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The inner solvation of a cylindrical capsule

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Solvents inside a cylindrical capsule exchange positions slowly on the NMR timescale.

This research was undertaken to determine the capacity of the cylindrical capsule **1** (Fig. 1) for small molecule solvents. Earlier experience showed that two molecules of benzene or toulene are encapsulated, but it seemed likely that for smaller solvents, even more could be accommodated. Molecules capable of surrounding three other molecules are rare[1] and the nonspherical shape of **1** raises possibilities of different environments when three or more guests are detained inside. We report here several cases of limited translational motion of a guest caused by other guests in **1**.

In solution, the deuterated solvents that are convenient media for NMR studies make it difficult to determine how many—and even which—solvents are detained. In the solid state, X-ray crystallography has provided many examples of large guest encapsulation, but disorder of smaller molecules leaves the number of solvents inside the resting state uncertain. The capsule's tendency to take up trace impurities from the solvents compounds the problem, but indirect methods, such as the use of solvent mixtures, have been successful in some cases.[2] We are now able to observe encapsulation either using the guest as solvent or in a deuterated solvent too large to fit in the capsule.

The NMR spectrum of **1** in neat $CHCl_3$ is shown in Fig. 2a. The encapsulated $CHCl_3$ molecules appear as two signals in a 2:1 ratio: the signal at 2.9 ($\Delta\delta$ = −4.3 ppm, 2 protons) is assigned to $CHCl_3$ molecules at the ends of the capsule, while the resonance at 6.0 ($\Delta\delta$ = −1.2 ppm, 1 proton) represents the $CHCl_3$ molecule located near the middle. The separate signals for the guests in two different environments show that exchange is slow on the NMR timescale. Indeed, no evidence of exchange of positions inside the capsule could be obtained. Instead, 1D GOESY experiments established exchange of the guests with bulk solvent at a rate of ~1 s^{-1}. The resonance for the guest in the center is also broadened and implies an increased rate of exchange of this $CHCl_3$ with $CHCl_3$ in the bulk solvent outside the capsule. Accordingly, the lowest energy pathway for exchange of positions inside the capsule involves dissociation of a guest from one position into the bulk medium then re-entry to the other position of the capsule.

The inner solvation of a capsule is a form of molecular recognition. Complementarity of shapes and chemical surfaces is involved but the proper filling of space is an additional requirement for capsules. The three solvent molecules (75 Å^3 each) occupy about 54% of the capsule's space (420 Å^3)—a figure close to the ideal for encapsulation of neutral guests.[3] The *concentration* of three $CHCl_3$ molecules inside the volume of the capsule is calculated to be ~12 M while outside the concentration of solvent $CHCl_3$ is 12.3 M. An independent measure of the capacity—and an expression of the tenacity—of this capsule for $CHCl_3$ is given by the following: evaporation of a $CHCl_3$ solution of the capsule followed by overnight drying fails to remove the encapsulated solvent; the NMR spectrum of the residue, redissolved in CD_2Cl_2, shows that three molecules of $CHCl_3$ are released by each capsule.

The NMR spectrum of isopropyl chloride $ClCH(CH_3)_2$ in the capsule using deuterated mesitylene as a cosolvent is shown in Fig. 2b. The signals appear in an unobscured region of the spectrum and show the two types of encapsulated molecules—

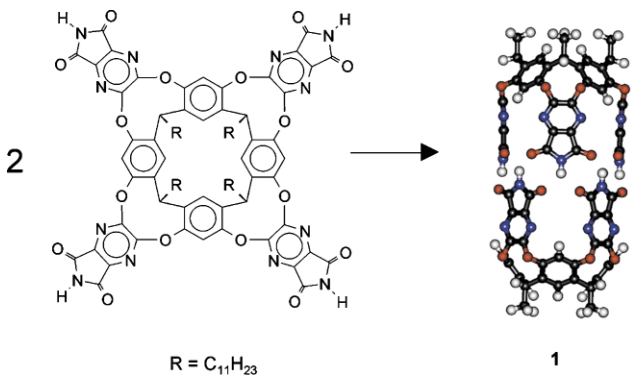

Fig. 1 Line drawing of the subunit and ball-and-stick model of the cylindrical capsule.

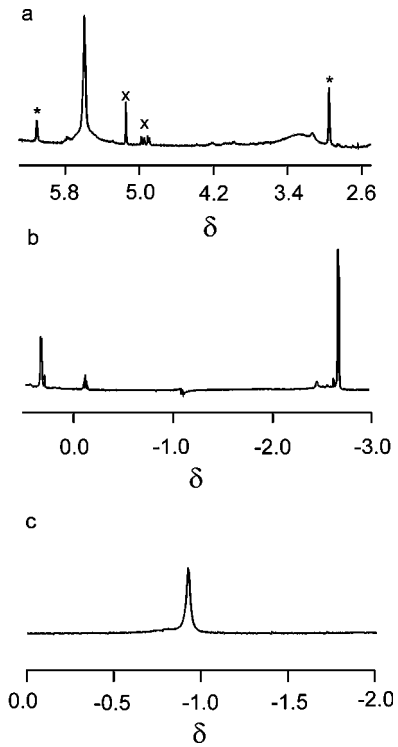

Fig. 2 NMR spectra (600 MHz) of encapsulated solvents in **1**: a) in $CHCl_3$ at 243 K the two locations of encapsulated solvent (marked *) show different chemical shifts and slow exchange, the signals at ~5 ppm (marked ×) represent amylene stabilizers in the solvent; b) in $ClCH(CH_3)_2$:mesitylene-d_{12} (2:1) at 303 K, the upfield doublet and the heptet represent two $ClCH(CH_3)_2$ guests at the ends of the capsule and the downfield doublet represents the $ClCH(CH_3)_2$ in the middle; c) in $ClCH_2$–CH_2Cl:mesitylene-d_{12} (2:1) at 303 K, the signal is due to guests at the ends of the capsule.

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those at the ends of the capsule and the one at the middle. Irradiation of the large doublet with either 0.4 or 1 s mixing times failed to show transfer to the small doublet, but transfer to the bulk solvent outside was evident. Again, an energetic barrier prevents the guest molecules from exchanging positions; they are too large to move past each other while within the capsule.

The longer and narrower 1,2-dichloroethane (DCE) in the same capsule shows somewhat different NMR characteristics (Fig. 2c). The upfield signal at ~ −0.9 ppm is in a region free of other resonances and it represents (by integration) the two DCE's at the ends of the capsule. The signal for the DCE in the middle is obscured by aliphatic resonances of the capsule itself and is somewhat distorted by the large signal for the DCE outside. A preparation of the capsule starting from perdeuterated dodecanal revealed the position of the centrally located DCE signal through a GOESY experiment. Again, exchange within the capsule is slow but it does occur on the NMR timescale: Irradiation of the DCE resonance at −0.9 ppm gave transfer to the signal for the DCE in the middle of the capsule at 2.1 ppm. The exchange was detected using 1D GOESY with a mixing time of 0.4 s at 273 K. Because exchange with bulk DCE also occurs, the rate could not be accurately determined. The conformational flexibility of DCE apparently permits its slithering motions from one position to another while in the cavity. The volume of DCE is slightly smaller than that of $CHCl_3$ and its occupancy (packing coefficient) is 53%. A modeled depiction of the encapsulated guests is given in Fig. 3.

The smaller CH_2Cl_2 in the capsule showed no distinct guest signals at room temperature or lower, even down to 223 K. Yet, the capsule shows its characteristic, symmetrically occupied spectrum. Either the guests exchange positions within the capsule or they exchange with exterior solvent, at rates rapid enough to result in line broadening on the time-scale of the NMR experiments. Both processes are likely to be faster for this smaller guest,[4] and we have no way of distinguishing between them. Modelling shows 4 CH_2Cl_2 guests can be accommodated and few steric clashes are encountered when one guest moves past the other. The plasticity of hydrogen bonds at the center of the capsule could also facilitate mobility of $CHCl_2$ guests (Fig. 4). In the presence of the larger guest, *p*-xylene, an unsymmetrically filled capsule was observed; one molecule each of *p*-xylene and CH_2Cl_2 was encapsulated with $\Delta\delta = -3.7$ ppm for the latter. The shift places the CH_2Cl_2 near the end of the capsule (Fig. 4).

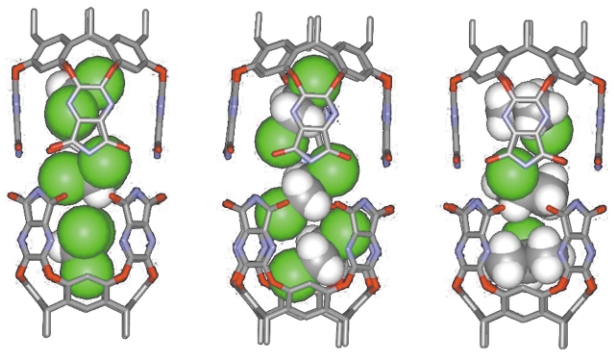

Fig. 3 Energy minimized structures of encapsulation complexes. Top: capsule **1** with $CHCl_3$ (left) $ClCH_2$–CH_2Cl (center) and $ClCH(CH_3)_2$ (right). The space filling models reflect the difficulty of positional exchange of the guests between the ends of capsule **1** and its middle while inside the capsule. The peripheral alkyl groups and some hydrogens of the hosts are removed for viewing clarity.

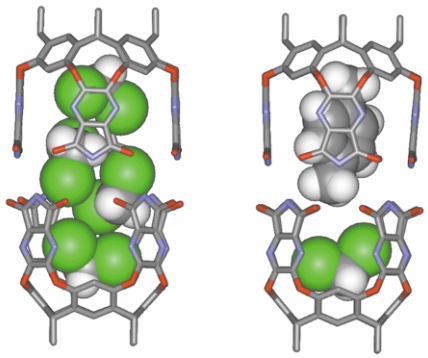

Fig. 4 Energy minimized structures of the capsule with guests. Left: four CH_2Cl_2 solvents are accommodated. Right: CH_2Cl_2 and *p*-xylene.

Encapsulation complexes can be assembled through metal/ligand interactions[5–7] or hydrogen bonding[8–10] and their interiors feature high symmetry—roughly spherical. They isolate their guests in space and time but their shapes do not hinder the motions of guests with respect to each other. The slow exchange on the NMR timescale gives information on complex stoichiometry and reports on the magnetic environments inside the capsule in a way that rapidly exchanging systems cannot. The present cases provide the first examples of guest induced limitations on translational mobilities, without resort to glassy matrices and low temperatures, or the isolation that is available at low pressures in the gas phase. Instead, the assemblies operate at equilibrium in the liquid phase, at ambient temperatures and on timescales ranging from milliseconds to hours. They offer physical organic chemistry an unprecedented view of behavior in the liquid phase.

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