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Cavitand Octa Acid Forms a Nonpolar Capsuleplex Dependent on the Molecular Size and Hydrophobicity of the Guest

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We have been exploring the use of a deep cavity cavitand known by the trivial name 'octa acid' as a photochemical reaction cavity for manipulating photochemical and photophysical properties of organic molecules. In the current study, we have monitored the micropolarity of the interior of the cavitand by recording the fluorescence of five different organic probes. They all indicate that the interior of octa acid capsuleplex (2:1, H/G complex) is nonpolar and does not contain water molecules in spite of the complex being present in water. The nature of the octa acid−probe complex in each case has been characterized by ^{1}H NMR data to be a 2:1 capsuleplex. Photophysical and ^{1}H NMR experiments were employed to probe the factors that control the structure of the complex, 2:2, 2:1, and 1:1. The data we have on hand suggest that the structure of the host/guest complex depends on the size and hydrophobicity of the guest molecule.

Introduction

The use of organized assemblies in controlling the excited and ground-state processes of organic molecules has received continued interest during the last three decades.[1−11] This interest has resulted in understanding and exploiting a variety of organized assemblies such as micelles, dendrimers, liquid crystals, polymers, gels, crystals, and both organic and inorganic hosts [cyclodextrins (CD), cucurbiturils (CB), calixarenes (CA), cavitands, cholic acids, clay, zeolites, mesoporous materials, etc.]. During the past decade, we have been examining the use of some of these assemblies, the water-soluble hosts such as CB, natural and functionalized CD, CA, Fujita's Pd host, micelles, dendrimers, and solid hosts such as zeolites and crystals, in particular, as reaction media with the main goal of identifying the common features, and comparing the properties of their reaction cavities.[12−30] Recently we have added a synthetic cavitand octa acid (OA) with dimensions shown in Scheme 1 to our arsenal of supramolecular hosts.[31,32] The eight carboxylic acids on both the top and bottom rims of this host make it water soluble under basic (pH ≈ 9.0) conditions. We believe this host to have significant potential as a reaction medium based on our limited studies.[33−39] To plan and rationalize selectivity within the OA cavity the needed understanding of the internal characteristics of the cavity has prompted us to explore features such as micropolarity and host/guest complexation behavior of OA.

In Scheme 2, schematic representations of various commonly used hosts, e.g., micelle, cavitand, capsule, and carcerand, and their corresponding host/guest complexes are presented. We emphasis the fact that, of the various hosts presented, both micelle and capsule are made up of more than one molecule and thus could be dynamic in character, i.e., the structure could be time dependent. It is important to recognize that carcerand (originally synthesized by Cram), in which the two cavitands that make up the capsule are covalently linked, has a time-independent

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(1) Whitten, D. G.; Russell, J. C.; Schmehl, R. H. *Tetrahedron* **1982**, *38*, 2455–2487.
(2) Ramamurthy, V. *Tetrahedron* **1986**, *42*, 5753–5839.
(3) Weiss, R. G. *Tetrahedron* **1988**, *44*, 3413–3475.
(4) Whitten, D. G. *Acc. Chem. Res.* **1993**, *26*, 502–509.
(5) Turro, N. J.; Graetzel, M.; Braun, A. M. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 675–696.
(6) Tung, C.-H.; Wu, L.-Z.; Zhang, L.-P.; Chen, B. *Acc. Chem. Res.* **2003**, *36*, 39–47.
(7) Turro, N. J. *Acc. Chem. Res.* **2000**, *33*, 637–646.
(8) Turro, N. J. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4805–4809.
(9) Scaiano, J. C.; Garcia, H. *Acc. Chem. Res.* **1999**, *32*, 783–793.
(10) Bohne, C. *Langmuir* **2006**, *22*, 9100–9111.
(11) Ramamurthy, V., Ed. *Photochemistry in Organized and Constrained Media*; VCH: New York, 1991.
(12) Kaanumalle, L. S.; Nithyanandhan, J.; Pattabiraman, M.; Jayaraman, N.; Ramamurthy, V. *J. Am. Chem. Soc.* **2004**, *126*, 8999–9006.
(13) Karthikeyan, S.; Ramamurthy, V. *J. Org. Chem.* **2006**, *71*, 6409–6413.
(14) Karthikeyan, S.; Ramamurthy, V. *J. Org. Chem.* **2007**, *72*, 452–458.
(15) Pattabiraman, M.; Kaanumalle, L. S.; Natarajan, A.; Ramamurthy, V. *Langmuir* **2006**, *22*, 7605–7609.
(16) Pattabiraman, M.; Kaanumalle, L. S.; Ramamurthy, V. *Langmuir* **2006**, *22*, 2185–2192.
(17) Pattabiraman, M.; Natarajan, A.; Kaanumalle, L. S.; Ramamurthy, V. *Org. Lett.* **2005**, *7*, 529–532.
(18) Kaliappan, R.; Kaanumalle, L. S.; Natarajan, A.; Ramamurthy, V. *Photochem. Photobiol. Sci.* **2006**, *5*, 925–930.
(19) Kaliappan, R.; Kaanumalle, L. S.; Ramamurthy, V. *Chem. Commun.* **2005**, 4056–4058.
(20) Kaliappan, R.; Maddipatla, M. V. S. N.; Kaanumalle, L. S.; Ramamurthy, V. *Photochem. Photobiol. Sci.* **2007**, *6*, 737–740.
(21) Arumugam, S.; Kaanumalle, L. S.; Ramamurthy, V. *J. Photochem. Photobiol., A* **2007**, *185*, 364–370.
(22) Arumugam, S.; Vutukuri, D. R.; Thayumanavan, S.; Ramamurthy, V. *J. Am. Chem. Soc.* **2005**, *127*, 13200–13206.
(23) Arumugam, S.; Vutukuri, D. R.; Thayumanavan, S.; Ramamurthy, V. *J. Photochem. Photobiol., A* **2007**, *185*, 168–171.
(24) Natarajan, A.; Mague, J. T.; Ramamurthy, V. *Cryst. Growth Des.* **2005**, *5*, 2348–2355.
(25) Natarajan, A.; Mague, J. T.; Ramamurthy, V. *J. Am. Chem. Soc.* **2005**, *127*, 3568–3576.
(26) Natarajan, A.; Mague, J. T.; Venkatesan, K.; Arai, T.; Ramamurthy, V. *J. Org. Chem.* **2006**, *71*, 1055–1059.
(27) Sivaguru, J.; Natarajan, A.; Kaanumalle, L. S.; Shailaja, J.; Uppili, S.; Joy, A.; Ramamurthy, V. *Acc. Chem. Res.* **2003**, *36*, 509–521.
(28) Sundaresan, A. K.; Ramamurthy, V. *Photochem. Photobiol. Sci.* **2008**, *7*, 155–1564.
(29) Gibb, C. L. D.; Sundaresan, A. K.; Ramamurthy, V.; Gibb, B. C. *J. Am. Chem. Soc.* **2008**, *130*, 4069–4080.
(30) Chen, J. Y. C.; Jayaraj, N.; Jockusch, S.; Ottavianai, M. F.; Ramamurthy, V.; Turro, N. J. *J. Am. Chem. Soc.* **2008**, *130*, 7206–7207.
(31) Gibb, C. L. D.; Gibb, B. C. *J. Am. Chem. Soc.* **2004**, *126*, 11408–11409.
(32) Liu, S.; Gibb, B. C. *Chem. Commun.* **2008**, 3709–3716.
(33) Kaanumalle, L. S.; Gibb, C. L. D.; Gibb, B. C.; Ramamurthy, V. *J. Am. Chem. Soc.* **2004**, *126*, 14366–14367.
(34) Kaanumalle, L. S.; Gibb, C. L. D.; Gibb, B. C.; Ramamurthy, V. *J. Am. Chem. Soc.* **2005**, *127*, 3674–3675.
(35) Kaanumalle, L. S.; Gibb, C. L. D.; Gibb, B. C.; Ramamurthy, V. *Org. Biomol. Chem.* **2007**, *5*, 236–238.
(36) Kaanumalle, L. S.; Ramamurthy, V. *Chem. Commun.* **2007**, 1062–1064.
(37) Natarajan, A.; Kaanumalle, L. S.; Jockusch, S.; Gibb, C. L. D.; Gibb, B. C.; Turro, N. J.; Ramamurthy, V. *J. Am. Chem. Soc.* **2007**, *129*, 4132–4133.
(38) Parthasarathy, A.; Kaanumalle, L. S.; Ramamurthy, V. *Org. Lett.* **2007**, *9*, 5059–5062.
(39) Sundaresan, A. K.; Ramamurthy, V. *Org. Lett.* **2007**, *9*, 3575–3578.

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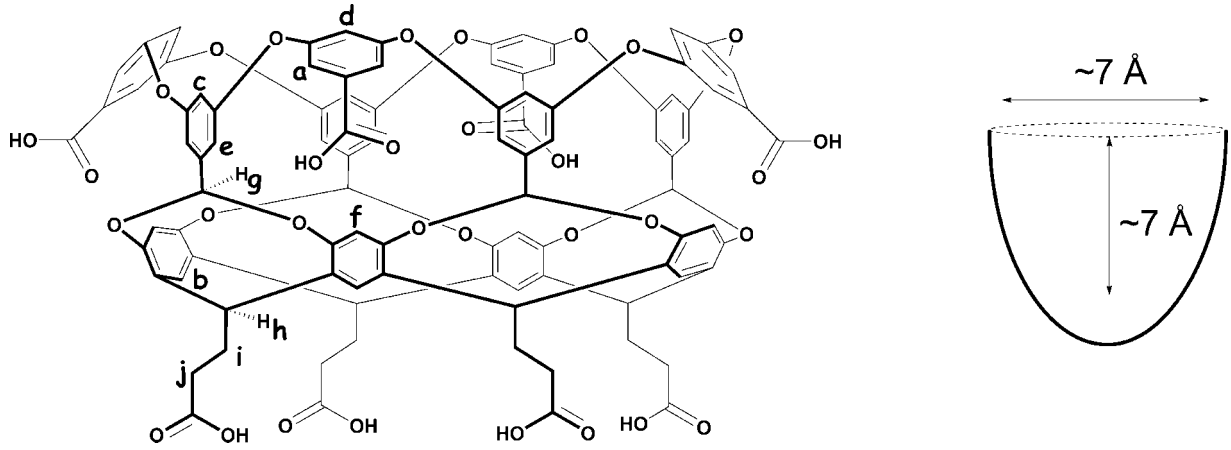
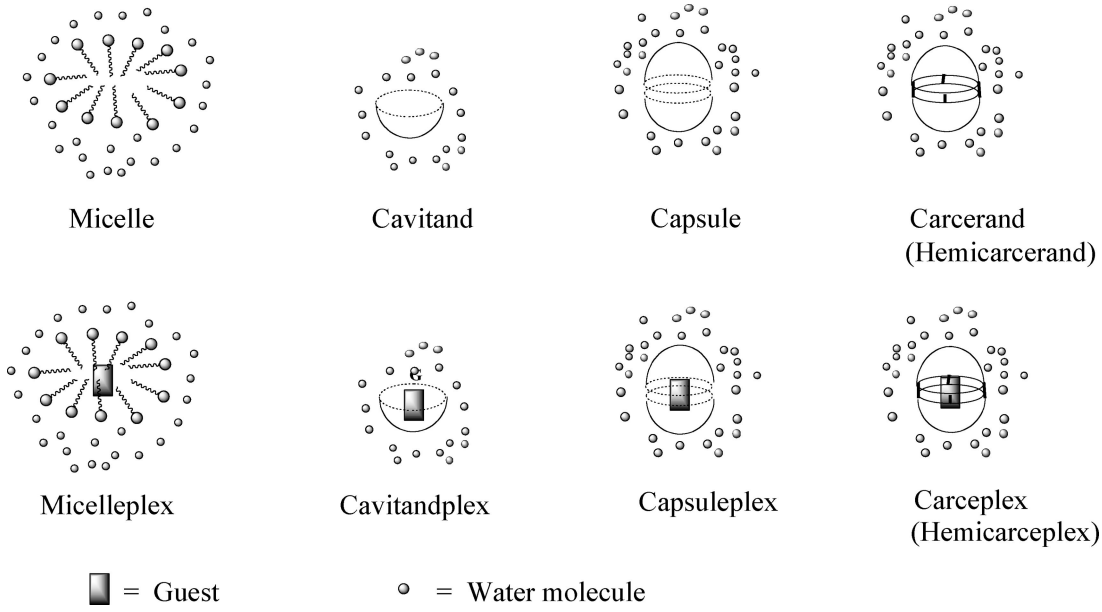
Scheme 1. Chemical structure and schematic representation of the host octa acid (OA); hydrogens in OA labeled a−j will be useful in examining the ^{1}H NMR spectra presented in the figures



Scheme 2. Definition of various possible host and host/guest complexes and their schematic representations



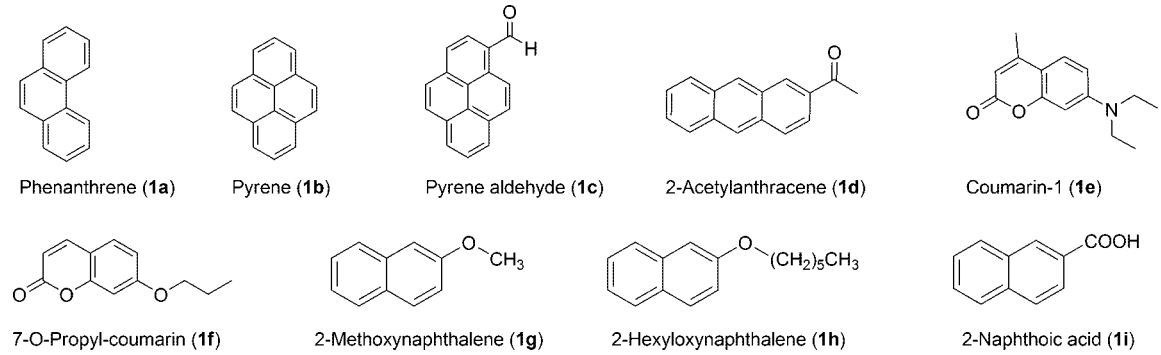
structure.[40−42] The structure that is relevant to this presentation is the capsuleplex that has a close similarity to carceplex. An important difference between the two is that in the former the guest is held within the capsule through weak interactions, while in the latter it is incarcerated through covalent linkages. In this report we deal with the cavitand octa acid that is capable of forming a 1:1 caviplex, or 2:1 and 2:2 capsuleplexes.

In order to be able to predict the effect of the host cavity on photochemical transformations of a guest it is important to know whether water molecules are present within the OA cavity, especially since the host/guest complexes are prepared in water. This knowledge would also help us understand the features [weak interactions between the host and the guest (ΔH) and/or release of the cavity bound water (ΔS)] that drive the complexation process. In this study, five organic molecules, pyrene,[43−45] pyrenealdehyde,[46−50] 2-acetylanthracene,[51,52] coumarin-1,[53,54] and 7-*O*-propylcoumarin[55−58] (Scheme 3, **1b**−**f**)) have been used as probes to monitor the polarity of the interior of the guest-occupied OA capsule. The absorption and emission maxima, intensity of emission and its vibrational pattern, and the excited singlet lifetime of these probes depend on the polarity of the medium in which they are present. Details of the mechanism by which the medium influences the above spectral properties are available in the literature and are not part of this presentation.

^{1}H NMR studies have been carried out to establish the nature of the OA−probe complexation process, as it is important to know the exact location of these probes during their emissive

(40) Warmuth, R.; Yoon, J. *Acc. Chem. Res.* **2001**, *34*, 95–105.
(41) Cram, D. J.; Tanner, M. E.; Thomas, R. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1024–1027.
(42) Cram, D. J.; Cram, J. M. *Container Molecules and Their Guests*; Royal Society of Chemistry: Cambridge, 1993.
(43) Nakajima, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 3272–3277.
(44) Kalyanasundaram, K.; Thomas, J. K. *J. Am. Chem. Soc.* **1977**, *99*, 2039–2044.
(45) Dong, D. C.; Winnik, M. A. *Photochem. Photobiol.* **1982**, *35*, 17–21.
(46) Kalyanasundaram, K.; Thomas, J. K. *J. Phys. Chem.* **1977**, *81*, 2176–2180.
(47) Kumar, C. V.; Chattopadhyay, S. K.; Das, P. K. *Photochem. Photobiol.* **1983**, *38*, 141–152.
(48) Lianos, P.; Cremel, G. *Photochem. Photobiol.* **1980**, *31*, 429–434.
(49) Kroning, P. *Z. Naturforsch.* **1973**, *28a*, 109–116.
(50) Kroning, P. *Z. Naturforsch.* **1974**, *29a*, 804–809.
(51) Tamaki, T. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 1761–1767.
(52) Tamaki, T. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 1756–1760.
(53) Nag, A.; Chakrabarty, T.; Bhattacharya, K. *J. Phys. Chem.* **1990**, *94*, 4203–4206.
(54) Van Gompel, J. A.; Schuster, G. B. *J. Phys. Chem.* **1989**, *93*, 1292–1295.

Scheme 3. Structures of organic molecules used as probes



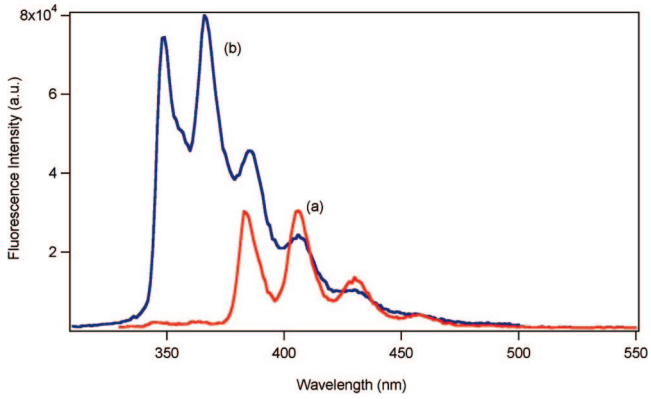


Figure 1. Fluorescence emission spectra of (a) 1×10^{-5} M phenanthrene in borate buffer (pH $\approx$ 9.0) and (b) phenanthrene@$(OA)_2$ in borate buffer (pH $\approx$ 9.0), Excitation wavelength: 300 nm.

process. Since we were also interested in understanding the factors controlling the formation of possible OA/guest complexes (2:2, 2:1, and 1:1), naphthyl derivatives **1g**−**i** (Scheme 3) were employed. We present results of ^{1}H NMR spectroscopy and fluorescence studies related to the micropolarity of OA capsule and host/guest complexation in this report.

Results and Discussion

Micropolarity of Octa Acid Capsule. *Host/Guest Inclusion Revealed by Emission Properties.* We used guest phenanthrene (**1a**) to probe how readily changes in emission properties of an aromatic molecule could be used to monitor the inclusion of a guest within the host OA capsule. Aromatic molecules known to aggregate in water show disparate emission behavior (different regions) of monomers and aggregates.[59−63] The emission of aggregates reverts to that of the monomer on dispersion. We used this feature to probe if aromatic molecules of the size of probes **1b**−**i** could be included within the OA cavity. As illustrated in Figure 1 emission spectra of phenanthrene in water in the presence and absence of OA are remarkably different. Upon excitation at 300 nm of a suspension of phenanthrene in borate buffer (10^{-5} M), a weak emission between 370−470 nm due to aggregates of phenanthrene was observed. Addition of 2 equiv of OA (2×10^{-5} M) to this suspension led to two interesting observations: Clearance of the turbid solution and the intense, structured, and blue-shifted fluorescence. The lifetime of the emissive state (53 ns) measured by a single photon counting technique was consistent with that of phenanthrene monomer S_1. Phenanthrene being a highly hydrophobic molecule was not soluble enough (1×10^{-3} M) to record ^{1}H NMR spectra in 10 mM borate buffer in D_2O. However, upon addition of 2 equiv of OA (2×10^{-3} M in 20 mM borate buffer in D_2O) to the solution, upfield-shifted phenanthrene proton signals were observed (Figure 2ii), a sign characteristic of guest−host complexation. ^{1}H NMR results confirmed that phenanthrene formed a 2:1 capsule with OA. NOESY spectrum confirmed interaction between host and guest protons (Supporting Information, Figures S1 and S2).

Table 1. Diffusion constants for the capsular assemblies of polarity probes with OA

complex	diffusion constant (cm^2/s)	complex	diffusion constant (cm^2/s)
1a@OA$_2$	1.45×10^{-6}	**1e@OA$_2$**	1.52×10^{-6}
1b@OA$_2$	1.46×10^{-6}	**1g$_2$@OA$_2$**	1.38×10^{-6}
1c@OA$_2$	1.33×10^{-6}	**1 h@OA$_2$**	1.26×10^{-6}
1d@OA$_2$	1.59×10^{-6}	**OA**	1.88×10^{-6}

We then examined inclusion of the micropolarity indicators **1b**−**f** within the OA host and the stoichiometry of host to guest (H/G) complexes by recording their ^{1}H NMR spectra. We then performed photophysical studies that established the interior of the OA capsule to be "dry" and nonpolar. Results of ^{1}H NMR studies of all five probes are presented first. On the basis of these studies we concluded that **1b-f** formed capsular 2:1 host/guest complexes.

Host/Guest Complex Structures Revealed by NMR Data. An upfield shift of the guest proton signals in the ^{1}H NMR spectra caused by the magnetic shielding provided by the aromatic walls of the host interior serves as an experimental test for inclusion of a guest within the OA cavity.[28,37,39] Such shifts were found to be the case with probes **1b**−**f.**

For example, ^{1}H NMR signal due to CHO in the case of 1-pyrenealdehyde that appeared at ~10 ppm in chloroform was upfield shifted to 8.5 ppm in aqueous solution containing OA (4×10^{-3} M) and **1c** (2×10^{-3} M) (Figure 2iii). Similarly, there was an upfield shift in the ^{1}H NMR signals due to the 2-acetylanthracene molecule (1×10^{-3} M) in the presence of 2 equiv of OA in D_2O (2×10^{-3} M, 10 mM borate buffer, pH $\approx$ 9.0) (Figure 2iv). The maximum upfield shift was noted for the $-COCH_3$ group whose signal was present at −0.5 ppm in the presence of OA (in chloroform solvent it appeared at 2.5 ppm).

(55) Wagner, B. D.; Fitzpatrick, S. J.; McManus, G. J. *J. Inclusion Phenom. Macrocycl. Chem.* **2003**, *47*, 187–192.
(56) Seixas de Melo, J. S.; Becker, R. S.; Macanita, A. L. *J. Phys. Chem.* **1994**, *98*, 6054–6058.
(57) Muthuramu, K.; Ramamurthy, V. *J. Org. Chem.* **1982**, *47*, 3976–3979.
(58) Muthuramu, K.; Ramamurthy, V. *J. Photochem.* **1984**, *26*, 57–64.
(59) Breslow, R. *Acc. Chem. Res.* **1991**, *24*, 159–164.
(60) Breslow, R.; Maitra, U.; Rideout, D. *Tetrahedron Lett.* **1983**, *24*, 1901–1904.
(61) Catalán, J.; Zimányi, L.; Saltiel, J. *J. Am. Chem. Soc.* **2000**, *122*, 2377–2378.
(62) Li, G.; McGown, L. B. *J. Phys. Chem.* **1994**, *98*, 13711–13719.
(63) Dutta, A. K. *Solid State Commun.* **1996**, *97*, 785–790.

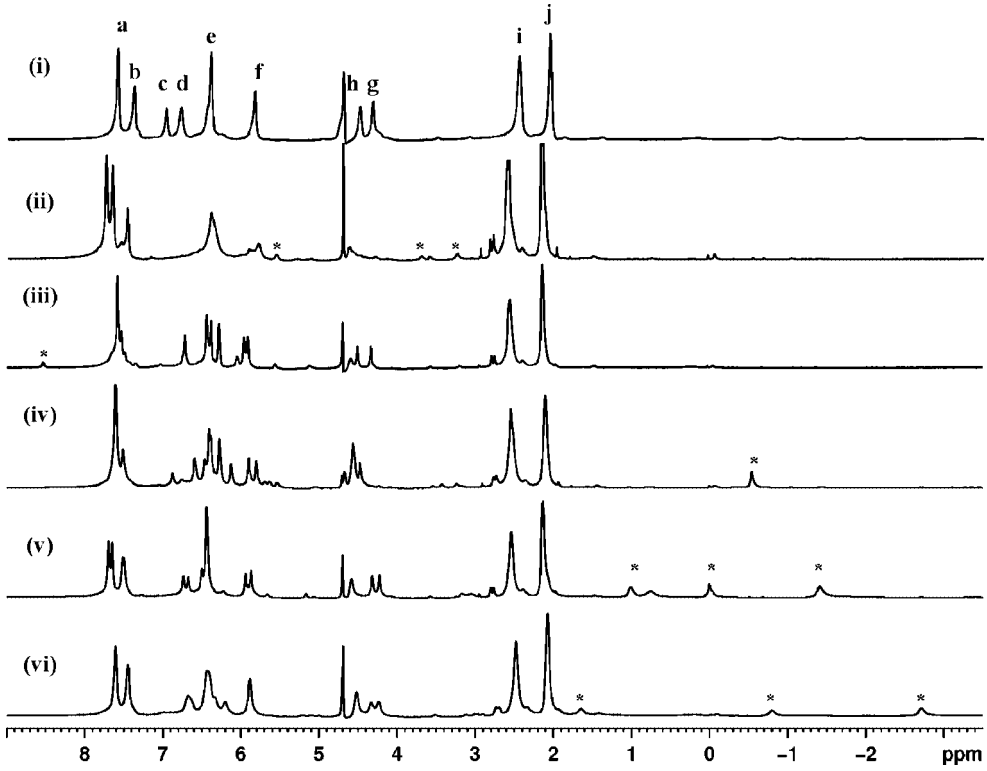


Figure 2. ^{1}H NMR spectra of (i) OA (1 mM), (ii) phenanthrene@OA_2, (iii) pyrenealdehyde @OA_2, (iv) 2-acetylanthracene@OA_2, (v) coumarin-1@OA_2, (vi) 7-propoxycoumarin @OA_2. [OA] = 1 mM in 10 mM borate buffered D_2O, [Guest] = 0.5 mM. Guest signals are marked with a * and those due to the host are labeled with letters. The aldehyde signal of pyrene aldehyde@$(OA)_2$ and the upfield signals of all other cases are marked. It was not possible to unequivocally identify the aromatic hydrogen signals of the guests.

An upfield shift of $\Delta\delta \approx 3$ ppm suggested that the molecule was encapsulated within the OA cavity. Examination of traces (v) and (vi) in Figure 2 confirms that the signals due to alkyl chains in **1e** and **1f** are shifted upfield. Such shifts confirm the inclusion of the guest molecules **1e** and **f** within the OA cavity.

The ratio of host to guest in each case was ascertained through titration experiments. Addition of guests **1b**−**f** beyond a 2:1 ratio (H/G) resulted in turbid solutions, suggesting that excess probe molecules remain in water as aggregates. Titration studies in each case suggested a 2:1 complex of host/guest. The pulse gradient spin−echo diffusion (PGSE) NMR experiments provided diffusion constants for the OA complexes of **1a**−**e** (Table 1), and these are in the same range obtained previously by us for several 2:1 complexes.[134−137]

Structures of all host/guest complexes were characterized by COSY and NOESY 2D ^{1}H NMR experiments (Supporting Information). Examination of the spectra provided in Figure 2 and Supporting Information (Figures S3−S6, S8, and S9) helped us confirm that probes **1c**−**f** formed a 2:1 capsule. The capsule formed by these guests lacking symmetry with two identical OA molecules would be dissymmetric with different capsular top and bottom halves to lead to different chemical shifts for identical hydrogens of OA in these regions. For example, with pyrenealdehyde as the guest, the signals due to H_e, H_f, and H_g are split; with 2-acetylanthracene, splitting of H_f and H_g ^{1}H signals were noted. Similar splitting of signals due to host $H_{a,c,f,g}$ protons by the unsymmetrical coumarin-1 (Figure 2v) and H_{a-g} protons in the case of 7-*O*-propylcoumarin as guests could be noticed (see also spectra in Supporting Information). The ^{1}H NMR studies clearly established that all five probes reside as single molecules within the capsule formed by two molecules of OA, and in the NMR time scale, one is longer than the excited singlet lifetime, and they do not venture into the aqueous exterior.

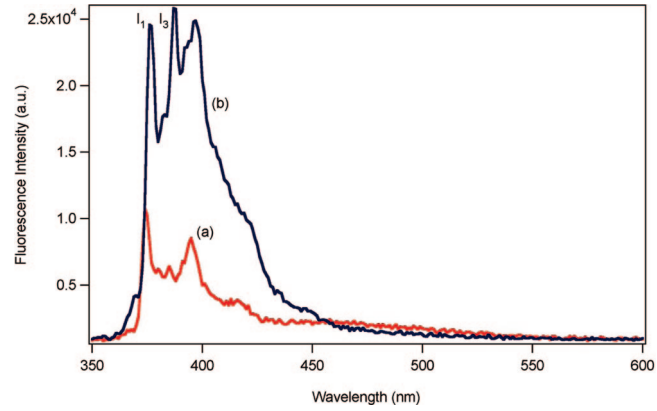


Figure 3. Fluorescence emission spectra in borate buffer (pH ≈ 9) of (a) 1×10^{-5} M pyrene and (b) pyrene@$(OA)_2$. Note the relative intensities of I_1 to I_3 in the two cases. Excitation wavelength: 320 nm.

Micropolarity Revealed by Emission Characteristics of Aromatic Probes. In this section we discuss the results obtained with five polarity probes that are established by NMR data to form a 2:1 capsule with OA. Five probes were employed to be sure that all parts of the capsule are covered. The results from the probes discussed individually led us to the same final conclusion: the capsule occupied by an aromatic probe molecule is dry and nonpolar.

Pyrene (**1b**) is an extensively used probe molecule to determine the micropolarity of the environment in which it resides.[43−45] Intensities of the various vibronic bands in its fluorescence, most importantly I_1 and I_3 bands, provide information about the polarity. It is known that in a polar medium, I_1/I_3 is greater than in a nonpolar environment. Thus, pyrene that formed a stable 2:1 capsule with OA seemed ideal to probe the interior of the capsule.

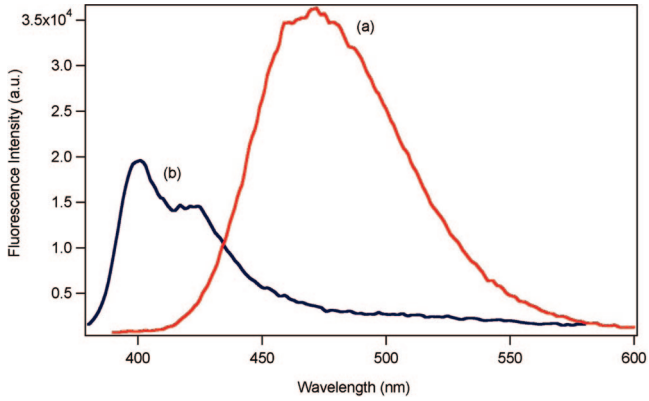


Figure 4. Fluorescence emission spectra in borate buffer (pH ≈ 9) of (a) 1×10^{-5} M pyrenealdehyde and (b) pyrenealdehyde@$(OA)_2$. Excitation wavelength: 330 nm.

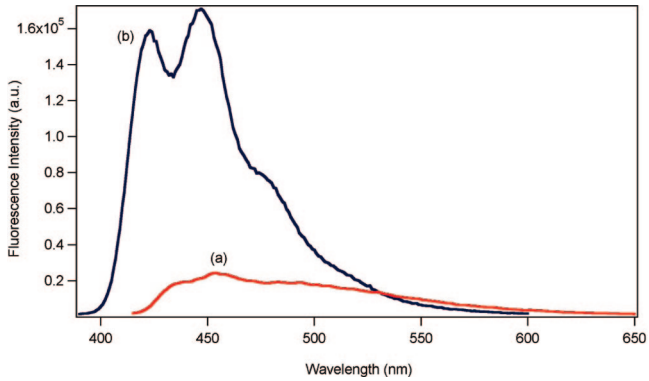


Figure 5. Fluorescence emission spectra in borate buffer (pH ≈ 9) of (a) 2-acetylanthracene and (b) 2-acetylanthracene@$(OA)_2$. Excitation wavelength: 330 nm.

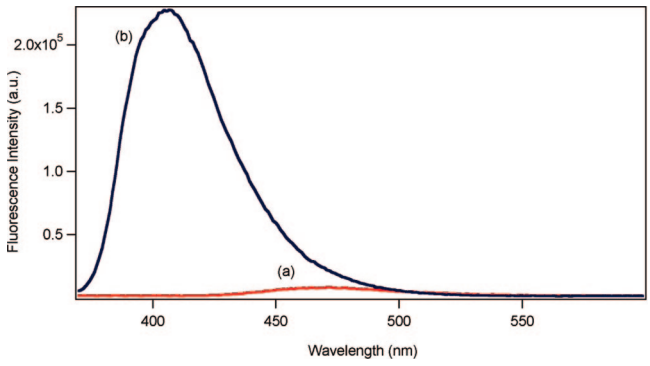


Figure 6. Fluorescence emission spectra in borate buffer (pH ≈ 9) of (a) coumarin-1 and (b) coumarin-1@$(OA)_2$. Excitation wavelength: 350 nm.

Pyrene is soluble in water at a concentration of 1×10^{-5} M. Upon excitation of pyrene in borate buffer (1×10^{-5} M), a monomer emission between 360−420 nm and a weak excimer emission with a maximum at 470 nm due to pyrene aggregates were recorded (Figure 3a). Addition of 2 equiv of OA (2×10^{-5} M) completely displaced the latter weak emission with an intense monomer emission (Figure 3b).

The excited-state S_1 lifetime of pyrene included in OA was measured to be 350 ns, indicating that pyrene resides as a single molecule within the OA capsule. The monomer emission with I_1/I_3 ratio of 1.01 is an indication that pyrene is emitting from an environment where there are no water molecules. Comparing I_1/I_3 value obtained in OA with those in various solvents reported

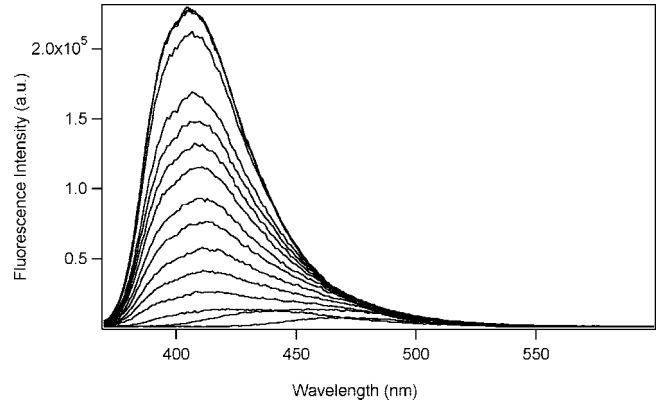


Figure 7. Variation in fluorescence of coumarin-1 (1×10^{-5} M; pH ≈ 9.0, 10 mM $Na_2B_4O_7$ in H_2O) with increased addition (from bottom to top) of OA in borate buffer (1×10^{-6} to 3×10^{-5} M). Note the shift in the maxima as well as increase in the intensity with increased concentrations of OA. Excitation wavelength: 350 nm.

in the literature, we conclude that the polarity of the host/guest capsule is similar to that of benzene. Considering the 24 benzene rings of the OA capsule, this similarity is not surprising.

Pyrenealdehyde (**1c**) has been established to show emission due to its two emitting states of $\pi\pi^*$ and $n\pi^*$ in polar and nonpolar media, respectively.[46,48] Such a switch in the emitting species results in a shift in the maximum wavelength of emission as well as changes in vibrational structure in the emission spectrum. Figure 4 provides emission spectra of pyrenealdehyde in water in the presence and absence of OA. The recorded structured, blue-shifted fluorescence emission of pyrenealdehyde encapsulated within OA suggests that the emission is from its $n\pi^*$ state. The structured excitation and absorption spectra are also characteristic of $n\pi^*$ state. These observed emission characteristics and the shorter lifetime (<2 ns) confirm the presence of the probe molecule in a nonpolar environment.

2-Acetylanthracene (**1d**) is known to show fluorescence in different wavelength regions in polar and nonpolar media.[51,52] The structured emission changes to structureless and red-shifts in polar solvents. Fluorescence emission of 2-acetylanthracene in borate buffer at a concentration of 1×10^{-5} M was weak and broad (420−550 nm), characteristic of polar environment (Figure 5a). Remarkably, fluorescence emission of 2-acetylanthracene@OA_2 (**1d** = 1×10^{-5} M; OA = 2×10^{-5} M) was intense, structured, and blue-shifted (400−500 nm; Figure 5b). On the basis of these results we conclude that 2-acetylanthracene is present in a nonpolar environment within the OA capsule. An overlay of the emission spectra of 2-acetylanthracene in benzene and in the host/guest complex (Supporting Information) supports our earlier conclusion that the polarity of the interior of the OA capsule is similar to that of benzene.

Coumarin-1 (**1e**) belongs to a family of laser dyes whose fluorescence quantum yield and lifetime increase with a decrease in solvent polarity.[53,54] Excitation of coumarin-1 at 350 nm in borate buffer showed a weak broad emission between 440 and 540 nm. As can be seen in Figure 6, there is significant enhancement in fluorescence and hypsochromic shift in the emission of coumarin-1 in the presence of OA (**1e** = 1×10^{-5} M; OA = 2×10^{-5} M). Figure 7 is the fluorescence titration showing spectral changes due to the addition of small increments of OA to coumarin-1 solution in borate buffer. These experiments unequivocally establish that, with incremental addition of OA, the probe was transferred from the polar (aqueous) to the nonpolar (OA capsule) environment. Fluorescence lifetime recorded for coumarin-1@OA_2 resulted in a single exponential decay with a

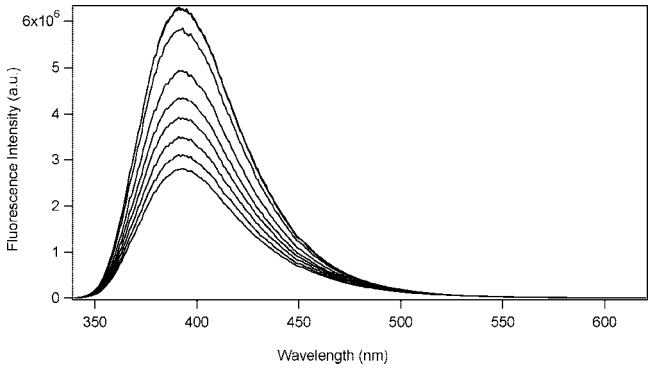


Figure 8. Variation in fluorescence of 7-*O*-propyl coumarin (2×10^{-5} M) with increased addition of OA in borate buffer (1×10^{-5} to 6×10^{-5} M, from top to bottom). Excitation wavelength: 320 nm.

lifetime of 4.17 ns. On the basis of literature precedents we attribute the increase in intensity and shift in the emission maxima to the twisted intramolecular charge transfer phenomenon. Similar to the other three probes, coumarin-1 also reports that the capsule interior is water free.

The last probe molecule we employed was 7-*O*-propylcoumarin (**1f**). Unlike the previous example, this molecule emits strongly in polar and weakly in nonpolar media, generally without any change in the emission maxima.[55,57,58] On the basis of our observations with the above four probes our expectation of a strong emission of this molecule in borate buffer to decrease on the addition of 2 equiv of OA was realized (Figure 8). The fluorescence titration conducted with this probe leading to fluorescence suppression is shown in Figure 8.

From the above studies it is clear that the interior of the OA capsule where the organic guest molecule resides is nonpolar, and most likely no water molecules are present. This observation is remarkable considering that the water used to dissolve the guest OA is excluded from its cavity.

Guest-Dependent H:G Complex Stoichiometry. In the examples discussed above, the hydrophobic probes **1a**−**f** of dimensions too large to fit within the cavity of a single OA molecule formed a 2:1 complex with it. One might then wonder: What happens if the guest molecule is small; will it form a 2:2 or 1:1 complex? Would a more water-soluble (hydrophilic) molecule complex with OA? How strong would such a complex be? To address these questions we have investigated the complexation properties by employing NMR and emission techniques of three probe molecules, 2-methoxynapthalene (**1g**), 2-hexyloxynaphthalene (**1h**), and 2-naphthoic acid (**1i**).

From the ^{1}H NMR titration spectra of 2-methoxynaphthalene with OA displayed in Figure 9 the upfield shifted (δ −0.75) methyl group signals indicate the methoxy group's location at the narrower end of OA capsule. The chemical shift due to the methyl remains independent of the amount of guest in the solution. This suggests that the complex is stable in the NMR time scale (compare with Figure 13). Formation of host/guest complex with 1:1 stoichiometry is suggested by the lack of change in the spectra on further addition of the guest. A symmetrical guest−host complex (2:2) formation, possible only through accommodation of two guest molecules within a capsule, was inferred from the absence of splitting of any of the host signals and confirmed by the results of emission studies. Emission spectra of 2-methoxynaphthalene in water upon addition of various amounts of OA are provided in Figure 10. We believe that the change from the exclusive emission from the monomer of 2-methoxynaphthalene at a concentration of 2×10^{-5} M in water to the emission from both the monomer ($\tau = 11$ ns) and excimer ($\tau = 39$ ns) upon

Figure 9. ^{1}H NMR titration experiment of 2-methoxynaphthalene with host OA. (i) OA (1 mM in 10 mM buffered D_2O), OA/2-methoxynaphthalene at (ii) 4:1, (iii) 4:2, (iv) 4:3, and (v) 4:4. Aliphatic guest resonances are marked with *.

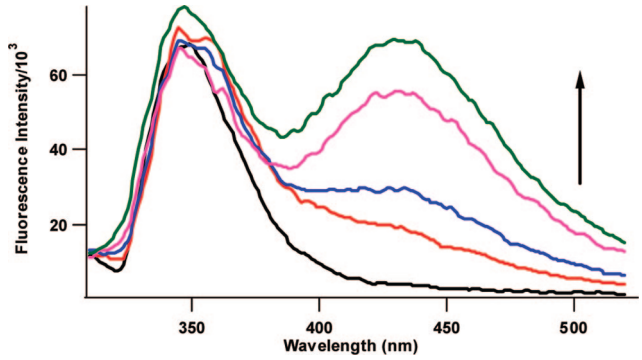


Figure 10. Fluorescence titration of 2-methoxynaphthalene (2×10^{-5}M) with OA host in borate buffer (10 mM), with varying concentration of OA from (bottom to top) 0 to 4×10^{-5}M. Excitation was carried out at 270 nm.

addition of OA confirms the inclusion of two molecules of the host within OA guest. Consistent with our conclusion the diffusion constant measured by PGSE NMR experiment was 1.38×10^{-6} cm^2/s (Table 1).

In contrast to the above results, a 2:1 capsule was formed with 2-hexyloxynaphthalene, a molecule longer than 2-methoxynaphthalene. ^{1}H NMR titration spectra of 2-hexyloxynaphthalene with OA are shown in Figure 11. Inclusion of the alkyl chain within OA is evident from the upfield shift of the ^{1}H NMR signals due to the hexyl chain. Further, the chemical shift of the alkyl chain independent of the amount of guest and host present in solution suggests that the host/guest complex is stable in the NMR time scale. This observation is similar to that noted with 2-methoxynaphthalene. An important observation was that addition of 2-hexyloxynaphthalene beyond 0.5 equiv of the host resulted in

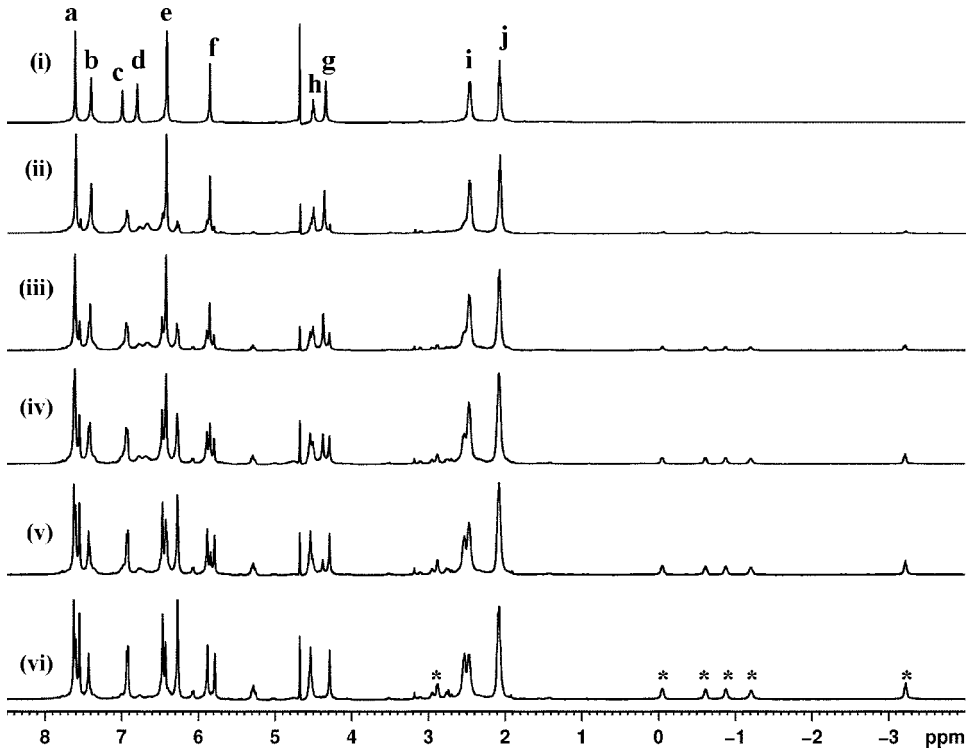


Figure 11. ^{1}H NMR titration experiment of 2-hexyloxynaphthalene with host OA. (i) OA (2 mM in 20 mM buffered D_2O), OA/2-hexyloxynaphthalene at (ii) 10:1, (iii) 5:1, (iv) 3:1, (v) 2.5:1 and (vi) 2:1. Aliphatic guest resonances are marked with *.

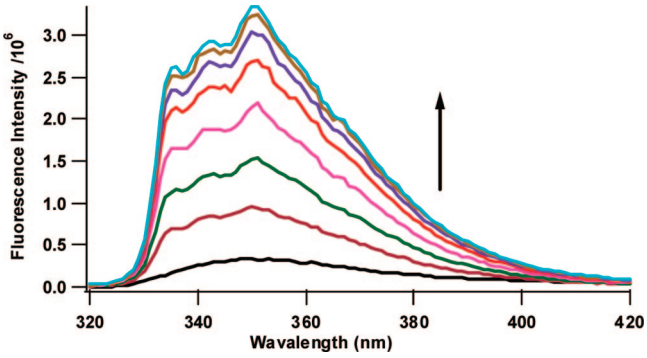


Figure 12. Fluorescence spectra of 2-hexyloxynaphthalene (2×10^{-5} M) with OA host in borate buffer (10 mM) at concentrations varying from (bottom to top) 0 to 1.4×10^{-4} M. Excitation was carried out at 270 nm.

signals due to uncomplexed guest molecules suggestive of this guest forming a 2:1 capsule with OA. Consistent with this result, the $^1H_{a-g}$ signals due to the host were split, suggesting that in presence of 2-hexyloxynaphthalene the top and bottom halves of the capsule are not symmetrically identical. In support of the inference that, unlike **1g** (2-methoxy), **1h** (2-hexyloxy naphthalene) forms a 2:1 complex, its emission spectrum in the presence of OA was also different. The weak monomer emission observed with the poorly water-soluble 2-hexyloxynaphthalene intensified upon addition of OA to the solution, and most importantly, emission due to excimer was absent (Figure 12). Consistent with the 2:1 complexation, the diffusion constant was measured to be 1.26×10^{-6} cm^2/s (Table 1). This difference in the nature of the emission between 2-methoxy- and 2-hexyloxynaphthalenes convincingly demonstrates the crucial role of the molecular size of the guest in complexation with the host.

As opposed to the above two 2-alkoxynaphthalenes, more hydrophilic and water soluble 2-naphthoic acid exhibited a different behavior. The ^{1}H NMR titration spectra are provided in Figure 13. We like to focus on two signals, one due to the guest (H_1) and another due to the host (H_e). Unlike the two 2-alkoxynaphthalenes discussed above, the chemical shifts of the above two signals in the 2-naphthoic acid/OA complex were not constant but changed with increased addition of the host OA. In Figure 14 the differences in the chemical shifts of H_1 (in the presence and absence of OA in buffer) are plotted with respect to the host/guest ratio. It is clear that there is a continuous shift in the signal position with the increased addition of OA. Even at 2:1 ratio (H/G) the chemical shift has not reached a plateau, and it is still shifting upfield. We believe that this is an indication that OA/2-naphthoic acid complex is not stable in the NMR time scale; there is an exchange between free and complexed states. This is quite different from what we noted with the two 2-alkoxynaphthalenes where the host/guest complexes (2:2 and 2:1) remained intact during the NMR time scale. In Figure 13 the diffusion constants for the guest and host molecules for various host/guest ratios are indicated. Once again the diffusion constants were dependent on the amount of the host/guest ratio in solution. In fact the diffusion constant of the guest, although decreased from 5.36×10^{-6} cm^2/s to 4.32×10^{-6} cm^2/s (Figure 13), did not reach that expected of a host/guest complex. Both chemical shift and diffusion constants that we measured at various host/guest ratios are an average of the ones due to free and complexed species. Water solubility and hydrophilicity of 2-naphthoic acid makes the host/guest complex less stable on the NMR time scale. Since even with 3 equiv of the host the saturation limit was not reached, we could not estimate the binding constant for this system. We believe that the OA forms a 1:1 complex with 2-naphthoic acid (cavitandplex, Scheme 2). At this stage we do not have unequivocal evidence for this. The point we wish to highlight is that the nature of the host/guest complex is dependent on the structure and hydrophobicity of the guest. Structures we visualize for the three hosts are represented in Figure 15. It is important to recognize that the structure of host/guest complex

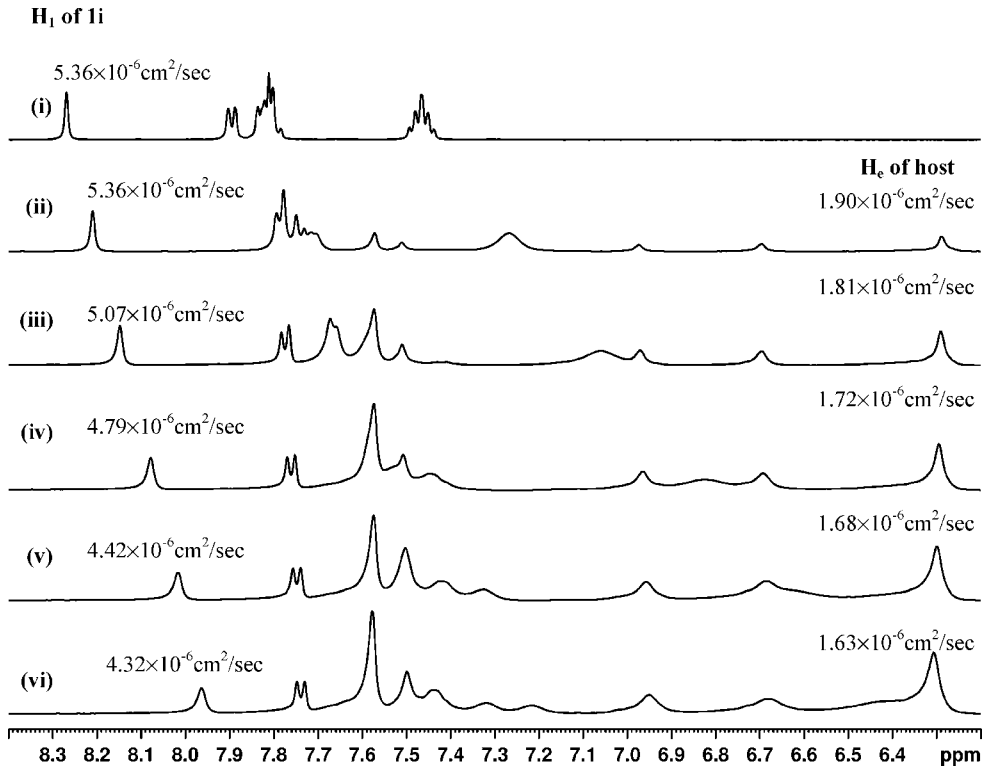


Figure 13. [1]H NMR titration experiment of 2-naphthoic acid with host OA. (i) 2-naphthoic acid (1 mM in 10 mM buffered D_2O), (ii) 2-naphthoic acid/OA 1:0.2, (iii) 2-naphthoic acid/OA 1:0.4, (iv) 2-naphthoic acid/OA 1:0.6, (v) 2-naphthoic acid/OA 1:0.8, and (v) 2-naphthoic acid/OA 1:1. Diffusion constant for the H_1 resonance of the guest and H_e resonance of the host are indicated at each host/guest ratio.

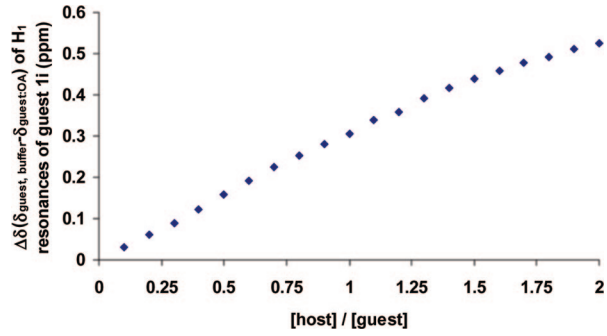


Figure 14. Variation of H_1 proton resonance of **1i** upon the addition of OA. [**1i**] = 1 mM.

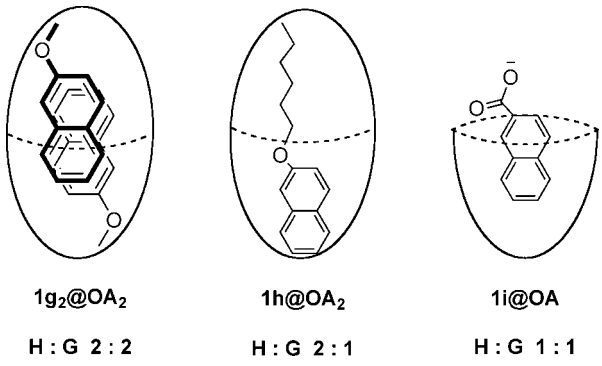


Figure 15. Cartoon representations of capsular assemblies of naphthalene derivatives **1g**−**i** with OA.

depends on a number of factors. Currently we have identified two of these, size and shape of the guest and its solubility (hydrophobicity) in water.

Summary

We have probed the interior features of the deep cavity cavitand octa acid that is currently being explored as a reaction cavity. This host, soluble in water at pH ≈ 9, forms a 1:1, 2:1, or 2:2 complex depending on the guest. Five independent probes form a 2:1 complex, and through their emission features they all report that the interior of OA capsule is benzene-like. We are currently exploring the energy-, electron-, and spin-transfer features of octa acid host.

Experimental Section

Materials and Methods. All probe molecules used in this study were purchased from Sigma-Aldrich/Acros Organics and were recrystallized twice prior to use. Octa acid (OA) was synthesized following a literature procedure.[1] Fluorescence spectra were recorded using an Edinburgh FC900 spectrofluorometer equipped with a xenon lamp. Fluorescence lifetime measurements were made using an Edinburgh single photon counter, fitted with a hydrogen arc lamp. All [1]HNMR spectra were recorded using a Bruker 500 MHz NMR at 27 °C. Spectral plots were generated using Igor Pro software. Diffusion constant measurements were made using a Bruker 500 MHz NMR spectrometer at 27 °C. Data were collected by using 'stebpg1s' pulse sequence (eight scans) and processed by T_1/T_2 relaxation module in the TOPSIN 2.1 software.

Photophysical Studies. A 1 mM stock solution of OA was made in 10 mM sodium tetraborate in water. Guest stock solutions (1 mM) were made in spectrophotometric grade chloroform. To chloroform evaporated (by bubbling nitrogen) were added appropriate amounts of each guest to a test tube with the required amounts of borate buffer and OA stock solution such that the guest and OA were at 1×10^{-5} M and 2×10^{-5} M concentrations, respectively. The same concentration and procedure was adopted for all seven guests.

General Protocol for Binding Studies by NMR. A [1]H NMR spectrum of 600 μL of 2 mM OA in 20 mM sodium borate buffer in D_2O was recorded. To this solution was added 0.25 equiv of guest (5 μL of a 120 mM solution in DMSO-d_6) in four stages, the mixture

was shaken well for about 5 min, and spectra were recorded after each addition. Each sample was also examined 24 h later. No differences were noticed between 5 min and 24 h spectra. In all cases complete complexation was observed upon addition of 0.5 equiv of guest. Further addition resulted in a turbid solution, and the NMR spectrum revealed the presence of both free and complexed guest. All 2D ^{1}H NMR experiments were carried out with samples containing 5 mM OA and 2.5 mM guest in 50 mM sodium tetraborate buffer in D_2O.

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Supporting Information Available: COSY and NOESY 2D ^{1}H NMR spectra of host/guest complexes; fluorescence emission spectrum of **1d** in octa acid and in benzene. This material is available free of charge via the Internet at http://pubs.acs.org.

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