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REVERSIBLE ENCAPSULATION OF TERMINAL ALKENES AND ALKYNES

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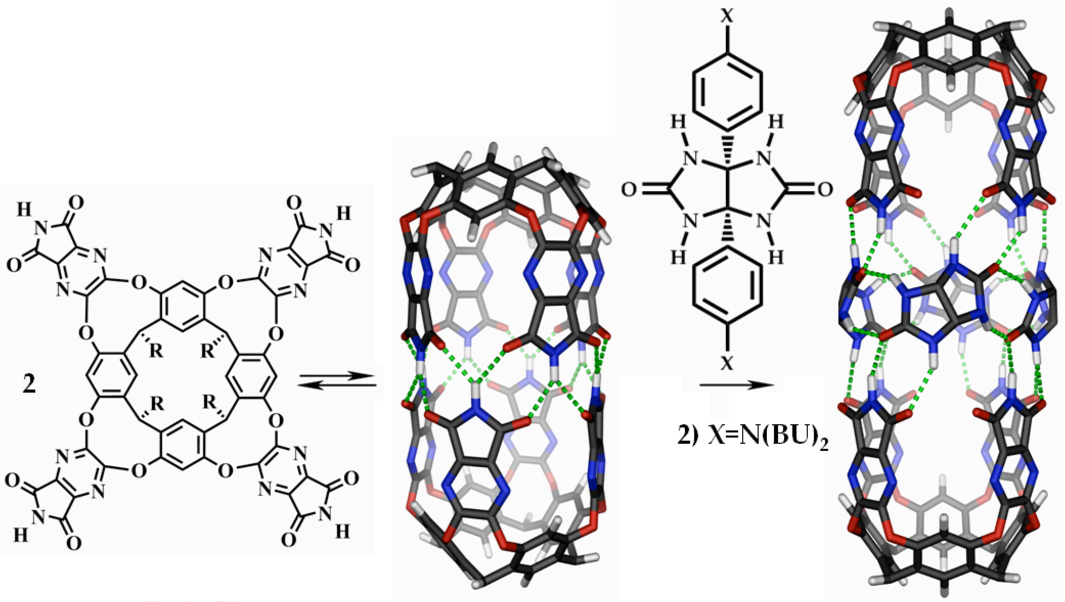
Dedicated to Prof. Ryoji Noyori on the occasion of his 70th birthday.

Abstract – Molecular encapsulation is a modern form of recognition in which a host completely surrounds a guest molecule. Unlike earlier covalent systems, reversible assembly allows the study of these complexes at equilibrium under ambient conditions. We show here that self-assembled capsules held together by hydrogen bonds surround a series of alkenes and alkynes that fill the space properly. These guests are frequently found in contorted conformations that reduce their length in order to fit inside and then make appropriate contacts with the capsule.

The chemistry of molecular recognition has always relied on heterocyclic structures, from crown ethers[1] and cryptands,[2] through molecular clefts[3] and even molecules that completely surround others. The original covalent carcerands[4] and cryptophanes[5,6] are being replaced by reversible encapsulation complexes: these rely on metal ligand interactions[7] or hydrogen bonding systems[8] in which many heterocycles can be found. Self-assembly is a general description of filling space and reversible encapsulation complexes involve a form of molecular recognition using finite spaces that need molecules to occupy them properly. The hydrogen bonded capsules come in many sizes but the long and narrow shape of the capsule **1.1**[9] (Figure 1) and its extended version **1.2$_4$.1** offer new opportunities for filling the space. The shapes define their molecular recognition capacities for alkenes and alkynes and we describe them here.



1 R=$C_{11}H_{23}$ **1.1** **$1.2_4.1$**

Figure 1: Line drawings of the resorcinarene subunit **1** and the glycoluril spacer **2**. The dimeric capsule **1.1** and the extended capsule **$1.2_4.1$** are modeled without peripheral alkyl and aryl groups for clarity.

The capsule **1.1** requires the presence of suitable guests for assembly; in those cases where a single guest is inappropriate, coencapsulation with another guest can lead to a stable arrangement.[10] Accordingly, suitable guests can include single molecules or combinations[11] of gases with liquids[12] and solids.[13] These encapsulation complexes are at equilibrium in the solution phase at ambient conditions and NMR methods offer a window for observation of molecules inside. Earlier we described the encapsulation of long chain normal alkanes such as dodecane, in the capsule **1.1**. The longest *n*-alkane accommodated was C_{14}, and this required coiling into a helical conformation.[14] With longer *n*-alkanes no encapsulation is seen, but the addition of excess glycolurils **2** gives a new assembly **$1.2_4.1$** that takes up alkanes from C_{15} to C_{19}.[15]

We examined a series of 1-alkenes and 1-alkynes within the original and extended capsule. The shorter alkenes C_{12} and C_{13}, are taken up by both capsules (Fig 2a-d). In the extended **$1.2_4.1$** the chemical shifts of the C_{15} and longer alkenes end move upfield; the methylenes near the methyl end of the guest move closer to the ends or nearer to the walls of the capsule. Accordingly, the long guests are seen to compress. They become shorter but thicker and helical coiling would result in both of these changes. The multiplicity of the signals results from the asymmetric electronic environment induced by the chiral arrangement of the four glycolurils. This is seen in the diastereotopic methylene signals, particularly those near the center of the assembly. The longest terminal alkene to fit into **1.1** is C_{14} and earlier studies showed that 7-*trans*-tetradecene was also a guest.[14] Thus it appears that a double bond anywhere along the 14-cabon chain would be accommodated. For the fully saturated C_{14}, extensive coiling was revealed along the chain by 2D NMR cross peaks between hydrogens on the *n* and *n*+4 carbons.

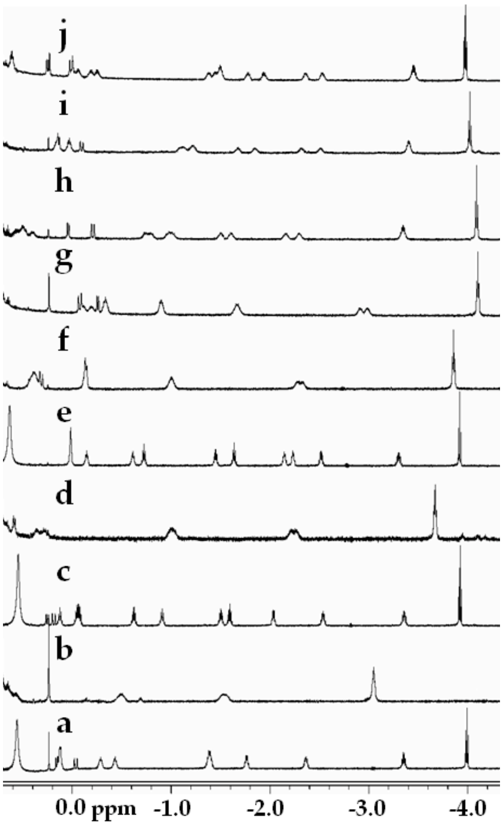


Figure 2: Encapsulation of terminal alkenes in **1.1** and **1.2$_4$.1**. Upfield regions of the ^{1}H NMR spectra (600 MHz, mesitylene *d*12) of **1.1** (2 mM) and terminal alkenes (15 mM): (a) 1-dodecene, (b) 1-dodecene and **2** (4 mM), (c) 1-tridecene, (d) 1-tridecene and **2** (4 mM) , (e) 1-tetradecene (f) 1-tetradecene and **2** (4 mM) (g) 1-pentadecene and **2** (4 mM), (h) 1-hexadecene and **2** (4 mM), (i) 1-heptadecene and **2** (4 mM) (j) 1-octadecene and **2** (4 mM).

The tapered ends of these capsules are unable to allow a “blunt” methyl group to penetrate deeply, but a “pointed” terminal acetylene is another matter. Probes using rigid (aromatic) spacers with terminal acetylenes showed that this narrowest of functional groups can approach the small opening of the resorcinarene subunit. Their NMR spectra showed that the acetylenic hydrogen experiences less shielding as it is forced deeper into the tapered end of the capsule where 4 benzene rings converge.[16] The same trend is observed for terminal alkynes in **1.1.** As the guest lengthens, the narrow, terminal acetylene must move deeper into the cavitand. The methyne hydrogen signals move downfield to -2.8, -1.7 and -0.3 ppm for 1-dodecyne, 1-tridecyne and 1-tetradecyne, respectively, as they experience a less shielding environment. In the extended cavity of **1.2$_4$.1** the methyne hydrogen signals move *upfield* to -2.3, -3.2 and -3.5 ppm for 1-tridecyne, 1-tetradecyne and 1-pentadecyne, respectively, as they approach the resorcinarene. But as the acetylenic hydrogen enters the tapered end of the cavitand, the signal begins to shift downfield as seen for 1-hexadecyne (-3.0 ppm).

The terminal alkynes also show an unexpected behavior in the extended capsule (Fig. 3). The NMR resonances for the methyl groups are invariably found at - 4 ppm, ($\delta\Delta \sim 4.8$ ppm) close to the maximum value ever seen for this function. It suggests the "blunt" methyl is at the deepest it can be in the resorcinarene ends of the capsule. For $C_{12} - C_{14}$ the chemical shifts of the nearby methylenes move, as they should, downfield, indicating a conformation that is relaxed and extended and (on average) away from the walls. But for $C_{14} - C_{16}$ the signals of these nearby methylenes move *upfield*. The downfield shift of protons surrounded by glycolurils has been previously noted,[17] but the upfield shift indicates the placement of the hydrogens nearer the pyrazine walls. A model of what may be happening is given in Figure 4C. The acetylene end of C_{16} is deep in the tapered end and the nearby methylenes are in an extended conformation that continues through - and is reinforced by - the constricted space of the glycolurils. This conformation places pressure on the far end of the guest and causes it to buckle, forcing the methylenes nearer the walls.

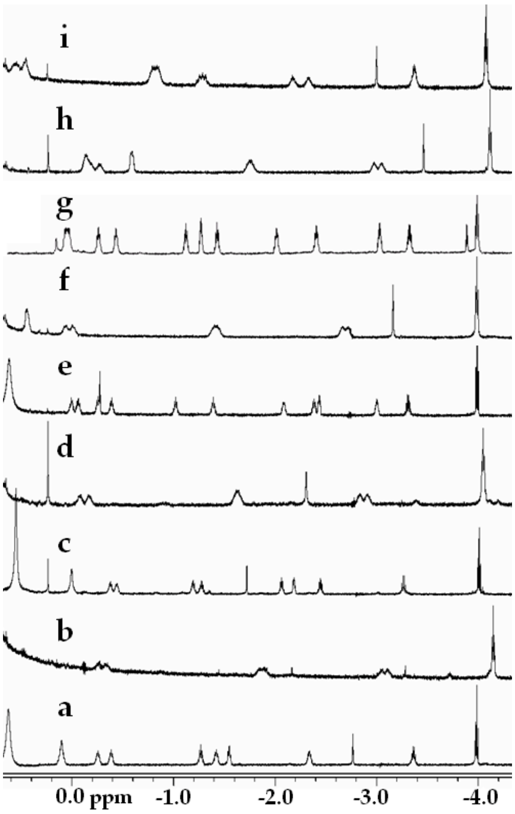


Figure 3: Encapsulation[18] of terminal alkynes in **1.1** and **$1.2_4.1$**. Upfield regions of the ^1H NMR spectra (600 MHz, mesitylene d_{12}) of **1.1** (2 mM) and terminal alkynes (15 mM): (a) 1-dodecyne, (b) 1-dodecyne and **2** (4 mM), (c) 1-tridecyne, (d) 1-tridecyne and **2** (4 mM) , (e) 1-tetradecyne, (f) 1-tetradecyne and **2** (4 mM) (g) 1-pentadecyne, (h) 1-pentadecyne and **2** (4 mM), (j) 1-hexadecyne and **2** (4 mM).

How do these alkenes and alkynes fill the capsules? For some time we have believed that the proper filling of space drives reversible encapsulation, perhaps even most recognition phenomena. This is ironic since the earliest, finite self-assemblies in solution had *no other function* than to fill space.[19] The shapes of the cavities involved are modeled in Figure 4. Both share the tapered ends imparted by the resorcinarenes, but the glycolurils of **$1.2_4.1$** constrict the volume near its middle.

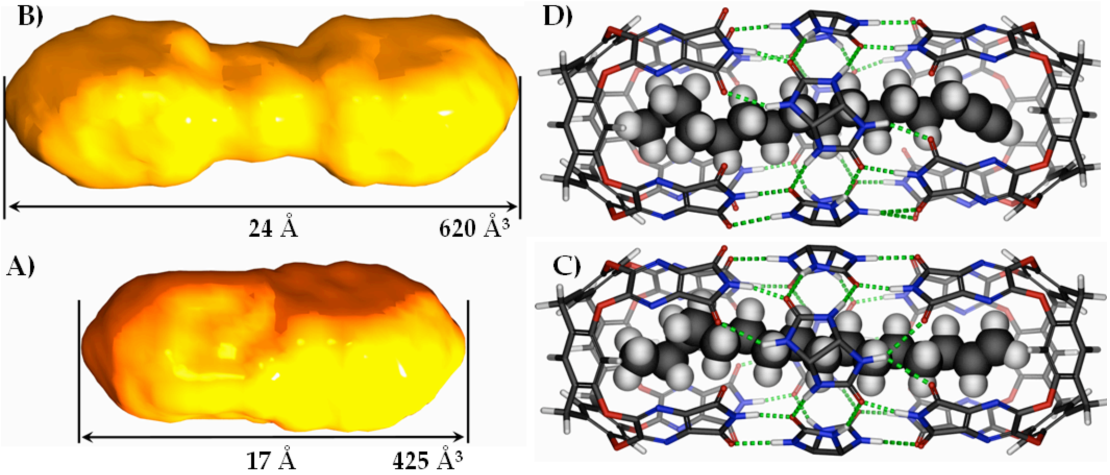


Figure 4: The shapes and volumes of the inner spaces of **1.1** (A) and the extended capsule **$1.2_4.1$** (B) as calculated by GRASP.[20] Complexes of 1-hexadecyne (C) and 1-hexadecene (D) are energy-minimized in the extended capsule. Some *gauche* conformations are seen in the guests near their methyl ends.

In solution, an optimal occupancy of ~ 55% of the volume is encountered for encapsulated liquids.[21] The value for encapsulated solids must be higher, in the range of 65-80% and probably centered around the value for closely packed spheres, 74%. The calculated packing coefficients (PC's) for the various complexes are given in the Table. The calculations assume fully-extended conformations for the guests and uncollapsed host walls (they were fixed). It is seen that the capsule **1.1** reaches a limit of 57% occupancy with C_{14} derivatives, or a few % lower if coiling is allowed. Much lower occupancies are calculated for the complexes of these hydrocarbons in **$1.2_4.1$**. The source of this discrepancy is unknown, but dissolved atmospheric gases may be coencapsulated in the extended system.[22]

Table: Packing coefficients (PC's) of guests in **1.1** and **$1.2_4.1$.** The lengths and volumes of the guests are calculated for their fully-extended conformations.

Guest	Volume (Å^3)	Length (Å)	PC(%) in 1.1	PC(%) in $1.2_4.1$
n-$C_{12}H_{24}$	210	15.6	49	34
n-$C_{12}H_{22}$	205	15.4	48	33

n-$C_{13}H_{26}$	226	16.8	53	37
n-$C_{13}H_{24}$	222	16.6	52	36
n-$C_{14}H_{28}$	243	18.0	57	39
n-$C_{14}H_{26}$	239	17.8	56	38
n-$C_{15}H_{30}$	260	19.3	61	42
n-$C_{15}H_{28}$	255	19.0	60	41
n-$C_{16}H_{32}$	277	20.5	65	45
n-$C_{16}H_{30}$	272	20.3	64	44
n-$C_{17}H_{32}$	294	21.8	69	47
n-$C_{18}H_{34}$	311	23.0	73	50

Many of the atoms that make up the host are sp^2 hybridized with their p orbitals directed inward, and the cavity can be thought of as coated with a thin layer of negative charge. Molecules of convex shape and coated with a thin layer of positive charge are complementary, provided that they can fit inside. In the cases at hand, the guest's contacts with the walls are CH-π attractions of the hydrocarbon with aromatic walls. The attractions operating here will also be on offer in fullerenes and carbon nanotubes when methods are developed to encapsulate hydrocarbons in them. The CH-π interaction[23] is also available in metal organic frameworks[24] and many other metal/ligand capsules that feature aromatic subunits as rigid structural panels. While gases have been the target guests to date, akenes and alkynes may also be fruitfully explored in the future.

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