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Self-Assembly of Resorcin[4]arene in the Presence of Small Alkylammonium Guests in Solution

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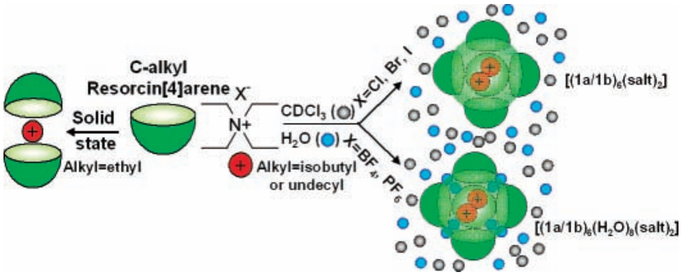
ABSTRACT

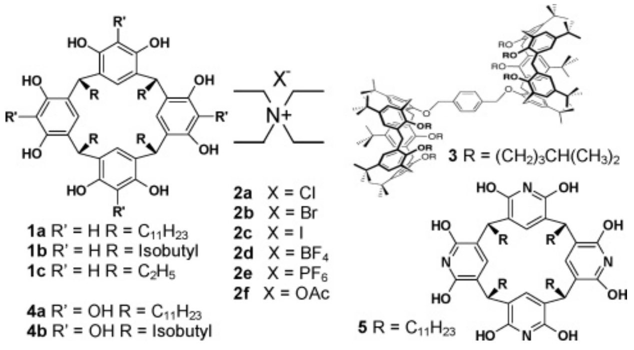


We followed the self-assembly of *C*-alkyl-resorcin[4]arene (1a,1b) in the presence of tetraethylammonium salts (2). The X-ray structure of *C*-ethyl-resorcin[4]arene (1c) in the presence of TEABr (2b), showed a dimer encapsulating one guest. However, diffusion measurements reveal that two molecules of tetraethylammonium are encapsulated within the hexameric capsule of 1a,b in chloroform, regardless of the anion. Most importantly, the anion affects the role of water in the self-assembly and the nature of the formed capsules.

The study of hydrogen-bonded molecular capsules has progressed rapidly over the past decade.[1−9] Both dimeric[1−4] and hexameric[1,5−9] hydrogen-bond capsules have been investigated in the solid state[5] and in solution.[6−9] Recently, we have shown, by diffusion NMR, that different resorcin[4]arenes and pyrogallol[4]arenes self-assemble spontaneously into hexameric capsules in a series of organic solvents.[6] Hexameric capsules of resorcin[4]arenes and pyrogallol[4]arenes with various guests were also reported in solution.[7,8] However, the guest affinity of these systems and the effect of guest molecules on the structure of the formed supramolecular complexes remain elusive.

Diffusion NMR has become an important technique for studying the self-assembly of supramolecular systems in solution.[10] It was shown that diffusion NMR is a powerful tool for probing encapsulation,[11] and the self-assembly of

Scheme 1



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resorcin[4]arene (**1**), pyrogallol[4]arene (**4**), and octahydroxypyridine[4]arene (**5**).[6,7,9,10]

Recently, the self-assembly of **1a** in the presence of relatively small guests, such as glutaric acid (**6**) and *β*-methyl-D-glucopyranoside (**7**) was studied by diffusion NMR.[7b] Aoyama and co-workers claimed that **1a** forms 1:1 and 2:1 complexes with **6**[12] and **7**,[13] respectively. However, diffusion NMR studies showed that **1a** forms hexameric capsules which encapsulate six and three molecules of **6** and **7**, respectively.[7b] These examples demonstrate the new insights that can be obtained when using diffusion NMR to study such systems.[7b]

Here, we used diffusion NMR to study the self-assembly of resorcin[4]arenes (**1a** and **1b**) in the presence of small guests, i.e., tetraethylammonium salts (**2**). Calculations and X-ray structures indicated that these guests are encapsulated in dimeric capsules of *C*-ethyl resorcin[4]arene (**1c**).[14,15a] It was also stated that, according to the ^{1}H NMR spectrum of **1a** and triethylammonium bromide, a dimer is formed in a $CDCl_3$ solution, which encapsulates one molecule of this salt.[15a] However, the diffusion data, acquired in chloroform solutions, show otherwise.

First, we examined the encapsulation of tetraethylammonium bromide (TEABr **2b**). When TEABr (**2b)** was added to the solution of **1a**, new signals appeared at δ −0.1 and 1.7 ppm, as was previously reported for triethylammonium bromide (Figure 1). These peaks were previously attributed to the encapsulated salt inside the cavity of the dimeric capsules.[15a] We repeated these experiments for all the other tetraethylammonium guests, and in all cases these new signals appeared at high field (Figure 1). We could not observe the signals of free guest molecules for all the different salts. According to the integration the ratio between **1a** and the new peaks of **2a**−**f** was 3:1 (data for **2f** are not shown). This is a very odd ratio since it indicates the formation of a trimer with one guest molecule or a hexamer with two guest molecules, and both these options were not suggested before for these systems. It should be noted that in a recent study Palmer et al. suggested that the high-field peaks observed when TEACl (**2a)** is added to **1a** may well represent three cations per hexamer or one cation within a dimeric capsule.[15b] To determine which of these aggregates is the main species in this chloroform solution we turned to diffusion NMR.[10]

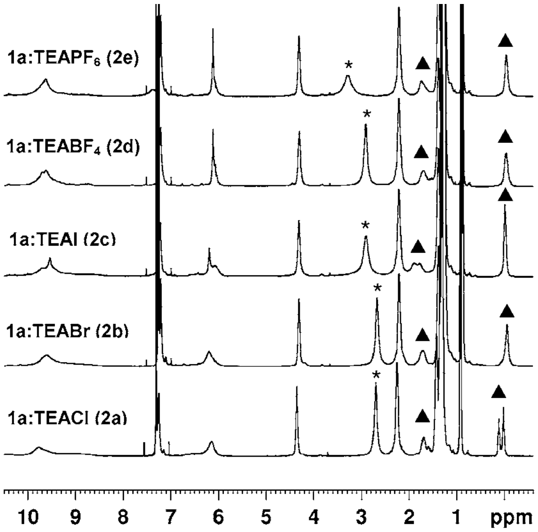

Figure 1. ^{1}H NMR spectra (400 MHz, 298 K) of **1a** in $CDCl_3$ in the presence of different tetraethylammonium salts (**2a**−**e**). The asterisk indicates the water peak and ▲ indicates the peaks of the encapsulated salts.

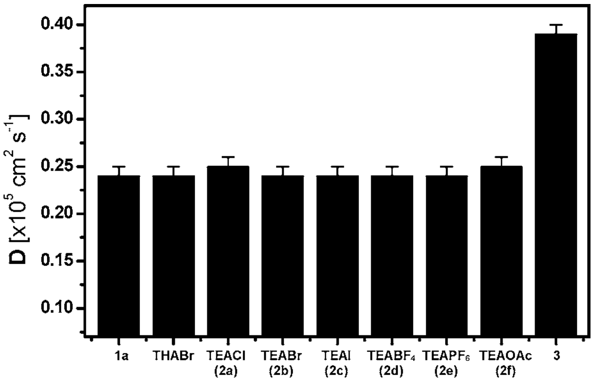

Figure 2. Diffusion coefficients of the peaks of **1a**, different encapsulated ammonium salts in the hexamers of **1a** and biscalix-[5]arene (**3**). Compound **3** has a molecular weight of 2398 g mol^{-1}, which is slightly higher than the molecular weight of the dimer of **1a**.

The diffusion coefficients of **1a** and the encapsulated salts **2a**−**f**, shown in Figure 2, were found to be very similar (0.24 ± 0.01 × 10^{-5} cm^2 s^{-1} 298 K, $CDCl_3$, 20 mM). These findings are reasonable since the encapsulated guest and the host diffuse as a single entity; thus, they must have the same diffusion coefficient. This value is consistent with the diffusion coefficient of a hexameric capsule of **1a** with

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tetrahexylammonium bromide (THABr) (Figure 2),[6a,16] and is also very similar to that previously obtained for the hexameric capsules of pyrogallol[4]arene (**4a**)[6c,d] and octahydroxypyridine[4]arene (Opy, **5**).[9] The diffusion coefficients of **1a** with **2a**−**f** are significantly lower than that of a biscalix[5]arene (**3**),[17] having a molecular weight of 2398 g mol^{-1}, which is slightly larger than that of the dimer of **1a** (Figure 2).

Since the values that were extracted for **1a** and the encapsulated tetraethylammonium guests were very similar to those obtained for the hexameric capsules of **1a**, **4a**,[6c,d] and **5**,[9] we concluded that **1a** self-assembles into a hexameric capsule even in the presence of small guests such as tetraethylammonium salts. Two molecules of the tetraethylammonium seem to be encapsulated within the hexameric capsule of **1a**, regardless of the anion of these salts. These results indicate that the self-assembly of this supramolecular system in chloroform solution is very much different from the dimeric structure found in the solid state.[14] Interestingly, we found exactly the same behavior for host **1b**. We found diffusion evidence only for hexameric capsules of **1b** with the studied salts (see Figures S1−S3 in the Supporting Information). Here, again, two tetraethylammonium molecules are encapsulated in each hexameric capsule.

It was shown that in systems where exchange and NOE interactions between nuclei that differ considerably in their diffusion coefficients exist, the signal decay extracted from pulsed gradient spin echo (PGSE) and pulsed gradient stimulated echo (PGSTE) diffusion sequences is monoexponential, whereas the signal decay extracted from the longitudinal eddy current delay (LED) and bipolar longitudinal eddy current delay (BPLED) diffusion sequences is not.[18] Therefore, we suggested that, in the present systems, non-monoexponential signal decay in the LED and BPLED experiments can serve as a good indication of exchange or NOE interactions between sites that differ in their diffusion coefficients.[18]

We decided to examine the role of water in the self-assembly of **1a** in the presence of the different salts (**2a**−**e**). Previously it was found, by diffusion NMR, that **1a** self-assembles into a hexameric capsule with eight water molecules.[6b] However, after the addition of THABr, **1a** encapsulates the salt and forms a hexameric capsule, where the water molecules are no longer part of the supramolecular structure.[16] We assumed that, owing to the π−cation interactions, THABr acts as a pseudotemplate for the self-assembly of the hexameric capsule of **1a** and that the assistance or the mediation of the water molecules is, therefore, less needed.[16] For this reason, we expected to find the same results for **2a**−**e**. However, when we measured the signal decay of the water peak in the $CDCl_3$ solutions of **1a** and **2a** and **2c**−**e**, by using the LED sequence surprising results were obtained, as shown in Figure 3.

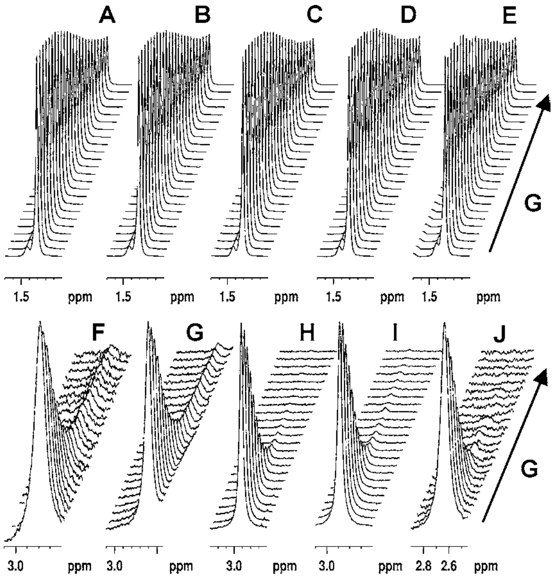

Figure 3. ^{1}H NMR signal decay as a function of the gradient strength (*G*) (400 MHz, 298 K) of one of the peaks of **1a** (A−E) and water (F−J) in a $CDCl_3$ solution with the following salts: $TEAPF_6$ **(2e)** (A and F), $TEABF_4$ **(2d)** (B and G), TEACl (**2a)** (C and H), TEAI (**2c)** (D and I), and THABr (E and J), as extracted from the LED sequence with a t_e of 50 ms.

Figure 3 shows that, although the same signal decay is observed for the peak of **1a** in all the different samples (Figure 3A−E), the signal decay of the water peak, in the presence of the different salts, differs dramatically (Figure 3F−J). Apparently, the water signal decay in the presence of **2a** and **2c** is monoexponential (Figure 3H and I, respectively), like that found for water in the presence of THABr[16] (Figure 3J), where water molecules are not part of the hexameric capsule. However, in the presence of **2d** and **2e** an extra slow diffusion component is observed only for the water peak (Figure 3G and F, respectively). Therefore, we suspected that, although **1a** forms hexameric capsules in the presence of **2a**−**f** that encapsulate two guest molecules, these capsules are not exactly the same for all the different anions.

We have previously shown that the additional extra diffusion component of the water signal develops during the eddy current delay (the t_e period) of the LED and BPLED sequences.[18] As this delay was increased, the extra component of the water signal decay became more pronounced.[18] To verify the reason for the difference in the water signal decay, we examined the effect of t_e on the water signal decay in the presence of two different salts: TEACl (**2a)** (Figure 4B−D) and $TEABF_4$ (**2d)** (Figure 4F−H). We also compared these water signal decays to those extracted from the PGSTE diffusion sequence, in which this delay does not exist and only monoexponential signal decay is expected (Figure 4A and E).

The signal decay of **1a** was not affected by the different pulse sequences or by the increase in the t_e delay (see Figures

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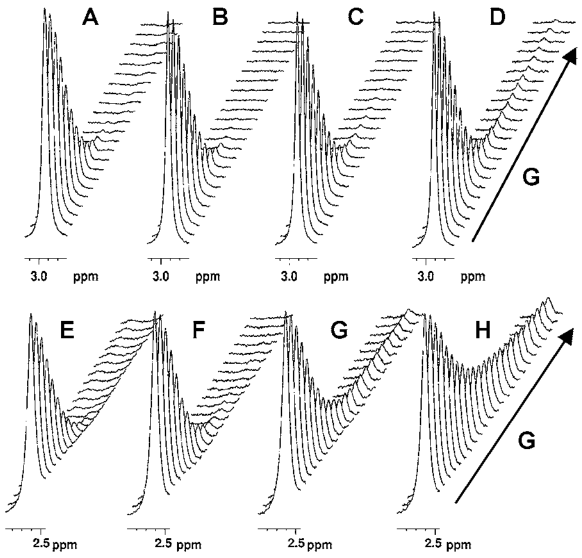

Figure 4. ^{1}H NMR signal decay as a function of the gradient strength (*G*) (400 MHz, 298 K) of the water peak in a $CDCl_3$ solution of **1a** with TEACl (**2a**) (A−D) and with $TEABF_4$ (**2d**) (E−H) as extracted from the (A and E) PGSTE diffusion sequence and the LED sequence with the following t_e's: (B and F) 5, (C and G) 50, and (D and H) 150 ms.

S4 and S5 in the Supporting Information). The water signal decay, however, was affected by the increase in the t_e delay both in the presence of **2a** (Figure 4B−D) and **2d** (Figure 4F−H), but not to the same extent. For the PGSTE and the LED sequence with a t_e of 5 ms, the same water signal decay was observed for both salts. This indicates that, indeed, by using a relatively short t_e, the LED sequence is degenerated into a PGSTE-like sequence and no bending in the water signal decay is observed. For **2a**, only for very long t_e's, could some deviation from linearity be observed. This is probably due to some exchange between the water molecules and the OH moieties on the aromatic rings of **1a**. However, for **2d** the effect of increasing the t_e on the water signal decay is much more significant. The additional extra diffusion component of the water signal can be observed for a t_e as short as 50 ms, which increases significantly for a t_e of 150 ms. These results indicate that exchange between the different populations of the water molecules is much more pronounced for the solution of **1a** in the presence of **2d** than in the presence of **2a**.

All these results indicate that the role of water in the self-assembly of **1a**, in the presence of different tetraethylammonium salts, differ when different anions are used. Apparently, when the anion is a halide such as in **2a**, **2b**, and **2c**, there are no water molecules that are part of the supramolecular system of the capsule, as was found for THABr.[16] These salts are sufficient to induce the formation of the hexameric capsule of **1a**, and there is no need for a significant number of water molecules in order to construct the supramolecular capsule. However, when the anion is BF_4^- or PF_6^-, the effect of t_e on the water signal decay is exactly as that obtained for water in a solution of **1a** in the absence of any salt, as demonstrated in Figure 5. Since the effect of t_e is the same both in the presence and absence of **2d** or **2e**, it is reasonable to assume that the role of the water molecules in the self-assembly of **1a** in these systems is the same. Therefore, we can conclude that in the presence of either **2d** or **2e**, **1a** self-assembles into $[\mathbf{1a}_6(H_2O)_8]$-type capsules that encapsulate two guest molecules, while in the presence of **2a**−**c**, **1a** self-assembles into a hexameric capsule without water molecules. The same results were also obtained for **1b**, (see Figure S3 in the Supporting Information).

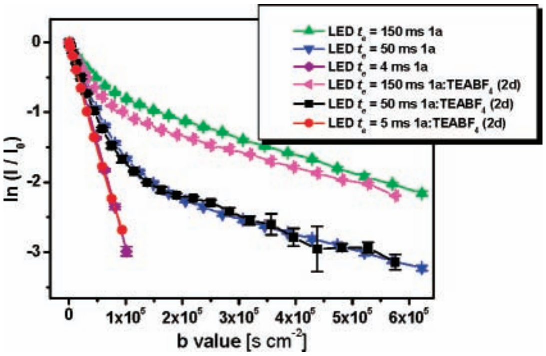

Figure 5. In of the normalized signal decay (In I/I_0) as a function of the *b* value for water in a $CDCl_3$ solution of **1a**, both in the absence and presence of $TEABF_4$ (**2d**), as extracted from the LED diffusion sequence with different t_e's.

In conclusion, diffusion NMR shows that **1a** and **1b** form hexameric capsules in chloroform solutions in the presence of different salts, even though dimeric capsules are found in the solid state. In addition, two molecules of the tetraethylammonium guests seem to be encapsulated within each hexameric capsule, regardless of the anion of these salts. However, we found that the role of water molecules in the self-assembly of **1a** and **1b** with TEAX is different for different anions. In the presence of **2a**−**c**, **1a** forms a $[\mathbf{1a}_6]$-type capsule, whereas with **2d** and **2e**, **1a** forms a $[\mathbf{1a}_6(H_2O)_8]$-type capsule. The same results were also obtained for **1b**.

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Supporting Information Available: ^{1}H and ^{13}C NMR data of the hexamers of **1a** and **1b**; Figures S1−S3 showing the same data as that shown in Figures 1−3 for *C*-isobutylresorcin[4]arene (**1b**). Figures S4 and S5 show the effect of t_e on the signal decay of **1a** and water in the presence of TEACl (**2a**) and $TEABF_4$ (**2d**), respectively.

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