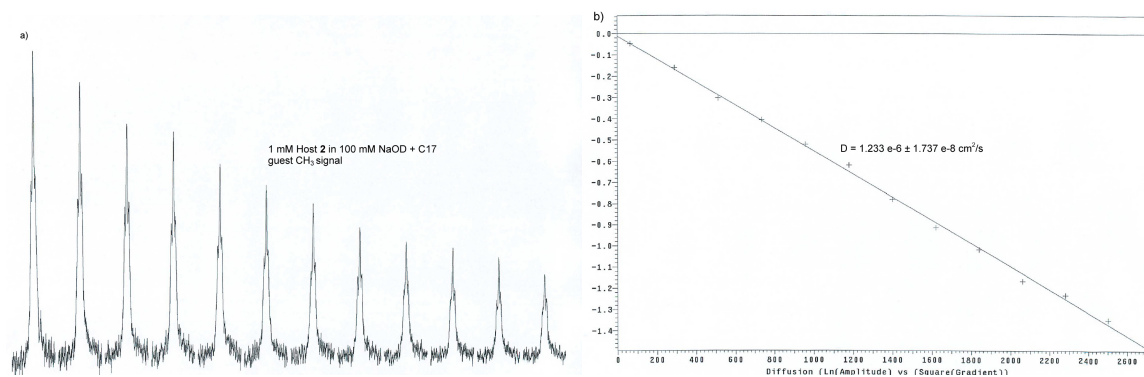
**Figure S7.** a) Decay of "d" proton signal; b) plot of the ln(amplitude) versus square of the gradient strength applied for 1 mM host 2 in 100 mM NaOD-D<sub>2</sub>O.



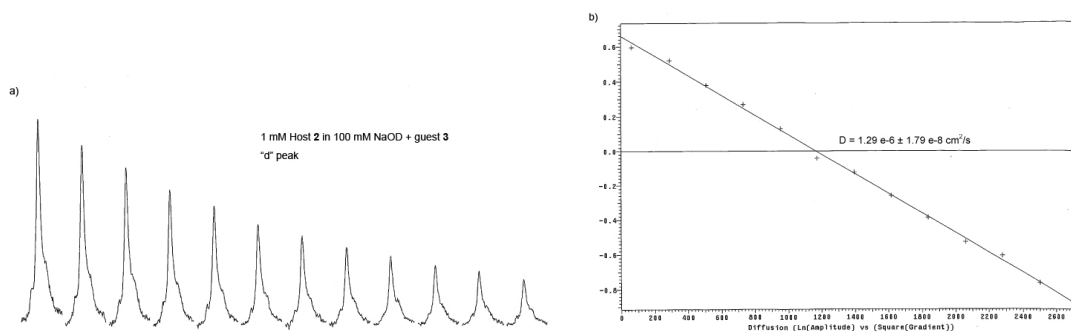
**Figure S8.** a) Decay of "d" proton signal; b) plot of the ln(amplitude) versus square of the gradient strength applied for 1 mM host 2 in 100 mM NaOD-D<sub>2</sub>O when fully bound with guest *n*-tetradecane (C14).



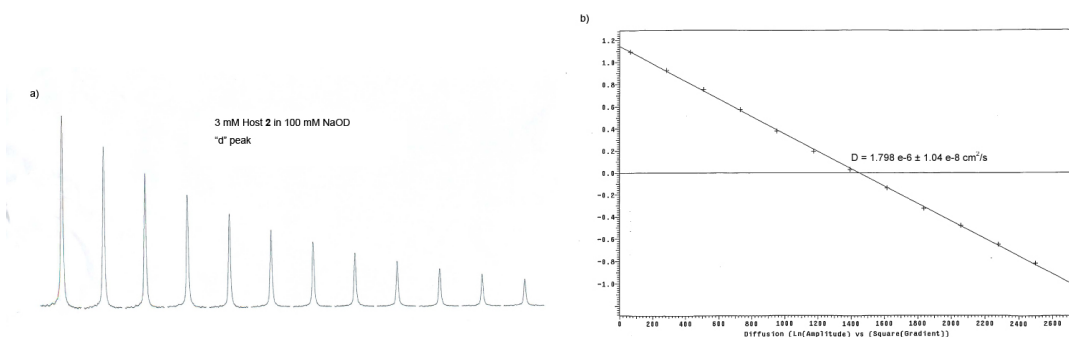
**Figure S9.** a) Decay of "d" proton signal; b) plot of the ln(amplitude) versus square of the gradient strength applied for 1 mM host 2 in 100 mM NaOD-D<sub>2</sub>O when fully bound with guest *n*-heptadecane (C17).



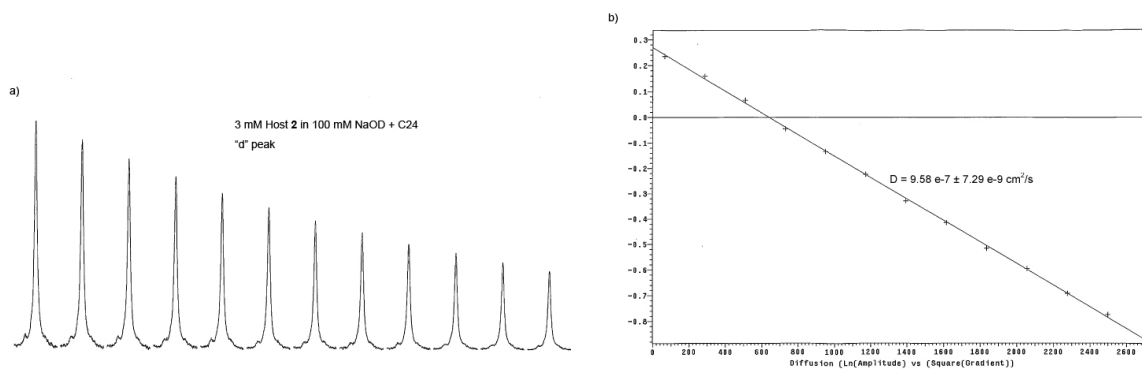
**Figure S10.** a) Decay of bound CH<sub>3</sub> signal; b) plot of the ln(amplitude) versus square of the gradient strength applied for 1 mM host 2 in 100 mM NaOD-D<sub>2</sub>O when fully bound with guest *n*-heptadecane (C17).



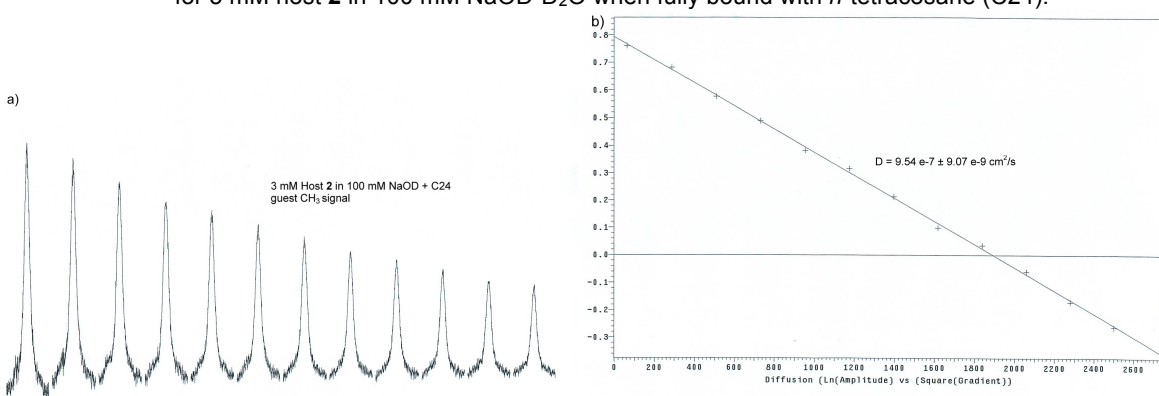
**Figure S11.** a) Decay of "d" proton signal; b) plot of the ln(amplitude) versus square of the gradient strength applied for 1 mM host 2 in 100 mM NaOD-D<sub>2</sub>O when fully bound with tetrahedral template 3.



**Figure S12.** a) Decay of "d" proton signal; b) plot of the ln(amplitude) versus square of the gradient strength applied for 3 mM host 2 in 100 mM NaOD-D<sub>2</sub>O.



**Figure S13.** a) Decay of “d” proton signal; b) plot of the  $\ln(\text{amplitude})$  versus square of the gradient strength applied for 3 mM host **2** in 100 mM NaOD-D<sub>2</sub>O when fully bound with *n*-tetracosane (C24).



**Figure S14.** a) Decay of bound guest CH<sub>3</sub> signal; b) plot of the  $\ln(\text{amplitude})$  versus square of the gradient strength applied for 3 mM host **2** in 100 mM NaOD-D<sub>2</sub>O when fully bound with *n*-tetracosane (C24).

**Table S2.** Diffusion Constants and Hydrodynamic Volumes of assemblies and their corresponding monomers.

Host or Host-guest system	$D$ (cm <sup>2</sup> /s)	HV (nm <sup>3</sup> )
1 mM Host <b>2</b> + 100 mM NaOD <sup>a</sup>	$1.95 \times 10^{-6}$	5.88
1 mM Host <b>2</b> + 100 mM NaOD + C14 <sup>a</sup>	$1.56 \times 10^{-6}$	11.5
1 mM Host <b>2</b> + 100 mM NaOD + C17 <sup>b</sup>	$1.24 \times 10^{-6}$	22.8
3 mM Host <b>2</b> + 100 mM NaOD <sup>a</sup>	$1.79 \times 10^{-6}$	7.60
3 mM Host <b>2</b> + 100 nM NaOD + C24 <sup>b</sup>	$9.62 \times 10^{-7}$	48.9

<sup>a</sup> Averages of measurements of H<sub>j</sub>, H<sub>d</sub>, and H<sub>f</sub> signals.

<sup>b</sup> Averages of measurements of H<sub>j</sub>, H<sub>d</sub>, H<sub>f</sub> and bound guest methyl signals.

## References

- (1) Liu, S.; Whisenhunt-Ioup, S. E.; Gibb, C. L. D.; Gibb, B. C. *Supramol. Chem* **2011**, *24*, 480.
- (2) Gan, H.; Benjamin, C. J.; Gibb, B. C. *J. Am. Chem. Soc.* **2011**, *133*, 4770.
- (3) Cohen, Y.; Avram, L.; Frish, L. *Angew. Chem. Int. Ed.* **2005**, *44*, 520.