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New Water-Soluble Organic Capsules Are Effective in Controlling Excited-State Processes of Guest Molecules

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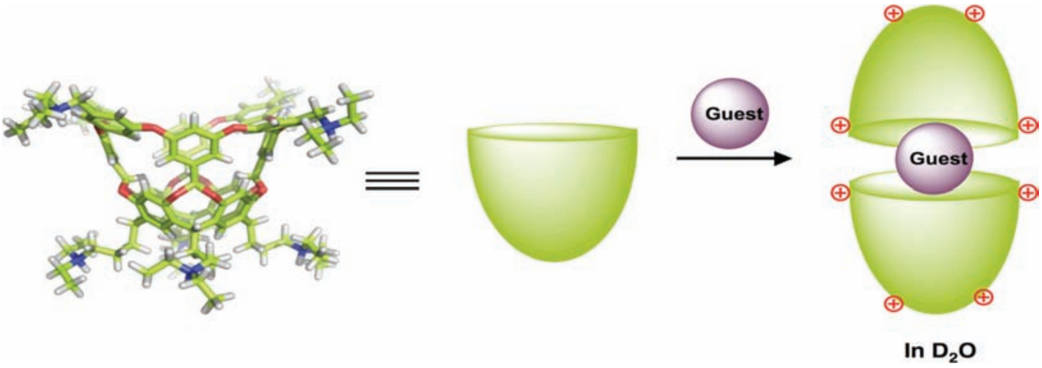
ABSTRACT



Synthesis, inclusion properties, and ability to control excited-state properties of two water-soluble hosts are presented. These hosts surround the guest molecule(s) by forming a capsular assembly. By constraining the guest and by providing very little free space, the host is able to alter the excited-state behavior of guest molecules. The excited-state chemistry and physics of guest molecules are distinctly different from those in organic solvents.

Following the pioneering contributions of Cram, Lehn, and Pederson, there has been continued interest in identifying host systems that would accommodate organic guest molecules yet constrain mobility to affect the course of thermal and photochemical reactions in solution.[1] During the last five decades, a variety of host systems such as calixarenes, resorcinarenes, cryptands, cavitands, and carcerands have been synthesized and examined in the context of host–guest complexation and used as reaction vessels.[2] However, most of them are soluble only in organic solvents. With the current emphasis on "sustainability", the search for a water-soluble host that could accommodate water-insoluble guest molecules within its confined cavity has gained momentum. Commercially available cyclodextrins have been extensively investigated in water in the context of enzyme mimics.[3] Cucurbutrils, functionalized calixarenes, and several hosts with metal frameworks have also been explored as reaction vessels in water with some success.[4] The guest included in all these hosts is exposed to water to some degree and is not fully encapsulated.

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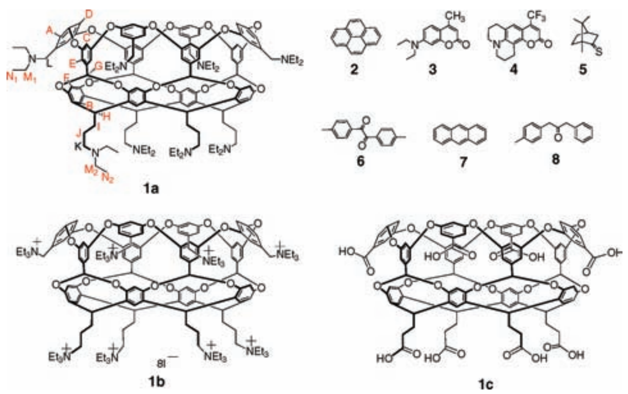

Figure 1. Structures of host and guests used for the study.

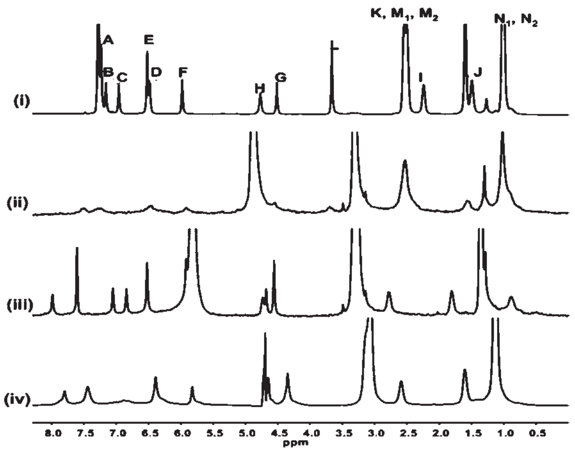

Figure 2. ^{1}H NMR spectra (500 MHz) of a 1 mM solution of **1a** in (i) $CDCl_3$, (ii) CD_3OD, and (iii) CD_3OD/DCl, and (iv) D_2O/DCl (pH ≈ 1).

Inspired by the report by Yoon and Cram[5] on a water-soluble hemicarcerand known as octa acid (Cram's octa acid), a few such water-soluble hosts have been reported recently.[6] Of these, a deep cavity cavitand also known as octa acid reported by Gibb (OA, **1c** in Figure 1) has been found to be exceptionally useful as a photochemical reaction cavity in water.[7] However, this host is soluble in water under basic conditions only. Recognizing its potential, we were interested in synthesizing new hosts with similar internal features but soluble in water either under acidic or neutral conditions. We report here the synthesis of two novel cavitands (amine and ammonium functionalized), their complexation properties, and their ability to influence photochemical and photophysical properties of included guest molecules. The host with amine functionality (**1a**, Figure 1) is soluble under acidic conditions in water and complements Gibb's OA soluble in basic aqueous solution. The host with tetraalkyl ammonium functionality (**1b**, Figure 1) is soluble in water under neutral conditions.

Structures of the two new hosts (**1a** and **1b**) and several guests, previously investigated in OA, used in this study are provided in Figure 1. Octa amine **1a** (OAM) was prepared by modification of the last two steps of the reported synthesis of OA (for the procedure, see the Supporting Information (SI)) and characterized by ^{1}H and ^{13}C NMR and ESI mass spectral data (SI). It is soluble in $CDCl_3$ and CD_3OD (see Figure 2 for ^{1}H NMR spectra) but not in water. Signal assignments in $CDCl_3$ (Figure 2) were made on the basis of the COSY spectrum provided as SI (Figure S4). To solubilize OAM in water, the amine groups had to be protonated first, which was accomplished by dissolving OAM in methanol + DCl solution (Figure 2). The white protonated OAM (P-OAM) powder obtained upon evaporation of CD_3OD was soluble in water and existed as aggregates at concentrations above 0.5 mM in water (see Figure S6 in the SI for ^{1}H NMR spectra in the concentration range 0.05−1 mM). Some of the signals in the ^{1}H NMR spectrum of P-OAM in D_2O were overlapping and broad and not as sharp as in $CDCl_3$. Inclusion of guests **2**−**8** (Figure 1) within P-OAM was accomplished by stirring together the above guests and P-OAM in water. Complexation was confirmed by comparing the ^{1}H NMR spectra of guest@P-OAM with that of guest@OA (see Figures S7 and S8 in the SI for ^{1}H NMR spectra). Evidence in favor of complexation comes from the large upfield shift of the ^{1}H NMR signals of the guest, especially that of nonaromatic protons in the case of guest@P-OAM complexes for **3**, **5**, **6**, and **8** (Figure 3). As seen in Figure 3, not surprisingly, the observed shifts are similar to those of guest@OA complexes. The stoichiometry of the complexes (1:2 or 2:2; guest to host ratio) was deduced from titration experiments (Figures S9−S15 in the SI). The stoichiometry of the complex was determined on the basis of the appearance of the ^{1}H NMR signals due to free guests during the titration experiments. Guests **2**, **3**, **4**, **6**, and **8** formed 1:2 complexes, while **5** and **7** formed 2:2 complexes. Under

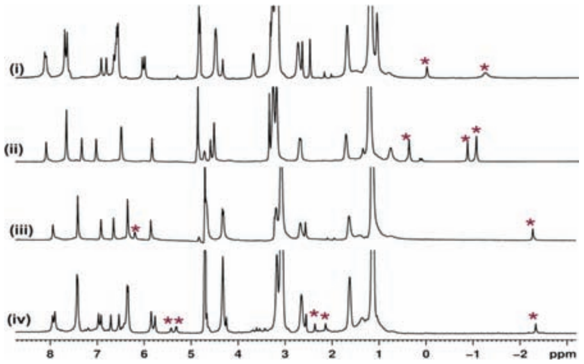

Figure 3. ^{1}H NMR spectra (500 MHz) (i) $\mathbf{3@1a_2}$ ([**1a**] = 1 mM; [**3**] = 0.5 mM), (ii) $\mathbf{5_2@1a_2}$ ([**1a**] = 1 mM; [**5**] = 1 mM, (iii) $\mathbf{6@1a_2}$([**1a**] = 1 mM; [**6**] = 0.5 mM), and (iv) $\mathbf{8@1a_2}$([**1a**] = 1 mM; [**8**] = 0.5 mM) in D_2O/DCl (pH ≈ 1). Upfield resonances of bound guest protons are marked with an asterisk.

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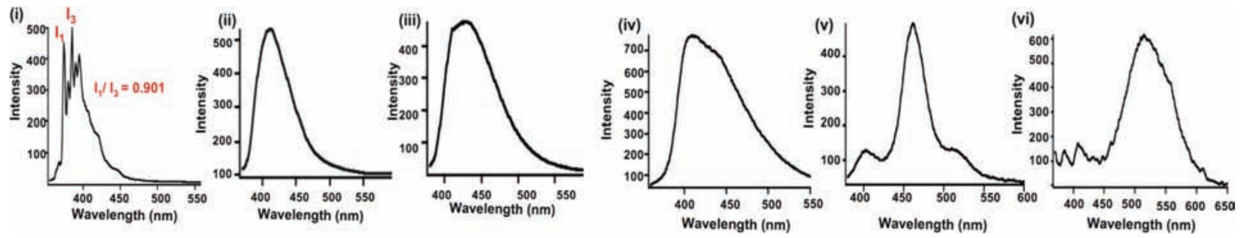

Figure 4. Fluorescence emission spectra of (i) **2**@**1a**$_2$ ((λ_{ex} = 320 nm, [**1a**] = 1 mM; [**2**] = 0.5 mM), (ii) **3**@**1a**$_2$(λ_{ex} = 350 nm, [**1a**] = 1 mM; [**3**] = 0.5 mM), (iii) **4**@**1a**$_2$((λ_{ex} = 400 nm, [**1a**] = 1 mM; [**4**] = 0.5 mM) in D_2O/DCl (pH ≈ 1), (iv) **5**$_2$@**1a**$_2$ ((λ_{ex} = 254 nm, [**1a**] = 0.5 mM; [**5**] = 0.5 mM), (v) **6**@**1a**$_2$((λ_{ex} = 310 nm, [**1a**] = 1 mM; [**6**] = 0.5 mM), and (vi) **7**$_2$@**1a**$_2$ (λ_{ex} = 350 nm, [**1a**] = 1 mM; [**7**] = 1 mM) in D_2O/DCl (pH ≈ 1).

conditions of excess host, no signals due to free guest molecules were noticed. Also upon slow addition of the guest to the host solution the chemical shift due to guest protons was constant, suggesting that in the NMR time scale all guest molecules, as long as there are enough host molecules, remain within the capsule without any apparent exchange between free and complexed guest molecules. Since the excited-state time scales are shorter than NMR time scale, we believe that the photochemical results reported below correspond to complexed guest molecules. Although complexation of guests with P-OAM was achieved in water, inclusion of these guests within OAM or P-OAM could not be achieved with $CDCl_3$ and CD_3OD as solvents. This suggested that the hydrophobic effect is most likely responsible for the host–guest capsule formation in water.

Having proved that P-OAM can encapsulate organic molecules in water, we were interested in probing the capsular interior and establishing its utility in manipulating the excited state behavior of guest molecules. Fluorescence spectra of **2**@P-OAM$_2$, **3**@P-OAM$_2$, and **4**@P-OAM$_2$ (Figure 4, i–iii) provided information on the interior polarity of the capsule. Pyrene with excimer emission in the absence of P-OAM showed only monomer emission in the presence of P-OAM with an I_1/I_3 ratio of 0.90 (intensity of vibrational band 1 vs 3 in the fluorescence emission; compare this with 1.01 for OA). Absence of excimer emission is consistent with ^{1}H NMR titration results that suggested pyrene forms a 1:2 complex in water. The observed I_1/I_3 ratio corresponded to the internal polarity being close to that of benzene (dipole moment: 2.28 and $E_{T(30)}$: 34.5). This conclusion is also supported by the fluorescence of **3** and **4**, which are established to show polarity-dependent fluorescence maxima.[8] The maxima of 412 nm for **3** and 480 nm for **4** correspond to an internal polarity slightly lower than ethyl acetate (dipole moment: 6.05 and $E_{T(30)}$: 38.1). These three probes suggest that no water molecules are included along with the guest within the P-OAM capsule.[9]

Anthracene (**7**), dimerizing readily and showing no excimer emission in solution, exhibited strong excimer emission when included within P-OAM. The emission spectrum of **7**$_2$@P-OAM$_2$ shown in Figure 4, vi, with strong excimer and weak monomer emissions is quite different from that in water in the absence of P-OAM. Anthracene excimer within the P-OAM capsule has a lifetime of 232 ± 12 ns (for excited state decay traces at three monitoring wavelengths, see Figure S19 in the SI) close to that in the crystals of anthracene (225 ns). In all cases, a minor secondary component with much shorter lifetime was noted, but this is unlikely to be due to 1:1 complex as the monitoring wavelength corresponds to excimer emission. Previously, such an emission in solution was recorded only in presence of OA.[10]

The next two examples deal with controlling phosphorescence properties of included guest molecules. Very few molecules show phosphorescence at room temperature in solution and that too only when oxygen is rigorously removed from solution. We attempted to record phosphorescence of camphorthione (**5**) and 4,4′-dimethylbenzil (**6**) included in P-OAM in water under aerated conditions. According to ^{1}H NMR titration studies, camphorthione forms a 2:2 complex and 4,4′-dimethylbenzil 1:2 complex with P-OAM. These two molecules upon excitation at room temperature showed intense phosphorescence when included within P-OAM (Figure 4, iv and v). Within the capsule, triplets of these two molecules had a long lifetime (53 ± 2 ms for **5** and 542 ± 27 ms for **6**, see Figures S20 and S21 in the SI). In the absence of P-OAM, self-quenching (**5**) and oxygen quenching (**5** and **6**) eliminated the phosphorescence in solution at room temperature. Thus, a P-OAM capsule similar to an OA capsule is capable of protecting the guest not only from ambient water but also from oxygen.[11]

We examined the photochemical behavior of the dibenzyl ketone **8** to test the effectiveness of the P-OAM capsule in controlling the excited state chemistry of included guests. In general, molecule **8** upon excitation in solution

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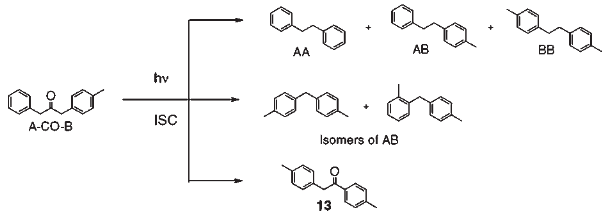
undergoes decarbonylation to the three diarylethanes AA, AB, and BB in a ratio of 1:2:1 (Scheme 1) to the exclusion of any rearrangement product.[12] However, irradiation of **8**@P-OAM$_2$ resulted equally in rearrangement and decarbonylation with product **9** and only AB and its rearranged products, respectively; no AA or BB products were obtained. These products clearly suggest that the reactive intermediate, the benzyl–phenyl acetyl radical pair, is trapped within the capsule during the entire duration of its transformation to final products. While such large amounts of AB formation have been noted previously in micelles,[13] 50% rearrangement product **10** has only been observed in the OA capsule. Thus, the P-OAM capsule holds guests and the derived reactive intermediates within it, allowing extraordinary reactions.[14]

Scheme 1. Reaction Manifold for the Photochemistry of **8**



Having identified a deep cavity cavitand (OAM) that would form capsular assemblies in water under acidic conditions, we were interested in synthesizing a deep cavity cavitand that would form host–guest complexes under neutral conditions in water. This led to the synthesis of octatriethylammonium iodide (**1b**, OTEAM). OAM upon treatment with ethyl iodide in DMF gave the host OTEAM. ^{1}H NMR spectra of this host in DMSO-d_6 and D$_2$O are provided in Figure 5. While the spectrum in DMSO-d_6 shows sharp signals corresponding to all hydrogens, that in D$_2$O is broad and not informative. Even at 0.05 mM, OTEAM remains aggregated in water (Figure S6 in the SI). However, addition of camphorthione (**5**) and 4,4′-dimethylbenzil (**6**) to OTEAM resulted in capsules in D$_2$O (see Figure S22 and S23 in the SI for ^{1}H NMR spectra). Consistent with the capsule formation, the diffusion constants measured by DOSY in these cases were slightly higher, 1.1×10^{-10} m^2 s^{-1}, than for the 1:1 complex of 1-admantane acetic acid with OTEAM (1.4×10^{-10} m^2 s^{-1}, see Figure S24 for DOSY spectra). Both **5** and **6** upon inclusion within the OTEAM capsule phosphoresced at room temperature (see Figure S25 in the SI). Preliminary studies indicated that this host did not include aromatic molecules such as anthracene, naphthalene, or pyrene. We are currently exploring the ability of this host to include other organic molecules and its value as a photochemical reaction cavity in water.

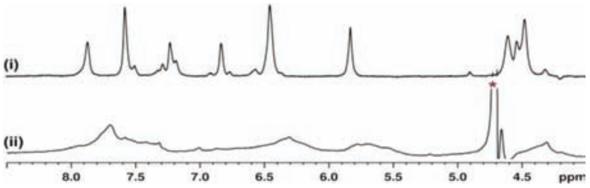


Figure 5. ^{1}H NMR spectra (500 MHz) of a 0.5 mM solution of **1b** in (i) DMSO-d_6 and (ii) D$_2$O. Residual water peak is marked with an asterisk.

We have disclosed here the synthesis and complexation abilities of two hosts resembling Gibb's octa acid and complementing it in their properties. Contrary to OA soluble in mildly basic aqueous conditions, one (OAM) is soluble under acidic aqueous conditions and the other (OTEAM) under neutral conditions in water. These two hosts could be used to modify the excited state chemistry of organic guests in water despite the complications due to aggregation. We are currently exploring the possibility of constructing a hetero capsule of OA and OAM in neutral aqueous solution and expanding the utility of OA, OAM, and OTEAM in materials and surface chemistry.

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Supporting Information Available. Synthetic procedures and spectral data for **1a** and **1b**, ^{1}H NMR titration spectra, emission decay traces, and emission spectra of guest@host complexes. This material is available free of charge via the Internet at http://pubs.acs.org.

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