Templated Assembly of Water-Soluble Nano-Capsules: Inter-Phase Sequestration, Storage, and Separation of Hydrocarbon Gases

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Nature relies heavily on the hydrophobic effect[1,2] to affect host−guest complexations and the self-assembly of supramolecular structures; the aqueous medium is frequently stultifying to noncovalent forces such as hydrogen bonds. A good deal of information pertaining to how the hydrophobic effect influences simple complexation processes has been garnered from synthetic host−guest systems. In contrast, models for discrete, well-defined self-assemblies driven by the hydrophobic effect remain relatively uncharted. Here we demonstrate that, in aqueous solution, hydrocarbon gases[3−6] are capable of templating the dimerization of deep-cavity cavitands to form nano-scale capsules. In the process, two gas molecules are encapsulated within the assembly. Nevertheless, binding is strong enough that gases can be sequestered directly from the gas phase. In addition, the observed differences in affinity between the guests allow the nano-capsules to affect a unique means of gas separation.[7]

The synthesis of host **1** (Figure 1) has been reported.[8] The cavitand possesses a large enforced, pseudo-conical cavity ca. 1 nm in diameter and depth. Importantly, the cavity also possesses a hydrophobic rim comprised primarily of aromatic rings that can π-stack in the capsular form. These structural features allow the host to dimerize around and internalize large guests, such as steroids.[8] In addition, within their essentially dry nano-environment, it is possible to both inhibit[9] and promote photochemical processes.[10] Reaction outcome−or the lack thereof−is specifically controlled by the shape complementarity of the guest and the inner walls of the capsule.

The ^{1}H NMR spectrum of host **1** (1 mM) in buffered (10 mM sodium tetraborate) aqueous solution is shown in Figure 2a. The sharpness of the signals suggests little in the way of aggregation, and that the host is essentially monomeric was confirmed by pulse-gradient stimulated spin−echo (PGSE) NMR; the diffusion constant of the host, $D = 1.82 \times 10^{-6}$ cm^2 s^{-1}, corresponds to a hydrodynamic volume of 7.2 nm^3 (Supporting Information). The addition of excess butane gas by bubbling through the solution led to several changes to the NMR spectrum (Figure 2b), the most significant of which for the host were for those hydrogen atoms pointing directly into the cavity. Thus, those in the 2-position of the "upper" row of resorcinarene rings (the *endo* positions[11]) shifted from 6.97 to 6.49 ppm, while the benzal hydrogens shifted from 4.50 to 4.38 ppm. No free butane was observed (1.28 and 0.88 ppm for the methylene and methyl groups, respectively). Instead, a broad signal, assumed to correspond to bound butane, was evident at ca. −0.75 ppm. A subsequent experiment revealed that binding could be carried out directly from the gas phase. Thus, without agitation, injection of 10 equiv of butane into the headspace over a buffered host solution resulted in the formation of a complex (Figure 2c) in which the host to guest ratio was 1:1. The sharp guest signals for bound butane, at −0.84 ppm (CH$_2$) and −1.35 ppm (CH$_3$), testify that butane has no distinct orientation within the cavity ($\Delta\delta = -2.12$ and -2.23 ppm, respectively). In contrast to free host **1**, a PGSE NMR experiment revealed a diffusion
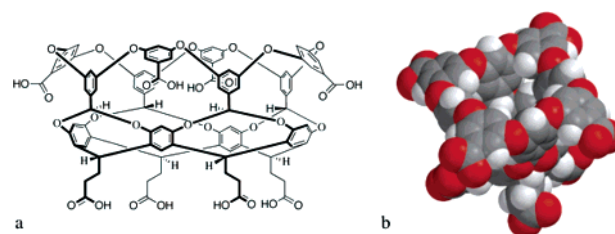

Figure 1. (a) Structure of deep-cavity cavitand **1**. (b) Space-filling model of cavitand **1** showing the enforced cavity and the wide, hydrophobic rim.
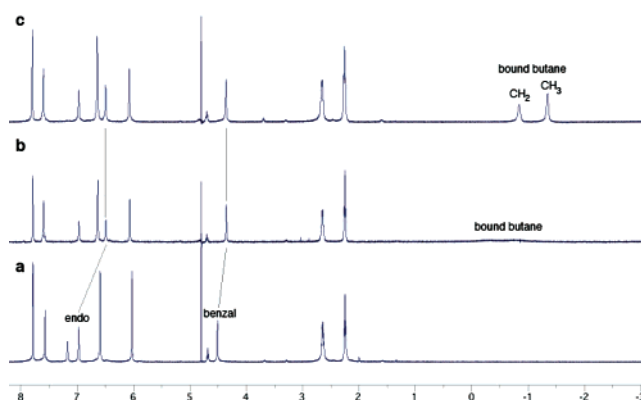

Figure 2. ^{1}H NMR spectra of (a) the free host **1** (1 mM, in 10 mM sodium tetraborate). (b) The same solution after butane gas was bubbled through the solution for 5 s. (c) The butane complex formed (after 18 h) by the addition of 200 μL (10 equiv) of the gas into the headspace above the solution of host **1**.

constant of $D = 1.42 \times 10^{-6}$ cm^2 s^{-1} for the butane complex, a value similar to the diffusion constant for the 2:1 capsular complex containing estradiol ($D = 1.36 \times 10^{-6}$ cm^2 s^{-1}). Thus, the direct absorption of butane gas from the headspace results in the formation of a 2:2 capsular complex with a hydrodynamic volume of 14.9 nm^3. Evidently, the difference between spectra b and c is a matter of excess guest. Diffusion studies using host signals reveal that both the samples are capsular, and that if the former was allowed to stand in an open flask, the bound butane signals sharpened over time to give a NMR spectrum identical to that in Figure 1c. However, NMR yields insufficient information to differentiate between the two likely candidates behind guest signal broadening: a kinetically less stable 2:3 complex or a change in guest exchange mechanism (from dissociative to associative as concentration increases).

^{1}H NMR was then used to investigate the kinetics of complexation from the gas phase. Injection of 20 equiv of butane into the headspace resulted−without agitation− in the encapsulation of the gas over a period of 12 h (Figure 3). Due to large errors in early sampling, initial rates could not be determined. Qualitatively, however, increases in the partial pressure of gas or concentration of **1** led to faster initial entrapment, while the absence of host led
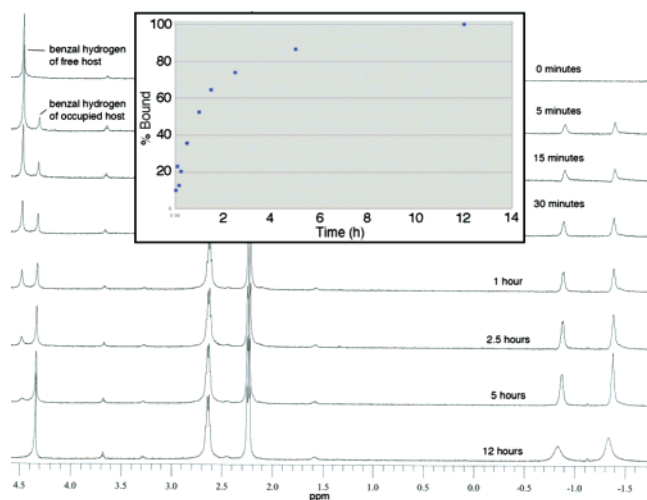
Figure 3. ^{1}H NMR spectra of the absorption of 20 equiv of butane gas by 0.8 mL of a 1 mM solution of cavitand **1** in 10 mM sodium tetraborate buffer. Inset: Absorption profile derived from the NMR data.

to an equilibrium concentration of butane of only 40 μM. It is interesting to compare this 40 μM value and the maximal solubility of butane in pure water (1.16 mM)[12] with the maximum storage capacity of aqueous solutions of **1**. In the case of the latter, it was possible to form 250 mM solutions of the 2:2 complex. Butane storage was "only" ca. 200 times greater than its maximal solubility in pure water because solutions of higher buffer concentration were too viscous to analyze by NMR.

Molecular encapsulation raises the question of the state of the entrapped matter.[13] Previous cases of the entrapment of single molecules of gas have described the contents as akin to the supercritical state.[4,5] Although arguments can be made about the appropriateness of comparing one guest molecule to its bulk state, the entrapment of two gas molecules blurs the distinction between these two cases. In the case at hand, the capsule has an internal volume of ca. 740 Å^3. Thus, the entrapment of two butane molecules corresponds to an occupancy factor ($\rho = V_{guest}/V_{cavity}$) of ca. 0.21. Thus, the content of this capsule is more akin to supercritical butane ($\rho = 0.19$) rather than liquid butane ($\rho = 0.47$). Alternatively, simplistically treating the contents as an ideal gas gives an alternative perspective. As each molecule occupies 37 nm^3 at standard temperature and pressure, the pressure inside the capsule equals 1×10^7 Pa or 100 atm.

We sought to quantify the quaternary complex and looked for evidence of a 1:1 complex. With regards to the latter, we examined the ^{1}H NMR spectrum of a 45 μM solution of the host in the presence of an excess of guest (Supporting Information). Under these conditions, new guest signals appeared at ca. 0.60 and 0.07 ppm, and an additional benzal H signal was evident at 4.45 ppm, the latter being indicative of free host and/or a noncapsular, 1:1 complex with a simple alkane. Both are likely present under these conditions, an assumption supported by the broadness of the guest signals which is indicative of a kinetically less stable complex in exchange with free guest. The ability to observe these species allowed us to determine a K_{app} value for the quaternary complex.[13] In the presence of 1 mM sodium tetraborate, a value of 1400 M^{-1} $\pm 20\%$ was recorded. Furthermore, as expected, the association constant increased significantly in the presence of NaCl. Thus, at 5 mM NaCl, a binding constant of $K_{app} = 30\,000$ M^{-1} $\pm 20\%$ was

noted, while in the presence of 14 mM NaCl, the K_{app} increased to a remarkable 100 000 M^{-1} $\pm 20\%$.

With these results in hand, the encapsulation of other hydrocarbon gases was examined. NMR demonstrated that, under similar conditions for the formation of the butane complex, propane also formed a quaternary complex. Slight broadening of the signals suggested a kinetically less stable species (Supporting Information). On the other hand, ethane was observed to only weakly bind in a 1:1 manner. It was not possible to accurately determine association constants for the propane complex because the gas is not sufficiently soluble in water. However, it was possible to perform a competition experiment (Supporting Information) between butane and propane and determine a relative binding constant for propane ($K_{rel} = 1/12$ $\pm 20\%$). This order of magnitude difference led us to investigate the possibility that butane could be selectively sequestered from the gas phase to affect a separation of the two hydrocarbons. In this experiment, to avoid agitation yet maintain a relatively rapid uptake of gas, a large excess of a 1:1 mixture of the two gases was introduced into the headspace above a solution of **1**. After 24 h, ^{1}H NMR analysis revealed that only butane had been absorbed into the aqueous solution, leaving a propane-enriched gas phase.

We have shown that the hydrophobic effect can lead to a remarkable templation and assembly processes involving host **1**, and that this process can separate butane and propane. The ability of this supramolecular system to separate the other hydrocarbon gases and how this is related to the presence of salting in and salting out species is now under investigation.

Supporting Information Available: NMR details of 1:1 complex formation, PGSE experiments, binding constant determinations, propane and ethane complexes, and competition experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

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