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Discrimination of Guests Encapsulation in Large Hexameric Molecular Capsules in Solution: Pyrogallol[4]arene versus Resorcin[4]arene Capsules

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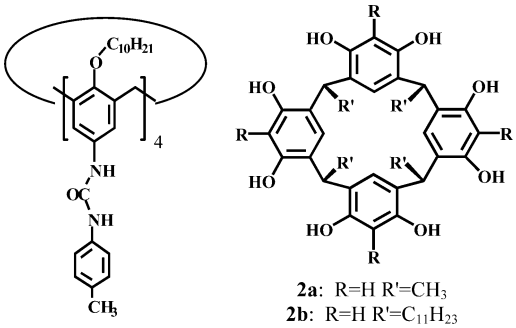
Molecular capsules, in general, and those based on hydrogen bonds, in particular, have attracted considerable interest in recent years.[1,2] One of the most intriguing characteristics of molecular capsules is their ability to isolate the encapsulated guests from the bulk. This may allow stabilization of the reactive intermediates[1b,3] and the catalysis of reactions.[1b,4] Therefore, understanding the factors that govern the affinity and the tendency of guests or, more importantly, series of guests toward the cavity of molecular capsules is important. Clearly, steric factors play a crucial role;[5] however, it was shown that electronic effects can also be very important, as demonstrated for the dimer of tetraureacalix[4]arenes such as **1**.[6,7]

In recent years, it was shown that resorcin[4]arene and pyrogallol-[4]arene systems, such as those shown in Chart 1, form large molecular capsules both in the solid state and in solution.[8,9] Shivanyuk and Rebek showed that **2b** forms a hexameric capsule with tetraalkylammonium salts and tetrabutylantimony bromide in wet chloroform solutions, affording a molecular capsule with a 6:1 stoichiometry.[8b,c] Recently, we showed, with the aid of diffusion NMR, that **2b** forms a hexameric capsule in a chloroform solution spontaneously.[8d,e] Kaifer very recently reported that **2b** encapsulates a cobaltocenium cation but not cobaltocene.[10] It was Mattay's group who first demonstrated that **3a** forms also a hexameric capsule in the solid state.[9a] Although they could not probe the structure in solution, Atwood and co-workers, who subsequently also prepared this molecular capsule, claimed that it appears to be stable even in polar solvents.[9b,c]

In the present Communication, we demonstrate that the hexameric capsules of the lipophilic resorcin[4]arene (**2b**) and pyrogallol-[4]arene (**3b**)[11] that have similar sizes and which are constructed from very similar building units have different affinities to different series of compounds. While the hexamer of **2b** can accommodate both neutral tertiary alkylamines and charged quaternary alkylammoniums, **3b** surprisingly encapsulates only the tertiary alkylamine series.

As part of our efforts to characterize and compare the self-assembly and characteristics of the molecular capsules of **2b** and **3b** in solution, and knowing that the hexamer of **2b** encapsulates a range of charged systems such as the different tetraalkylammonium salts,[8b] we decided to explore the affinity of the hexameric capsule of **3b** with respect to those salts. On the basis of Kaifer's work, one could conclude that, as in the smaller dimers based on tetraureacalix[4]arenes,[6,7] there is a preference for charge guests in these systems.[10] Therefore, we were surprised that all of our attempts to probe encapsulation of any of these tetraalkylammonium salts in the hexameric capsule of **3b** failed as shown in Figure S1 in the Supporting Information. These attempts included the addition of tetraalkylammonium salts of different sizes to the $CDCl_3$ or the $CHCl_3$ solutions of **3b** at different concentrations and stoichiometric ratios both before and after addition of varying amounts of CD_3-OD. We also attempted to encapsulate these salts by first dissolving

Chart 1



the salts in the $CDCl_3$ solutions and then adding **3b** that was isolated from its methanolic solution where it is in its monomeric form. In these attempts, tetraalkylammonium salts with different anions (Cl^-, Br^-, PF_6^-, BF_4^-) were used. In all of these experiments, we were unable to observe the typical high field chemical shifts of the encapsulated alkylammonium salts.[8b−d] This is demonstrated for the tetrahexylammonium bromide (THABr) case in Figure S1 of the Supporting Information. In experiments that were performed on solutions of **3b** in $CHCl_3$, the addition of the alkylammonium salts had no effect on the peaks of the encapsulated chloroform peak at about 5.1 ppm. This implies that the intact hexamer encapsulates only solvent molecules. At this stage, we decided to attempt the encapsulation of noncharged molecules in the hexamer of **3b**, and the tertiary alkylamines seemed to be the first choice worth trying.

Figure 1 shows sections of the ^{1}H NMR spectra of **3b** in $CHCl_3$ before (Figure 1A) and after addition of trihexylamine (Figure 1B). Figure 1C shows these sections of the ^{1}H NMR spectra after addition of DCl to the solution shown in Figure 1B. DCl was used to transform the neutral tertiary amines into their respective ammonium salts without significantly affecting the size of the guests, thus concentrating on electronic rather than on steric factors. These spectra clearly demonstrate that the addition of trihexylamine resulted in a displacement of the encapsulated $CHCl_3$ molecules and the encapsulation of the trihexylamine molecules. Addition of DCl that formed, in situ, the ammonium salt resulted in ejection of the guest and reencapsulation of the chloroform molecules (Figure 1C). The same sections of the ^{1}H NMR spectra for **2b** and trihexylamine in a $CHCl_3$ solution are shown in Figure 1D−F. Here, it is clear that both the amine and the ammonium salt are encapsulated in the hexameric capsule. In these spectra, a residual peak of encapsulated chloroform molecules is still observable both in the amine and in the ammonium cases. Figure 2 shows the ^{1}H NMR spectra in $CDCl_3$ solutions of **2b** and **3b** with tributylamine both before and after addition of DCl. From these spectra, it is clear that the tertiary amine is indeed encapsulated in both capsules.

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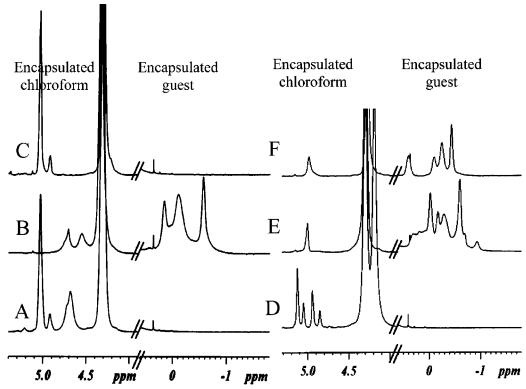

Figure 1. Sections of the ^{1}H NMR spectra (400 MHz, 298 K) of the hexameric capsules of **3b** (A−C), and **2b** (D−F) in $CHCl_3$ (A) and (D), after addition of trihexylamine (B) and (E), and after the addition of DCl (C) and (F).

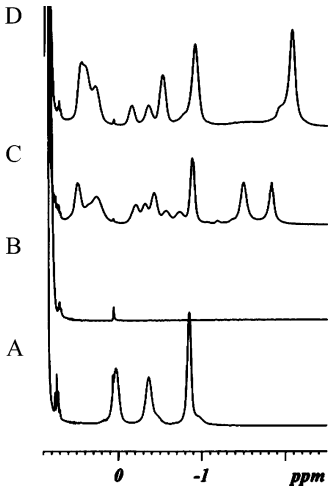

Figure 2. Sections of the ^{1}H NMR spectra (400 MHz, 298 K) in $CDCl_3$, of (A) the hexameric capsule of **3b** in the presence of tributylamine, (B) same as (A) after the addition of DCl, (C) the hexameric capsule of **2b** in the presence of tributylamine, (D) same as (C) after the addition of DCl.

Addition of DCl clearly results in the ejection of the in situ formed tributylammonium salt only for the capsule of **3b**. The same results were obtained for tripentylamine and trioctylamine and their respective ammonium salts.

To verify that in all cases we are dealing with the hexameric capsules of **2b** and **3b**, we measured the diffusion coefficients of these systems by diffusion NMR[12] using the stimulated echo diffusion sequence[12a] in some of these samples where the line shape was suitable for such experiments. The diffusion coefficients extracted for these systems are tabulated in Table S1 (see Supporting Information). These values provide additional independent verification that the structures of the hexameric capsules of **2b** and **3b** are maintained after addition of the amines and, more importantly, after the addition of DCl to their chloroform solutions that resulted in the in situ formation of the respective ammonium salts. Indeed, it can be seen from the data that the diffusion coefficients of **2b** and **3b** remained constant and low and, in all cases measured, the encapsulated species had the same diffusion coefficients as the capsules within experimental error. Moreover, when we could not identify encapsulated guests, we identified peaks of the encapsulated chloroform molecules when the spectra were collected in $CHCl_3$. Here again, the diffusion coefficients of these peaks were the same as those of the peaks of the hexameric capsules. Figure 2 reveals yet another difference in the behavior of the encapsulated guests in the different capsules. For example, tributylamine is tumbling freely in the cavity of **3b** (see Figure 2A), while both tributylamine and its quaternary salt are not freely tumbling in **2b**, resulting in a much more complexed spectrum for the encapsulated species in each case (see Figure 2C and 2D as compared to 2A). In fact, for the butyl guests we found an average of about one and two encapsulated species per hexamer in the case of **3b** and **2b**, respectively. Preliminary studies show that the encapsulation and ejection processes of the charged and uncharged guests are all completed within a few minutes.

In conclusion, we demonstrated that **3b** can encapsulate only the neutral tertiary alkylamines while **2b** accommodates both the amines and the respective ammonium salts. Although **2b** and **3b** form hexameric capsules in chloroform and although the building units in both hexamers are very similar, it is clear that **3b** encapsulates only the noncharged amine guests. This indeed seems to be a general observation as it was found for guests containing alkyl chains of four, five, six, and eight carbons. In fact, in **3b**, the protonation of the tertiary amines resulted in the ejection of the guests from the capsules, implying that such systems can, in principle, operate as a molecular pH switch.

Supporting Information Available: Figure S1 showing the ^{1}H NMR spectra of the hexameric capsules of **2b** and **3b** in the presence of tetrahexylammonium bromide. Table S1 showing the diffusion coefficients of chloroform, the guests, and the hexameric capsules of **2b** and **3b** in the presence of tertiary amines before and after the addition of DCl (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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