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SOLID GUESTS IN REVERSIBLE ENCAPSULATION HOSTS

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Abstract - The space inside a cylindrical capsule host is probed with a series of adamantane guests. The results indicate that higher packing coefficients are possible for solid guests than for liquids or gases in encapsulation complexes.

Studies of reversible encapsulation have revealed a number of newly discovered phenomena unique to molecules within molecules. These comprise amplification of concentrations,[1] coencapsulation of multiple guests,[2] stabilization of reactive intermediates,[3] acceleration of reactions[4] and even catalysis.[5] An older question concerns the optimal filling of space in these complexes. Earlier, we found that a packing coefficient of about .55 was desirable for the liquid state[6] and recently a value of about 0.40 for gases was proposed.[7] Here, we examine some very densely packed structures using solid adamantane derivatives as guests in order to find appropriate values for solids within these complexes.

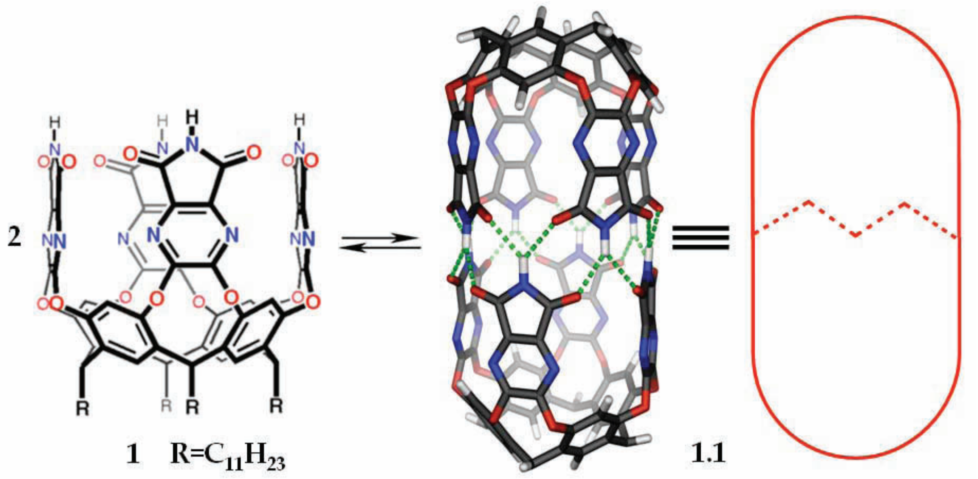
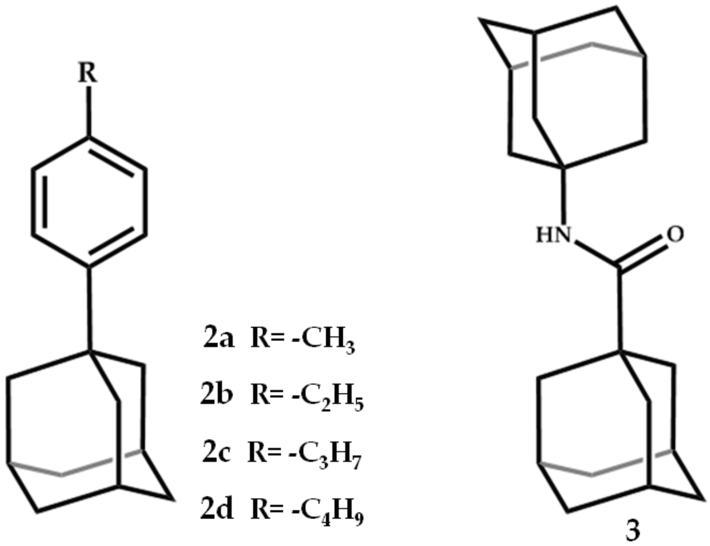


Figure 1. Line drawing of the resorcinarene subunit **1** and a model of the dimeric capsule **1.1**. The cartoon representation of the capsule is also shown.

We used the cylindrical capsule[8] **1.1** (Figure 1) in this study because its behavior with 2,2-paracyclophane and coencapsulated guests[9] suggested that high packing coefficients could be achieved with consequent limitations of guest rotation within the capsule. A series of guests **2a-d** (Figure 2) were prepared using an adamantane as an anchor species, covalently bound through a rigid phenyl spacer to increasingly larger alkyl groups - methyl through butyl. These were synthesized by well-established literature methods.[10] In addition, the bisadamantyl amide **3** was encapsulated.



3

Figure 2. Line drawings of the guests.

Encapsulation of these in **1.1** occurs in the largest deuterated commercial solvent available, mesitylene-*d*$_{12}$. The relevant parts of the NMR spectra are shown in Figure 3 along with the calculated packing coefficients (P.C.). It is seen that on average the N-H resonances move *upfield* with increasing length of the guest. This would be expected if the increased pressure inside the capsule leads to weakening the hydrogen bonds that hold the system together. At the other end of the spectrum, the upfield regions show that the terminal methyl “knobs” are shifted upfield by $\delta\Delta$ 4.3 - 4.8 ppm. These values are close to that provided by the nuclear independent chemical shift calculations of Schleyer;[11] applied to this capsule, a maximum value of -5.5 ppm is calculated.[12] The depth of the methyl group, its position in the resorcinarene tapered end and its contact points with the walls of the capsule are not easily predicted since the alkyl chains have some flexibility. The signals of the adamantane hydrogens, however, show a monotonic upfield shift with increasing guest length indicating their positions near the capsule’s tapered ends. The relatively short amide **3** showed somewhat lower upfield shifts. This may be caused by the attractive interactions of the secondary amide with the capsule's seam of hydrogen bonds.

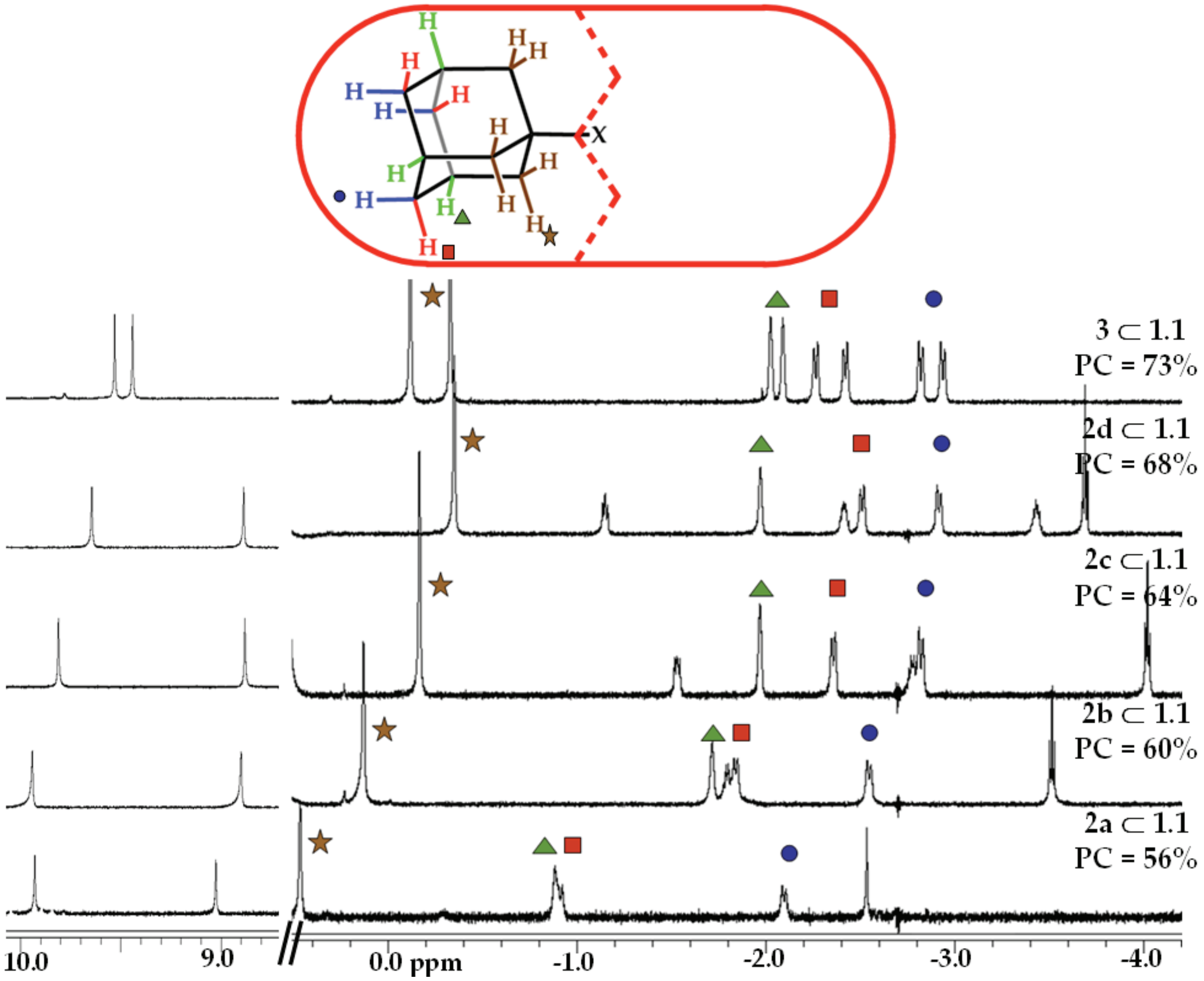
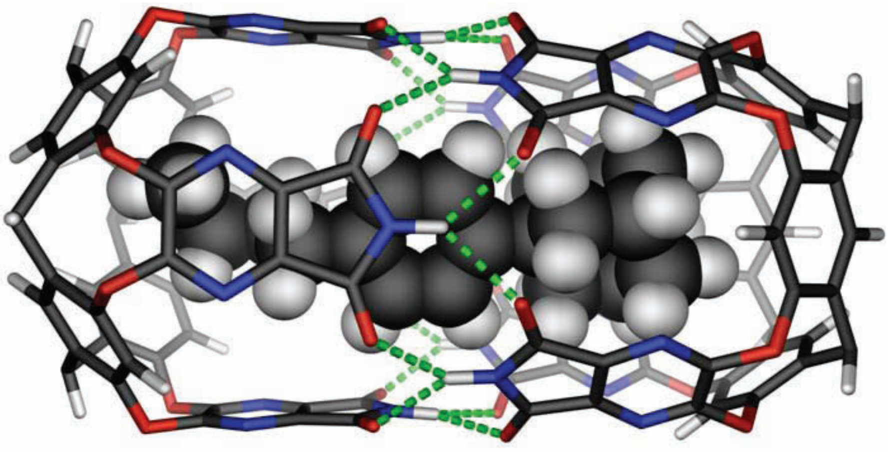
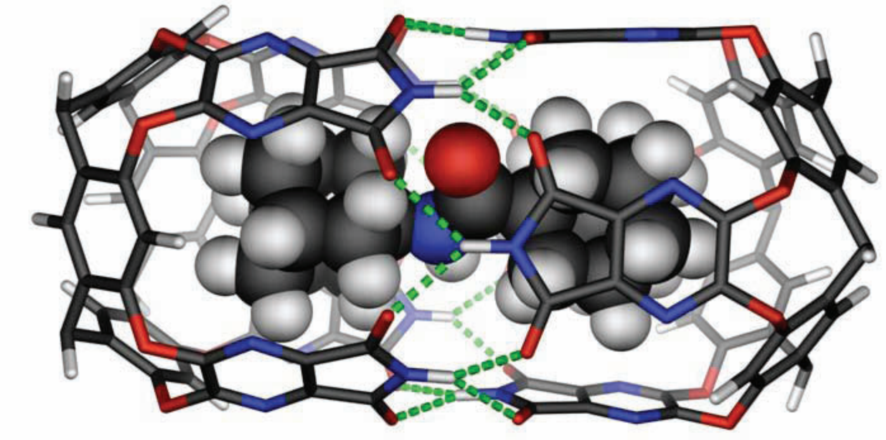


***Figure 3*.** Parts of the ^{1}H NMR spectra (600MHz, mesitylene d_{12}) of **1.1** (2mM) with all guests (15mM): (a) **2a**, (b) **2b**,(c) **2c**, (d) **2d**,and (e) **3**. Packing coefficients (P. C.) are also given.

The shape of adamantane is not particularly congruent to these tapered ends and it is not known to what extent the capsule itself deforms to accommodate such a blunt guest. The modeled complexes are shown in Figure 3 for the n-butyl **2d** and the amide guest **3**. The latter shows the highest packing coefficient of about .73, close to the value of closely packed spheres (.74) typical of most organic solids.



2d in 1.1



3 in 1.1

Figure 4. Energy minimized (AM-1) models of encapsulated **2d** and **3** in the capsule.

It is, at the very least, impolite to discuss phase when only a few molecules are involved and this is the case here. Nonetheless, it is reassuring to see that encapsulation of solid guests can lead to much higher packing coefficients than that, say, of gases.[13] This behavior was anticipated some 40 years ago by Kitaigorodski[14] and is still relevant today. Earlier synthetic receptors such as clefts recognized the surface features of their targets,[15] but the capsules that more or less surround their targets deal must also accommodate appropriate molecular volumes.

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