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Octahydroxypyridine[4]arene Self-Assembles Spontaneously To Form Hexameric Capsules and Dimeric Aggregates

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Abstract: In recent years it has been observed that resorcin[4]arenes and pyrogallol[4]arenes form hydrogen-bonded hexameric capsules in nonpolar solvents. In the present study we have used NMR spectroscopy, with an emphasis on diffusion NMR, to investigate the self-assembly and the aggregation mode of solutions of octahydroxypyridine[4]arene (**1b**) in chloroform. In spectroscopic studies, the hexameric capsule of *C*-undecylresorcin[4]arene (**2b**) was used as a reference compound and in some cases also as an internal reference. The current diffusion NMR spectroscopy study shows, in contrast to a previous report, that compound **1b** self-assembles spontaneously into hexameric and dimeric aggregates in solutions in chloroform. The ^{1}H NMR and diffusion NMR spectroscopic studies on a solution of **1b** in $CHCl_3$ show the presence of new upfield-shifted peaks, which diffuse with the same diffusion coefficient as the hexameric peaks in the spectrum. Therefore, these new upfield-shifted peaks were attributed to encapsulated $CHCl_3$ molecules. Interestingly, diffusion NMR measurements showed that the addition of trifluoroacetic acid (6.7 equiv), which had no effect on the hexameric capsules of **2b**, led to the disassembly of the hexamer and the dimer of **1b** into its monomers. Therefore, we conclude that compound **1b** self-assembles spontaneously into hexameric capsules in nonpolar organic solvents, as do resorcin[4]arenes **2b** and **2c** and pyrogallol[4]arenes **3a** and **3b**.

Keywords: hexameric capsules · hydrogen bonds · NMR spectroscopy · self-assembly · supramolecular chemistry

Introduction

Over the last decade hydrogen-bonded molecular capsules have attracted much interest.[1,2] First, dimeric capsules based on tetraureacalix[4]arenes were characterized.[3] Then, hydrogen-bonded hexameric capsules based on resorcin[4]arenes and pyrogallol[4]arenes became the focus of attention.[4,5] In 1997, a seminal paper in this field by MacGillivray and Atwood reported the spectacular solid-state structure of the hexameric capsule of *C*-methylresorcin[4]arene (**2a**, Scheme 1).[4a] In 1999, Mattay and co-workers reported the solid-state structure of the hexameric capsule of *C*-isobutylpyrogallol[4]arene (**3a**, Scheme 1).[5a] In 2001, Shivanyuk and Rebek demonstrated that *C*-undecylresorcin[4]arene (**2b**) forms hexameric capsules in a water-saturated chloroform solution in the presence of suitable guest molecules, such as tetrahexylammonium bromide and tetrabutylantimony(V) bromide.[6,7] Therefore, it was assumed that guest molecules are required to induce the formation of such hexameric capsules in solution. By using diffusion NMR spectroscopy, we later demonstrated that molecules such as resorcin[4]arene and pyrogallol[4]arene self-assemble spontaneously to form hexameric capsules in solution in chloroform, and in other organic solvents, without the addition of a specific guest molecule.[8,9] With diffusion NMR spectroscopy, we demonstrated that resorcin[4]arenes **2b** and **2c** self-assemble into hexameric capsules with eight water molecules, that is, $[(\mathbf{2b})_6(H_2O)_8]$ and $[(\mathbf{2c})_6(H_2O)_8]$, whereas pyrogallol[4]arenes **3a** and **3b** form $\mathbf{3a}_6$- or $\mathbf{3b}_6$-type capsules (Scheme 1).[9a,c,e] Furthermore, several complexes of resorcin[4]arene **2b**, which were prepared by Aoyama and co-workers during the 1990s and showed 1:1

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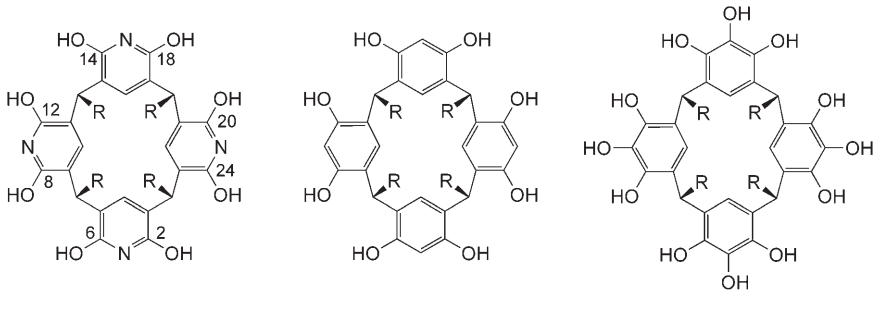
Supporting information for this article is available on the WWW under http://www.chemeurj.org/ or from the author. Figure S1 shows the diffusion-ordered spectroscopy (DOSY) of a 1:1 mixture of **1b**/**2b** (20:20 mM) in $CDCl_3$. Figure S2 shows the ^{1}H NMR spectra of **1b** (20 mM) in $CHCl_3$ in the absence and in the presence of TFA (1, 2, and 3 μL). Table S1 is a summary of the diffusion coefficients of **1b** (20 mM) and **2b** (20 mM) and a 1:1 mixture of **1a**/**2b** in the presence and in the absence of TFA (1 or 3 μL) in $CDCl_3$ and a sample of **1b** (20 mM) in $CHCl_3$.



1a: R=isobutyl
1b: R=$CH_2(CH_2)_9CH_3$

2a: R=methyl
2b: R=$CH_2(CH_2)_9CH_3$
2c: R=isobutyl

3a: R=isobutyl
3b: R=$CH_2(CH_2)_9CH_3$

Scheme 1. The structures of octahydroxypyridine[4]arenes (**1**), resorcin[4]arenes (**2**), and pyrogallol[4]arenes (**3**).

and 2:1 stoichiometric complexes of **2b** with glutaric acid and methyl β-D-glucopyranoside,[10] respectively, were investigated by diffusion NMR spectroscopy.[11] These recent studies proved that these complexes are, in fact, hexameric capsules of **2b** with six encapsulated glutaric acid molecules (i.e., 6:6 stoichiometry) and three encapsulated methyl β-D-glucopyranoside molecules (i.e., 6:3 stoichiometry).[11] These results demonstrate that the hexameric capsules of resorcin[4]arenes and pyrogallol[4]arenes are much more common than previously believed.[11]

Pyridine analogues of resorcin[4]arenes and pyrogallol[4]arenes, namely 2,6,8,12,14,18,20,24-octahydroxypyridine[4]arene, were first synthesized by Mattay and co-workers in 2001 by direct acidic condensation of 2,6-dihydroxypyridine with several aldehydes.[12] The crystal structure of *C*-tetraisobutyloctahydroxypyridine[4]arene (**1a**, Scheme 1) was reported and showed the formation of a head-to-head dimer with a perfect cone (*rccc*) conformation.[12] In addition, NMR studies performed on three different concentrations of *C*-tetra-*n*-undecyloctahydroxypyridine[4]arene (**1b**) in $CDCl_3$ by Mattay and co-workers showed two sets of signals that were attributed to the monomer and to the assembled dimer of **1b**.[13] Additionally, no indication of encapsulated $CHCl_3$ was found when the ^{1}H NMR spectrum of **1b** was recorded in $CHCl_3$.[13] Mass spectra of **1b** in the presence of different organic acid guest molecules showed peaks that were attributed to the encapsulated guest molecules in the dimer of **1b**. Furthermore, for high concentrations of acid, no dimers were observed by using mass spectrometry.[13]

Over the last decade we have demonstrated the added value and the new insights that one can obtain from diffusion NMR spectroscopy when studying supramolecular systems in solution.[8,9,11,14,15] In particular, we have demonstrated the suitability of using diffusion NMR spectroscopy for characterizing hydrogen-bonded molecular capsules.[3g–h,8,9,11] Owing to the spontaneous formation of hexameric capsules of compounds **2b**, **2c**, **3a**, and **3b** in organic solvents, both in the presence and in the absence of any guest molecules, we decided to investigate the aggregation mode of a solution of compound **1b** in chloroform.

Results and Discussion

C-Tetra-*n*-undecyl-2,6,8,12,14,-18,20,24-octahydroxypyridine[4]arene (**1b**, Scheme 1) was synthesized according to the procedure described in the literature.[12] The ^{1}H NMR spectrum of **1b** in $CDCl_3$ afforded the same spectrum as that reported earlier by Mattay and co-workers.[13] The ^{1}H NMR spectrum of a solution of **1b** (20 mM) in $CDCl_3$ revealed the two sets of peaks that were previously assigned to the monomer and the dimer of **1b**.[13] Sections of the ^{1}H NMR spectrum of **1b** are shown in Figure 1b. Diffusion NMR[15,16] measurements on this sample showed that these two sets of peaks do, indeed, differ in their diffusion coefficients. However, the set of peaks previously assigned[13] to

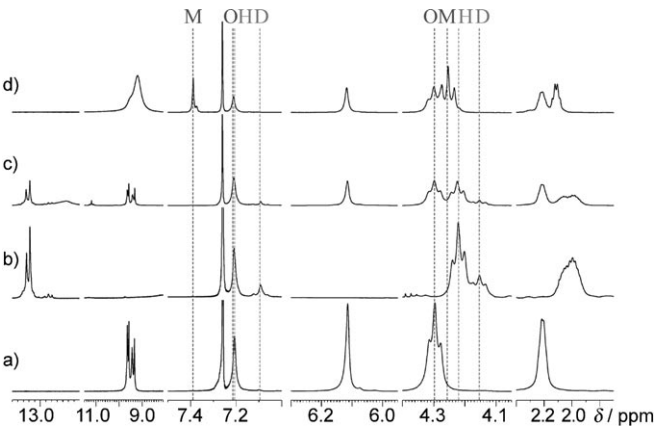


Figure 1. Sections of the ^{1}H NMR spectra ($CDCl_3$, 298 K) of a) resorcin[4]arene **2b** (20 mM), b) octahydroxypyridine[4]arene **1b** (20 mM), c) a 1:1 mixture of **1b**/**2b** (20:20 mM), and d) a 1:1 mixture of **1b**/**2b** (20:20 mM) in the presence of TFA (3 μL, 135 mM). The dotted lines outline some significant peaks of the hexamer of **2b** (O), the hexamer of **1b** (H), the dimer of **1b** (D), and the monomer of **1b** (M).

the dimer of **1b** was found to have a diffusion coefficient ($((0.236\pm0.001)\times10^{-5})$ cm^2s^{-1}, 20 mM, $CDCl_3$) that is very close to that of the hexameric capsules of **2b** and **3b**,[8,9] which are compounds whose molecular weights are very similar to that of **1b**. The set of peaks previously assigned to the monomer of **1b** was found to have a higher diffusion coefficient ($((0.350\pm0.008)\times10^{-5})$ cm^2s^{-1}, 20 mM, $CDCl_3$). However, this value is lower than that expected for a monomer of **1b** in this solvent system, as was shown for compound **2b**.[8] Based on these diffusion results we suspected that the previously assigned dimer of **1b** is in fact a hexameric aggregate and most likely, a hexameric capsule, as in the cases of compounds **2b**, **2c**, **3a**, and **3b**.[6–9] Moreover, the diffusion NMR results seem to indicate that the peaks previ-

ously assigned to the monomer of **1b** are in fact those of the dimer of **1b**.

To further verify the nature of the species that prevail in a solution of **1b** in chloroform, the following experiments were performed: First, **2b** (20 mM) was added to a sample of **1b** (20 mM) for use as an internal reference for the hexameric species (Figure 1c). The rationale behind this experiment was that if **1b** does indeed aggregate to form a hexamer, then both of the hexamers (i.e., those of **1b** and **2b**) should be very similar in size and shape, and therefore, should have very similar diffusion coefficients under the same experimental conditions (solvent, concentration, and temperature). Sections of the ^{1}H NMR spectra of **1b** (20 mM), **2b** (20 mM), and a solution that contained a 1:1 mixture of **1b**/**2b** (20:20 mM)in the presence and absence of trifluoroacetic acid (TFA; 3 μL, 135 mM) are shown in Figure 1.

The spectrum of the 1:1 mixture of **1b**/**2b** (Figure 1c) is a superposition of the spectra of **2b** (Figure 1a) and **1b** (Figure 1b). The addition of TFA (3 μL, 135 mM) had no effect on the spectrum of **2b**, however, it affected the spectrum of **1b** and the two sets of peaks were transformed into a single set of peaks with slightly different chemical shifts. Diffusion measurements performed on the 1:1 mixture of **1b**/**2b** (20 mM) revealed three diffusion coefficients for the three peak systems that were observed.

Figure 2 shows the signal decay of one representative peak of **2b** and representative peaks of the two peak systems of **1b** in the 1:1 mixture of **1b**/**2b** (20:20 mM). Interestingly, we found that the diffusion coefficient of the slower-diffusing set of peaks of **1b** ($((0.237\pm0.004)\times10^{-5})$ cm^{2}s^{-1} (20 mM) was similar to that of **2b** ($((0.234\pm0.001)\times10^{-5})$ cm^{2}s^{-1} (20 mM), which is known to be a hexamer when dissolved in $CDCl_3$ (see also Figure 3 and Figure S1 of the Supporting Information). This data further corroborated the assumption that the slow-diffusing set of peaks of **1b** actually represents a hexameric assembly of **1b** rather than a dimeric species. Interestingly, the addition of TFA (3 μL, 135 mM) to the sample that contained a 1:1 mixture of **1b**/**2b** (20 mM) gave rise to a new set of peaks for **1b** (see Figure 1d) with no observed changes in the chemical shifts of **2b**. As for the diffusion coefficients, the addition of TFA (3 μL, 135 mM) to the sample resulted in a much higher diffusion coefficient for the new set of peaks of **1b** ($((0.431\pm0.007)\times10^{-5})$ cm^{2}s^{-1}, 20 mM, $CDCl_3$). This value is even higher than that obtained for the fast-diffusing set of peaks of **1b** prior to the addition of TFA. However, TFA had no significant effect on the diffusion coefficient of the **2b**, which was ($((0.242\pm0.001)\times10^{-5})$ cm^{2}s^{-1} (20 mM, $CDCl_3$; see Figures 2 and 3). This result led us to believe that the addition of TFA (3 μL, 135 mM) breaks the hexameric and dimeric aggregates of **1b** into monomers, thus substantiating the assumption that the solution of **1b** in chloroform is actually a mixture of dimeric and hexameric aggregates.

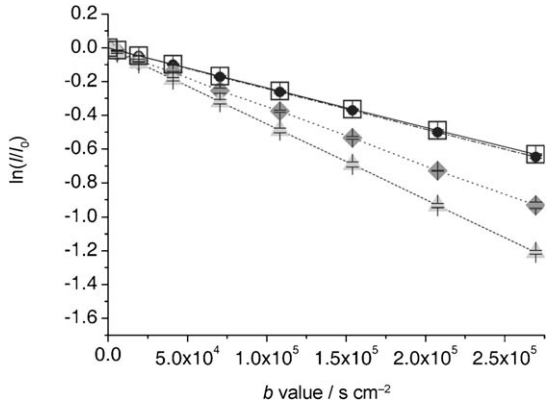


Figure 2. The natural log of the normalized signal decay (ln I/I_0) versus the b values in a 1:1 sample of **1b**/**2b** (20:20 mM) in $CDCl_3$ at 298 K for representative peaks of the hexameric capsule of **2b** (□), the hexameric (●) and dimeric (◆) aggregates of **1b**, and the monomer of **1b** (▲), which was obtained after the addition of TFA (3 μL, 135 mM) to the 1:1 sample of **1b**/**2b** (20:20 mM).

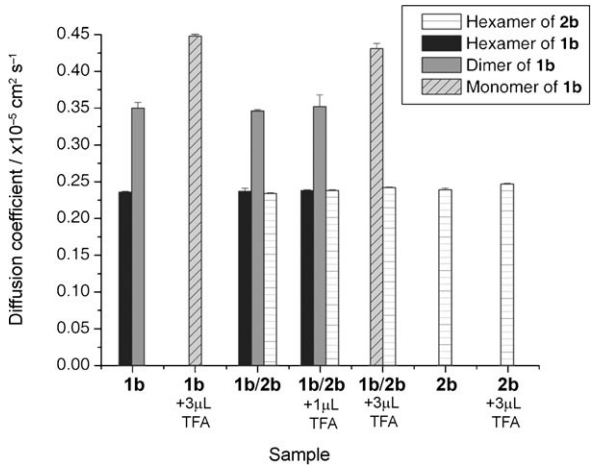


Figure 3. A graphical summary of diffusion coefficients of **1b** (20 mM), **2b** (20 mM), and a 1:1 mixture of **1b**/**2b** (20:20 mM) in $CDCl_3$ at 298 K in the absence and in the presence of TFA (1 μL, 45 mM or 3 μL, 135 mM). All diffusion coefficients [cm^{2}s^{-1}] have been multiplied by a factor of 10^5.

In the diffusion measurements on a sample of **2b** (20 mM) in $CDCl_3$ with TFA (3 μL, 135 mM), we found a slight rise in the diffusion coefficient of the hexameric capsule from ($(0.239\pm0.002)\times10^{-5}$) in the absence of TFA to ($((0.247\pm0.001)\times10^{-5})$ cm^{2}s^{-1} in the presence of TFA (see Figure 3). Therefore, we separately measured the diffusion coefficients of samples of **1b** (20 mM) and **2b** (20 mM) in $CDCl_3$ both before and after the addition of TFA (1 μL, 45 mM, or 3 μL, 135 mM). The diffusion coefficients obtained for all of the systems measured are presented graphically in Figure 3. (The numerical values are presented in Table S1 in the Supporting Information.) All of this data clearly demonstrates that the spectrum of **1b** consists of hexameric and dimeric aggregates that are disrupted upon the addition of TFA (3 μL, 135 mM), but does not necessarily imply that these aggregates are capsular in nature.

To establish whether or not the hexameric aggregates of **1b** were actually hexameric capsules, we investigated the ^{1}H NMR spectrum of **1b** in $CHCl_3$. In protonated media in the presence of such capsules, one would expect to find en-

capsulated solvent peaks that are shifted upfield relative to the bulk solvent peak. These peaks originate from a slow exchange on the NMR timescale between the encapsulated and bulk $CHCl_3$ molecules. For the resorcin[4]arene[8,9e] and pyrogallol[4]arene[9e] capsules, these new peaks appear between $\delta = 4.7$ and 5.2 ppm. A comparison of the ^{1}H NMR spectra of **1b** (20 mM) in $CDCl_3$ (Figure 4a) and in $CHCl_3$

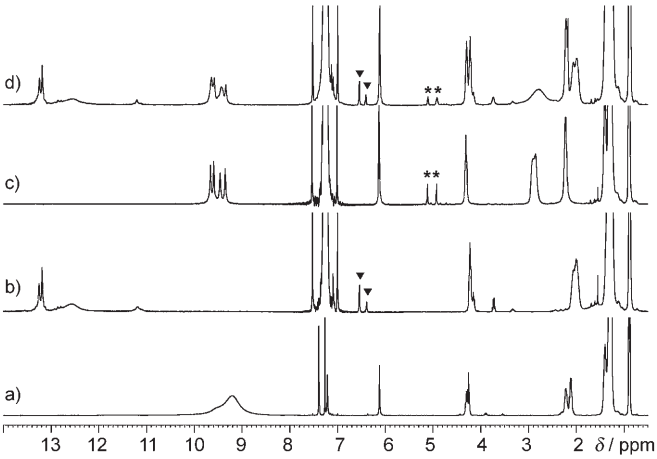


Figure 4. ^{1}H NMR spectra at 298 K of a) **1b** (20 mM) in $CDCl_3$, b) **1b** (20 mM) in $CHCl_3$, c) **2b** (20 mM) in $CHCl_3$, and d) a 1:1 mixture of **1b**/**2b** (20:20 mM) in $CHCl_3$. The encapsulated chloroform peaks of **1b** are located between $\delta = 6.37$ and 6.55 ppm and are marked with ▼, and the encapsulated chloroform peaks of **2b** are located between $\delta = 4.82$ and 5.15 ppm and are marked with asterisks (*).

(Figure 4b) shows two new additional peaks at $\delta = 6.37$–6.39 and 6.53–6.55 ppm, which were attributed to the encapsulated chloroform molecules. The diffusion coefficient of **1b** (30 mM) in $CHCl_3$ was $((0.252 \pm 0.006) \times 10^{-5})$ $cm^2 s^{-1}$ and the diffusion coefficients of these two new peaks were $((0.248 \pm 0.003) \times 10^{-5})$ and $((0.249 \pm 0.002) \times 10^{-5})$ $cm^2 s^{-1}$, respectively. These findings prove that the hexameric aggregates formed when **1b** is dissolved in chloroform are in fact hexameric capsules. These results imply that **1b** shows similar behavior to that of compounds **2b**, **2c**, **3a**, and **3b** in solution in chloroform.[8,9,11]

We also recorded the ^{1}H NMR spectrum and the diffusion coefficients of the 1:1 mixture of the two compounds (i.e., **1b** and **2b**) in $CHCl_3$ (Figure 4d). Figure 4c shows the ^{1}H NMR spectrum of **2b** in $CHCl_3$; this shows that the NMR spectrum of the 1:1 mixture of **1b**/**2b** in Figure 4d is the superposition of the two ^{1}H NMR spectra of **1b** and **2b** in $CHCl_3$ (Figure 4b and c, respectively). There were no traces of new encapsulated solvent peaks and no evidence of any formation of heterohexamers of compounds **1b** and **2b** was obtained. This result implies that the self assembly of **1b** and **2b** proceeds with complete self-sorting and no heterohexamers are formed. These results are similar to earlier findings that no heterohexamers were formed in the mixtures of **2b** with **3b** or **2c** with **3a**.[9e] Moreover, integration of the new peaks showed that about six to seven molecules of $CHCl_3$ are encapsulated in each hexameric capsule. Interestingly, the addition of TFA (3 μL) to **1b** (20 mM) in $CHCl_3$ resulted in the disappearance of the peaks between $\delta = 6.37$ and 6.55 ppm that were assigned to the encapsulated $CHCl_3$ molecules (see Figure S2 in the Supporting Information).

The formation of hexameric and dimeric aggregates was further supported by analyzing the ^{13}C NMR spectra obtained. We found that at higher concentrations the hexameric fraction increases, as expected, and that a sample of **1b** (100 mM) in chloroform mainly contains the hexameric species of **1b**. Figure 5a and b shows the aromatic section of the ^{13}C NMR spectra of **2b** and **1b**, respectively, whereas Figure 5c shows the aromatic region for a 1:1 mixture of **1b**/**2b** (20:20 mM) in chloroform. Figure 5c shows that the aromatic spectra of the hexameric capsules of **1b** and **2b** consist of five and six carbon peaks, respectively, and that of the dimer of **1b** consists of three carbon peaks. The addition of TFA (1 μL, 45 mM) to the mixture (Figure 5d) changed the ratio of hexamer to dimer in the mixture to ≈1:1 and left **2b** unaffected. Further addition of TFA (up to a total of 3 μL) to the mixture of **1b**/**2b** (Figure 5e) resulted in the disassembly of the hexamers and dimers of **1b** to monomers and left the hexamers of **2b** unaltered. Figure 5 shows that for the hexameric capsule of **1b**, as with that of **2b**, all carbons in the aromatic ring are chemically nonequivalent, which implies that the hexamers have a reduced symmetry. The dimer of **1b** has only three carbon peaks, as does the monomer of **1b**.

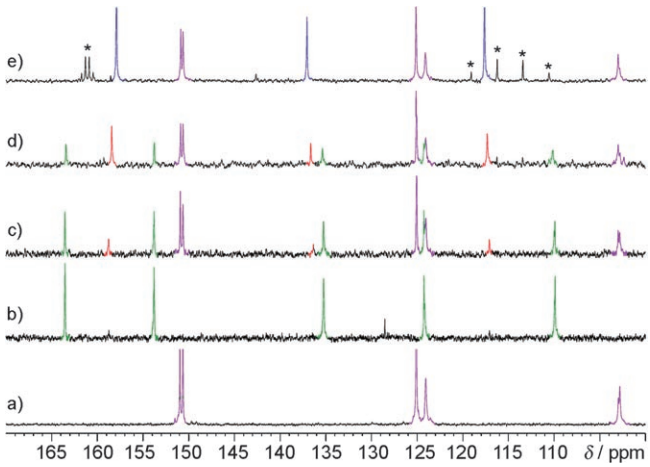


Figure 5. The aromatic sections of the ^{13}C NMR spectra of solutions in $CDCl_3$ at 298 K for a) **2b** (70 mM), b) **1b** (100 mM), c) a 1:1 mixture of **1b**/**2b** (20:20 mM) in the absence and in the presence of TFA (1 μL (d) and 3 μL (e)). Peaks of the hexamer of **2b** are in purple, peaks of the hexamer of **1b** are in green, peaks of the dimer of **1b** are in red, and peaks of the monomer of **1b** are in blue. The peaks marked with asterisks (*) are the two carbons of TFA in the sample.

Conclusion

In conclusion, we have demonstrated that in contrast to a recent report, a solution of **1b** in chloroform self-assembles spontaneously to form hexameric and dimeric aggregates

that are in thermal equilibrium. The hexameric aggregate is the major species in the 5 to 100 mM concentration range. The hexameric aggregates are molecular capsules under these conditions. In addition, the hexameric capsules of **1b** and **2b** do not form heterohexamers and six to seven equivalents of TFA disrupt the hexamers and dimers of **1b**, but leave the **2b** hexamers intact. This behavior matches previous findings for resorcin[4]arenes and pyrogallol[4]arenes in solution in chloroform and demonstrates the added value of using diffusion NMR when studying noncovalent supramolecular systems in solution.

Experimental Section

Materials: All starting materials, guest molecules, reagents, and the deuterated solvent $CDCl_3$ were purchased from Aldrich (Milwaukee, WI) and used as supplied. *C*-Tetra-*n*-undecyl-2,6,8,12,14,18,20,24-octahydroxypyridine[4]arene **1b** was prepared as previously described.[12]

Sample preparation: The samples in $CDCl_3$ and $CHCl_3$ were prepared by dissolving **1b** in the appropriate solvent up to a total volume of 0.3 mL. The titration of the various samples with TFA (1 and 3 μL) was done by adding 10 or 30 μL from a 10:1 diluted sample of TFA in $CDCl_3$ to the NMR tube.

NMR methods: NMR diffusion measurements were performed by using a 400 MHz Avance Bruker NMR spectrometer equipped with a "Great1" gradient system capable of producing magnetic field pulse gradients in the z-direction of about 50 G cm^{-1}. All experiments were carried out by using a 5 mm inverse probe. All diffusion measurements were performed in a 4 mm NMR tube that was inserted into a 5 mm NMR tube, which acts as a thermal insulating system and increases the accuracy and reproducibility of the diffusion measurements by reducing the chance of convection in the sample. This precaution is more important when diffusion NMR experiments are performed on nonviscous solvents with low boiling points and heat capacities. The measurements were all performed at 298 K. Diffusion measurements were performed by using an LED sequence with sine-shaped pulse gradients.[17]

^{1}H NMR diffusion measurements were performed at least three times and the reported diffusion coefficients are the mean ± the standard deviation of at least three experiments. Only data in which the correlation coefficients of $\ln(I/I_0)$ versus $\gamma^2\delta^2G^2(2/\pi)^2(\Delta-\delta/4)$ (in which γ is the gyromagnetic ratio, G is the pulsed gradient strength, and Δ and δ are the time separation between the pulsed gradients and their duration, respectively), which are generally termed the "diffusion weighting" and are denoted as the b values, were higher than 0.999 were reported.

The diffusion experiments were performed by using the LED pulse sequence with the following parameters: for the ^{1}H NMR diffusion measurements the sine-shape pulsed gradients (4 ms in duration) were incremented from 0 to 36 G cm^{-1} in 10 or 20 steps, and the pulse gradient separations (Δ) were either 30 or 60 ms. For a Δ value of 30 ms, the echo time, the mixing time, and eddy current delay were 20, 20, and 50 ms, respectively. For a Δ value of 60 ms, the echo time, the mixing time, and eddy current delay were 20, 50, and 50 ms, respectively.

[1] a) M. M. Conn, J. Rebek, Jr., *Chem. Rev.* **1997**, *97*, 1647–1668; b) V. Böhmer, M. O. Vysotsky, *Aust. J. Chem.* **2001**, *54*, 671–677; c) F. Hof, S. L. Craig, C. Nuckolls, J. Rebek, Jr., *Angew. Chem.* **2002**, *114*, 1556–1578; *Angew. Chem. Int. Ed.* **2002**, *41*, 1488–1508.

[2] a) L. C. Palmer, J. Rebek, Jr., *Org. Biomol. Chem.* **2004**, *2*, 3051–3059; b) J. Rebek, Jr., *Angew. Chem.* **2005**, *117*, 2104–2115; *Angew. Chem. Int. Ed.* **2005**, *44*, 2068–2078.

[3] For tetraureacalix[4]arenes, see: a) K. D. Shimizu, J. Rebek, Jr., *Proc. Natl. Acad. Sci. U.S.A.* **1995**, *92*, 12403–12407; b) O. Mogck, E. F. Paulus, V. Böhmer, I. Thonodorf, W. Vogt, *Chem. Commun.* **1996**, 2533–2534; c) B. C. Hamann, K. D. Shimizu, J. Rebek, Jr., *Angew. Chem.* **1996**, *108*, 1425–1427; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1326–1329; d) O. Mogck, V. Böhmer, W. Vogt, *Tetrahedron* **1996**, *52*, 8489–8496; e) O. Mogck, M. Pons, V. Böhmer, W. Vogt, *J. Am. Chem. Soc.* **1997**, *119*, 5706–5712; f) L. Frish, S. E. Matthews, V. Böhmer, Y. Cohen, *J. Chem. Soc. Perkin Trans. 2* **1999**, 669–671; g) L. Frish, M. O. Vysotsky, S. E. Matthews, V. Böhmer, Y. Cohen, *J. Chem. Soc. Perkin Trans. 2* **2002**, 88–93; h) L. Frish, M. O. Vysotsky, V. Böhmer, Y. Cohen, *Org. Biomol. Chem.* **2003**, *1*, 2011–2014; i) A. Shivanyuk, M. Saadioui, F. Broda, I. Thondorf, M. O. Vysotsky, K. Rissanen, E. Kolehmainen, V. Böhmer, *Chem. Eur. J.* **2004**, *10*, 2138–2148.

[4] For resorcin[4]arenes, see: a) L. R. MacGillivray, J. L. Atwood, *Nature* **1997**, *389*, 469–472; b) I. E. Philip, A. E. Kaifer, *J. Am. Chem. Soc.* **2002**, *124*, 12678–12679; c) A. Shivanyuk, J. Rebek, Jr., *J. Am. Chem. Soc.* **2003**, *125*, 3432–3433; d) M. Yamanaka, A. Shivanyuk, J. Rebek, Jr., *J. Am. Chem. Soc.* **2004**, *126*, 2939–2943; e) I. E. Philip, A. E. Kaifer, *J. Org. Chem.* **2005**, *70*, 1558–1564.

[5] For pyrogallol[4]arenes, see: a) T. Gerkensmeier, W. Iwanek, C. Agena, R. Fröhlich, S. Kotila, C. Näther, J. Mattay, *Eur. J. Org. Chem.* **1999**, 2257–2262; b) J. L. Atwood, L. J. Barbour, A. Jerga, *Chem. Commun.* **2001**, 2376–2377; c) J. L. Atwood, L. J. Barbour, A. Jerga, *Proc. Natl. Acad. Sci, U.S.A.* **2002**, *99*, 4837–4841; d) S. J. Dalgarno, S. A. Tucker, D. B. Bassil, J. L. Atwood, *Science* **2005**, *309*, 2037–2039.

[6] A. Shivanyuk, J. Rebek, Jr., *Proc. Natl. Acad. Sci. U.S.A.* **2001**, *98*, 7662–7665.

[7] A. Shivanyuk, J. Rebek, Jr., *Chem. Commun.* **2001**, 2424–2425.

[8] L. Avram, Y. Cohen, *J. Am. Chem. Soc.* **2002**, *124*, 15148–15149.

[9] a) L. Avram, Y. Cohen, *Org. Lett.* **2002**, *4*, 4365–4368; b) L. Avram, Y. Cohen, *Org. Lett.* **2003**, *5*, 1099–1102; c) L. Avram, Y. Cohen, *Org. Lett.* **2003**, *5*, 3329–3332; d) L. Avram, Y. Cohen, *J. Am. Chem. Soc.* **2003**, *125*, 16180–16181; e) L. Avram, Y. Cohen, *J. Am. Chem. Soc.* **2004**, *126*, 11556–11563; f) L. Avram, Y. Cohen, *Org. Lett.* **2006**, *8*, 219–222.

[10] a) Y. Aoyama, Y. Tanaka, S. Sugahara, *J. Am. Chem. Soc.* **1989**, *111*, 5397–5404; b) Y. Tanaka, Y. Kato, Y. Aoyama, *J. Am. Chem. Soc.* **1990**, *112*, 2807–2808; c) Y. Kikuchi, K. Kobayashi, Y. Aoyama, *J. Am. Chem. Soc.* **1992**, *114*, 1351–1358; d) Y. Kikuchi, Y. Tanaka, S. Sutarto, K. Kobayashi, H. Toi, Y. Aoyama, *J. Am. Chem. Soc.* **1992**, *114*, 10302–10306.

[11] T. Evan-Salem, I. Baruch, L. Avram, Y. Cohen, L. C. Palmer, J. Rebek, Jr., *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 12296–12300.

[12] T. Gerkensmeier, J. Mattay, C. Näther, *Chem. Eur. J.* **2001**, *7*, 465–474.

[13] M. L. Letzel, B. Decker, A. B. Rozehenko, W. W. Schoeller, J. Mattay, *J. Am. Chem. Soc.* **2004**, *126*, 9669–9674.

[14] a) O. Mayzel, Y. Cohen, *J. Chem. Soc. Chem. Commun.* **1994**, 1901–1902; b) O. Mayzel, O. Aleksiuk, F. Grynszpan, S. E. Biali, Y. Cohen, *J. Chem. Soc. Chem. Commun.* **1995**, 1183–1184; c) A. Gafni, Y. Cohen, *J. Org. Chem.* **1997**, *62*, 120–125; d) L. Frish, F. Sansone, A. Casnati, R. Ungaro, Y. Cohen, *J. Org. Chem.* **2000**, *65*, 5026–5030; e) L. Avram, Y. Cohen, *J. Org. Chem.* **2002**, *67*, 2639–2644; f) L. Frish, N. Friedman, M. Sheves, Y. Cohen, *Biopolymers*, **2004**, *75*, 46–59.

[15] a) Y. Cohen, L. Avram, L. Frish, *Angew. Chem.* **2005**, *117*, 524–560; *Angew. Chem. Int. Ed.* **2005**, *44*, 520–554; b) Y. Cohen, L. Avram, T. Evan-Salem, L. Frish, *Analytical Methods in Supramolecular Chemistry* (Ed.: C. A. Schalley), Wiley-VCH, Weinheim, **2006**.

[16] a) P. Stilbs, *Prog. Nucl. Magn. Reson. Spectrosc.* **1987**, *19*, 1–45; b) T. Brand, E. J. Cabrita, S. Berger, *Prog. Nucl. Magn. Reson. Spectrosc.* **2005**, *46*, 159–196.

[17] J. S. Gibbs, C. S. Johnson, Jr., *J. Magn. Reson.* **1991**, *93*, 395–402.

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