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Expanded Capsules with Reversibly Added Spacers

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Hydrogen-bonded capsules are usually self-assembled from identical and self-complementary modules. This structural feature provides synthetic economy and leads to phenomena such as self-sorting when different capsules are present in the same solution.[1] Two-component capsules of this sort are rare. They most often emerge when one of the components is the solvent,[2] but they have also been assembled through design by Kobayashi[3] and Reinhoudt.[4] We report here a two-component case that involves expansion of an *existing* capsule with a reversibly added spacer. This unprecedented behavior may be compared to adding leaves to expand a table. We show the encapsulation of larger, previously inaccessible guests in the extended cavity.

The cylindrical host capsule **1.1**[5] (Figure 1) forms readily by dimerization of **1** when, and only when, suitable guests are present in the noncompeting solvent mesitylene-d_{12}. Typical guests include benzanilide, dicyclohexyl carbodiimide, and dimethyl stilbene **2**. The longer alkylated aryls **3** and **4** are too large to be encapsulated. Even normal alkanes are accepted within **1.1**, and among them tetradecane ($C_{14}H_{30}$) is the longest one accommodated.[6] As shown in Figure 2a, *n*-$C_{15}H_{32}$ is not encapsulated, but addition of excess glycoluril **5a** produces the characteristic upfield signals of an encapsulated species (Figure 2b). Moreover, normal alkanes up to $C_{21}H_{44}$ are now accommodated (Figure 2c−e): *a new and longer capsule is present!*

What is the composition of the new assembly? Integration of the appropriate ^{1}H NMR signals of spectra 2b−e (and Supporting Information) indicates that *four* glycolurils are involved in the assembly with the original capsule and the single guest. The signal for the cavitand's imide N−H resonance shifts downfield from 10 ppm in typical complexes of **1.1** to 13 ppm in the new capsule, indicating contact of the N−H with a superior hydrogen bond acceptor. There are *two* signals for the glycoluril N−H's, one at ∼9.3 ppm and another at ∼7.5 ppm, and these undergo chemical exchange in the EXSY spectra. This indicates that the new capsule has reduced symmetry but the glycoluril units can change orientations within the assembly. Diffusion-ordered spectroscopy (DOSY) can distinguish the NMR signals of different species according to their diffusion coefficients, and Cohen has shown its unique applicability to encapsulation complexes.[7] For the cases at hand, DOSY showed that peaks of the expanded capsule and those of the guests represent the same assembly which has a larger diffusion coefficient than complexes of **1.1**. Glycoluril **5b** gives parallel results, and a mixture of **5a** and **5b** gives at least four capsular assemblies. The evidence is summarized in the structural proposal of Figure 3.

The hydrogens on C_2/C_{14} and C_4/C_{12} of *n*-pentadecane in the new capsule show two signals in NMR spectra (Figure 2b). A slightly different pattern holds for *n*-heptadecane: C_2/C_{16} and C_3/C_{15} are doubled, as are C_2/C_{18}, C_3/C_{17}, and C_4/C_{16} of *n*-nonadecane. Similar patterns are seen for C_{16}, C_{18}, and C_{20} (see Supporting Information). These carbons bear diastereotopic hydrogens as a consequence of gauche conformations along the backbone. Figure 4 proposes a structure for encapsulated *n*-heptadecane with gauche

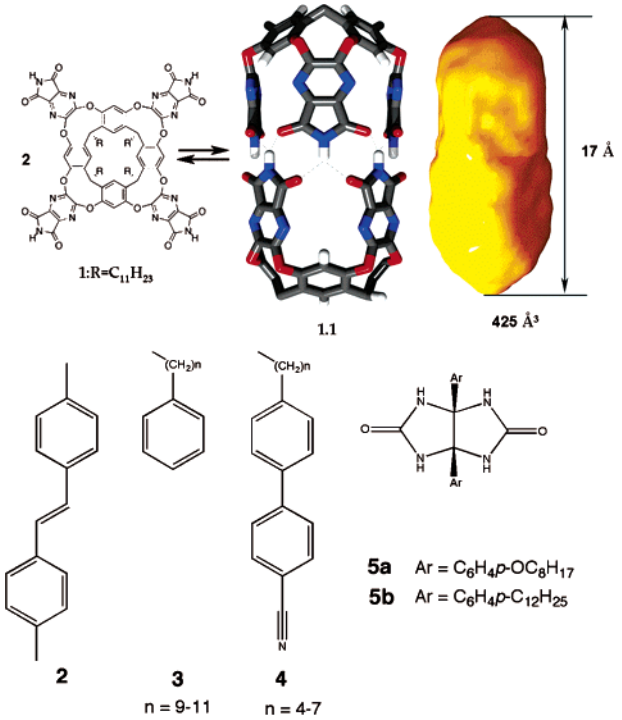

Figure 1. (Top) Tetraimide cavitand **1**, the dimeric, capsule **1.1**, and the shape of the space inside. Peripheral alkyl groups have been deleted. (Bottom) Some of the guests and glycoluril spacers used.

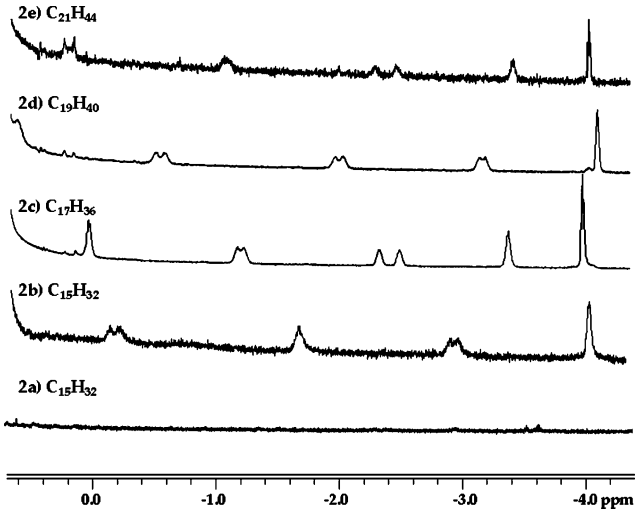

Figure 2. Upfield regions of the ^{1}H NMR spectra (600 MHz, mesitylene-d_{12}) of **1.1** (2 mM) with normal alkanes (15 mM): (a) pentadecane, (b) pentadecane + **5a** (6 mM), (c) $C_{17}H_{36}$, (d) $C_{19}H_{40}$, and (e) $C_{21}H_{44}$, all with **5a** (6 mM). For $C_{16}H_{34}$, $C_{18}H_{38}$, and $C_{20}H_{42}$, see Supporting Information.

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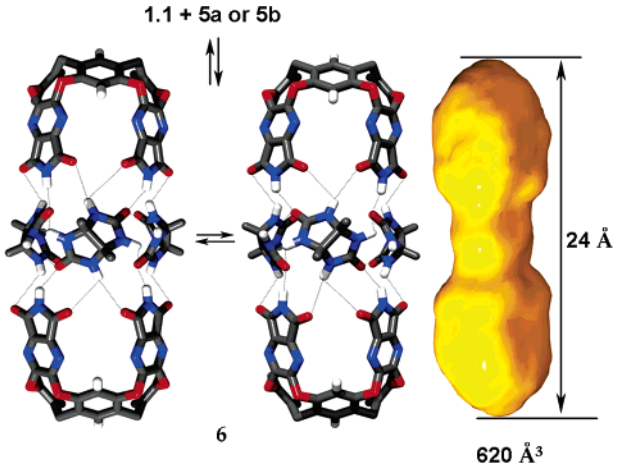

Figure 3. Proposed structure for the expanded capsule and a calculated model of the space inside. Peripheral alkyl groups and some capsule "walls" have been removed for viewing clarity.

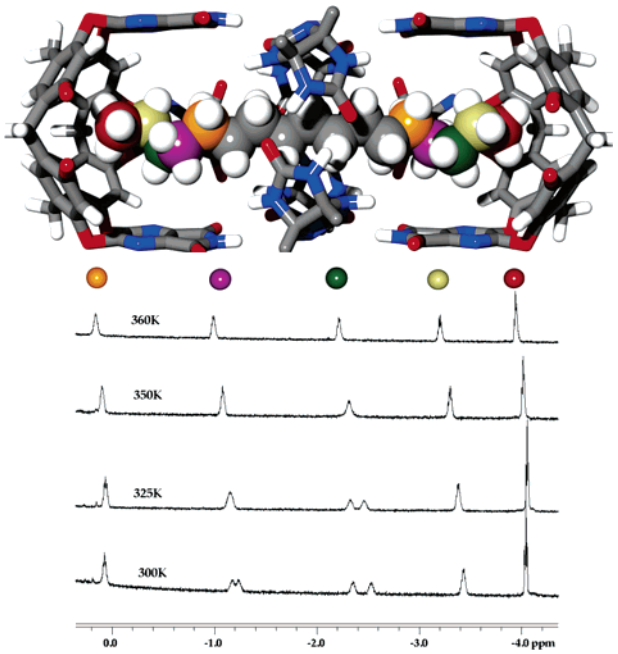

Figure 4. (Top) Model of encapsulated *n*-heptadecane in the expanded assembly (peripheral groups and the front "walls" omitted for clarity). (Bottom) Upfield regions of the ^{1}H NMR spectra (600 MHz, mesitylene-d_{12}) with **1** (2 mM), **5a** (6 mM), and heptadecane (15 mM) at various temperatures.

conformations about the C_2-C_3 and the C_3-C_4 bonds. The temperature-dependent NMR spectra are also shown, and the diastereotopic signals coalesce on heating.

A number of other guests that cannot be accommodated in **1.1** were taken up in the new assembly, including longer alkenes, acetylenes, and the alkylated arenes **3** and **4** (see Supporting Information). Two molecules of *p*-xylene are also encapsulated in a self-assembled complex of eight molecules, held together by weak intermolecular forces. Finally, the expansion of the capsule is—at least partly—reversible. Addition of **2** to a solution of C_{17} in the new capsule gave additional signals for the encapsulation of **2** in **1.1** (see Supporting Information). Apparently, an optimal guest fit can shift the equilibrium to capsule **1.1** and extrude the spacer elements. In the absence of a suitable guest, mixtures of **1** and **5a** or **5b** show neither capsule **1.1** nor capsule **6** in the NMR spectra.

In summary, a hydrogen-bonded, dimeric capsule can be reversibly expanded with four glycoluril spacers that increase the cavity's volume by ~200 Å^3 and its length by ~7 Å. Accordingly, a variety of longer alkanes and other guests are encapsulated in the new assembly. The expanded capsule also offers broadened possibilities for new isomerism[8] and suggests that increasingly complex capsules may emerge from other spacers with hydrogen-bonding capabilities and curved surfaces.

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Supporting Information Available: ^{1}H NMR spectra of encapsulated $C_{16}H_{34}$, $C_{18}H_{38}$,$C_{20}H_{42}$, and alkylated aryls **3** and **4** in **6**, as well as DOSY data. This material is available free of charge via the Internet at http://pubs.acs.org.

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