Host–Guest Systems

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Gas Behavior in Self-Assembled Capsules**

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Self-assembly is generally about filling space, and reversibly formed capsules are specific examples of spaces needing molecules to occupy them appropriately. In solution, an optimal occupancy of about 55 % of the space is accounted for by the liquid;[1] the value for encapsulated solids must be higher, somewhere in the range 65–80 %.[2] The situation is less clear for gases even though they were the first guests to be studied in self-assembled capsules,[3] covalent cryptophanes,[4] hemicarcerands[5] fullerenes,[6] and metal–organic frameworks (MOFs).[7] We have now observed the simultaneous encapsulation of several gas molecules within capsule **1·1** (Figure 1) and report here their occupancy in this capsule and related spaces. Their behavior raises questions about the phase experienced by a few molecules confined in reversibly formed capsules.

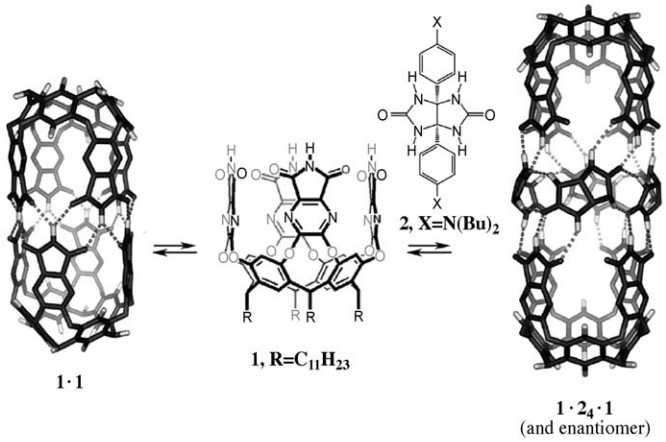

Figure 1. Structures of the resorcinarene subunit **1** and the glycoluril spacer **2**. The dimeric capsule **1·1** and the extended capsule **1·2₄·1** are modeled without peripheral alkyl and aryl groups for clarity.

The assembly of capsule **1·1** requires the presence of suitable guests, including combinations[8] of gases with liquids[9] and solids.[10] When **1** is dissolved in cyclopropane-saturated [D_{12}]mesitylene, three cyclopropane guests can be detected inside the capsule. Sharp signals are seen for the guests in the NMR spectra (Figure 2) with separate reso-

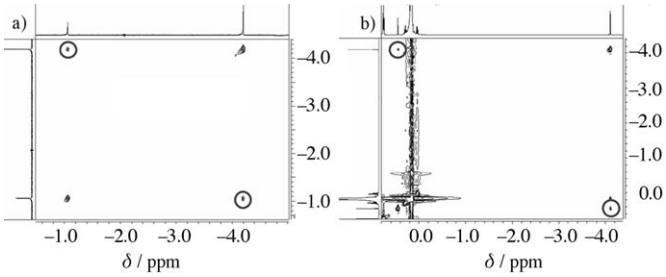

Figure 2. 2D EXSY NMR spectra of encapsulated cyclopropane; mixing times 300 ms. Spectra were obtained from solutions of a) **1.1** (2 mM) or b) **1.2₄.1** (2 mM) in (gas-saturated) [D_{12}]mesitylene. The signal at $\delta = +0.45$ ppm in (b) corresponds to the guest near the belt of glycoluril molecules while the large signal at $\delta \approx 0.2$ ppm is that of free cyclopropane in [D_{12}]mesitylene. Cross-peaks are circled.

nances observed for the cyclopropane molecule at the center of the capsule ($\delta = -1.1$ ppm) and the two cyclopropane molecules at the ends ($\delta = -4.2$ ppm). The spin-lattice relaxation time (T_1) for the cyclopropane guests located at the ends of the cavity is 14 s and that at the center of the capsule shows a T_1 value of 12 s. These values are long because there are few protons on the inner surface of the capsule; accordingly, accurate integration requires delay times of considerable length (40 s). When an excess of glycoluril **2** is present, the same experiment gives a new assembly **1·2₄·1**[11] which contains four encapsulated cyclopropane molecules. Again, separate signals are seen for the two guests near the ends of the cavity ($\delta = -4.1$ ppm) and the two guests near the central glycoluril units ($\delta = +0.45$ ppm). The observed downfield shift of the signals corresponding to protons surrounded by such glycoluril units has already been reported by us.[12]

Cross-peaks are seen in the 2D EXSY spectrum[13] of encaspulated cyclopropane (Figure 2a), which indicates that the guests exchange positions within the capsule at rates measurable on the NMR timescale. They also show exchange with external cyclopropane molecules. The activation barrier for the exchange inside the capsule **1·1** was determined as 17.5 kcal mol^{-1}, by using magnetization exchange rate constants. The 2D EXSY spectrum of cyclopropane in the extended capsule **1·2₄·1** also shows cross-peaks (Figure 2b), which indicates that the four cyclopropane molecules move past each other. This exchange process shows a slightly higher activation barrier of 18.5 kcal mol^{-1}, presumably because the space near the center of the assembly is constricted.

Parallel experiments with different guests reveal that two butane guests are encapsulated in **1·1** and three in **1·2₄·1**

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(Figure 3). Signals from the central butane molecule in the ^{1}H NMR specrum of the latter are obscured by those of the capsule, but cross-peaks in the 2D spectra indicate the exchange of butane positions. The butane guests also slip past each other at rates observable on the NMR timescale.

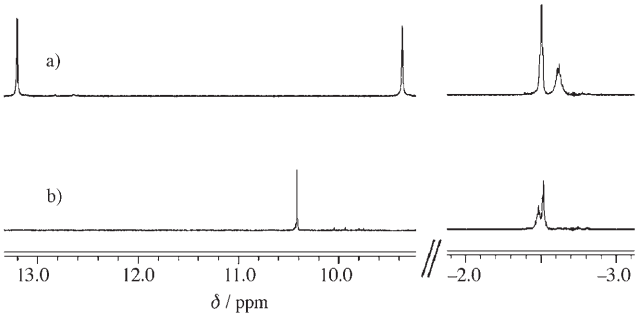

Figure 3. ^{1}H NMR signals of encapsulated *n*-butane and imidic proton of the capsule of solutions of a) **1·1** (2 mM) and b) **1·2$_4$·1** (2 mM) in (gas-saturated) [D_{12}]mesitylene. Signals for the imide N-H proton move downfield from $\delta = 10.4$ ppm in the spectrum of **1·1** to 13.2 ppm in that of the extended capsule **1·2$_4$·1**.

Although the space inside a capsule is not rigorously well-defined (Figure 4), modeling studies can give reasonable self-consistent estimates provided that the capsule walls do not collapse. We used GRASP[14] to calculate cavity volumes of 425 Å^3 in **1·1** and 620 Å^3 in **1·2$_4$·1**. The pressure inside the cavity can then be calculated, even if only one or a few molecules of the gas are present. For the cases reported here, simple calculations reveal how far these systems are from ideal. At one atmosphere, a mole of an ideal gas occupies 22.4×10^{27} Å^3 (22.4 L), or each molecule enjoys a space of about 37000 Å^3, which is nearly 90 times the space in the capsule **1·1**. Accordingly, three ideal gas molecules at ambient temperature in the capsule **1·1** would be at approximately 270 atm, yet the system is at equilibrium at room temperature with cyclopropane in mesitylene at about one atmosphere. A

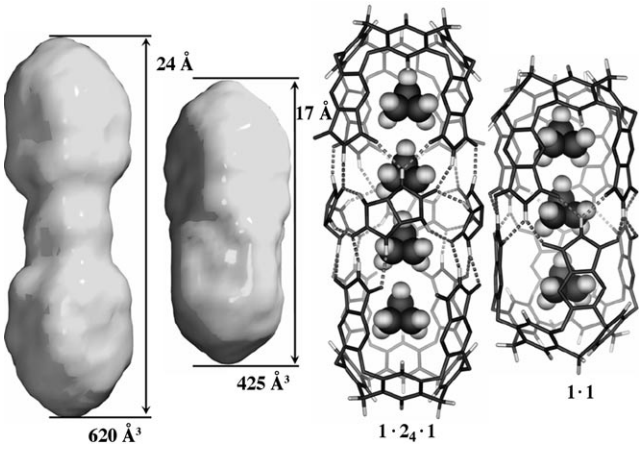

Figure 4. Left: The shapes and volumes of the inner spaces of **1·1** (425 Å^3) and the extended capsule **1·2$_4$·1** (620 Å^3) as calculated by GRASP. Right: Modeled structures of the encapsulation complexes of cyclopropane.

pressure of around 1000 atm for encapsulated cyclopropane in **1·1** is calculated using the van der Waals equation. Calculations on the extended capsule give about 240 atm for four (ideal gas) cyclopropane molecules in **1·2$_4$·1**. In a similar system, a single molecule of methane in the "tennis ball"[15] gives a pressure of 540 atm as an ideal gas and greater than 900 atm as a van der Waals gas. Even so, complete encapsulation is observed at ambient temperature as methane is gently bubbled through a solution of the tennis ball in chloroform.

Saunders[16] has addressed this conundrum. He points out that pressure is discontinuous when only a few molecules are involved, a pressure of 2000 atm can be calculated for a single helium atom in C_{60}, and even two helium atoms have been detected inside. Saunders, Komatsu and co-workers[17] inserted ^{3}He into an open-cage C_{60} derivative under equilibrating conditions and measured a pressure of approximately 3000 atm for a single guest, a value reasonably close to the original estimate. We have yet to observe reversible encapsulation complexes of a given capsule with different numbers of the same guest molecule inside, although the same guest can appear in two different capsules at equilibrium.[18] For the cases where an integral number of a single guest is inappropriate, coencapsulation with another guest can lead to a stable arrangement.[19,20]

The calculated pressures are, of course, unrealistic because the collisions with the walls are not elastic or "hard sphere". Instead of conceptualized surfaces that merely define the volume, these capsules are made up of aromatic subunits and attraction of the gas to these groups must lower the potential energy and thus the pressure of the gas. The nature of the guest's contacts with the walls—collision and recoil at one extreme and temporarily stuck to the inner surface on the other—is not known. The contacts between the host and guest could involve one, two, or three hydrogen atoms for a single cyclopropane molecule, and more contacts for butane. The lowering of the pressure corresponds to about 1–2 kcal mol^{-1} for each cyclopropane guest, a value comparable with typical CH–π interactions.[21] The attractions operating here also occur in fullerenes, carbon nanotubes, metal–ligand[22] or hydrophobic[23] capsules, and MOFs—all of which feature aromatic subunits as rigid spacers. The mechanical properties and sizeable areas of aromatic panels are a universal feature of these synthetic containers and are essential for isolating molecules within them. They provide softer, polarizable, electron-rich linings that contrast with the hard, tightly framed hydrogen-bond lattices of water in clathrates or the mineral-laden arrays present in typical zeolites.

Table 1 gives the packing coefficients (PCs) for encapsulated cyclopropane, butane, and hexane. The largest observed PCs are around 40 for the gas molecules inside the capsules. In contrast, the behavior of hexane is quite liquidlike. The NMR spectrum of the complex of **1·1** with hexane shows two hexane guests that tumble rapidly.[9] In **1·2$_4$·1** two hexane guests can be seen at the ends of the capsule and a third can be seen in the central space. In either capsule, hexane molecules fill slightly more than 50% of the space. This finding is in accordance with the analysis of Kitaigorodsky,[24] who noted

Table 1: Encapsulation of gaseous guests in **1**· and **1·2$_4$·1** at 295 K and ambient pressure.

Guest (vol, Å^3)	Number of guests PC[a]			PC[b]			
	1	2	3	1	2	3	4
CH_3-CH_3 (46)	11	22	33	7	15	22	30
$(CH_2)_3$ (56)	13	26	**39**	9	18	27	**36**
CH_3-$(CH_2)_2$-CH_3 (80)	19	**38**	57	13	26	**39**	52
CH_3-$(CH_2)_4$-CH_3 (113)	27	**53**	80	18	36	**54**	72

[a] Packing coefficients calculated for the cylindrical capsule **1·1** with cavity of 425 Å^3 [b] Packing Coefficients calculated for the extended capsule **1·2$_4$·1** with a cavity of 620 Å^3. The bold values represent observed occupancy.

that packing coefficients are a useful indication of phase: for simple aromatic compounds such as benzene a packing coefficient above 68% represents the solid state, 58% the liquid phase, and less than 51% is gaseous state.

The problems of storage, transport, labeling,[25] and sensing of gases — particularly those involved in alternative energy sources — make them timely targets of molecular recognition studies.[26] Ironically, the earliest,[27] most complex,[28] and finite self-assembled systems in solution had no other function than to fill space; it appears now that the proper filling of space drives most encapsulation phenomena[29] and perhaps even molecular recognition events in general. In summary, we note that a simple formula describes the encapsulation of gases in these very real containers: a stable arrangement results when approximately 40% of the space is occupied.

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