INTRODUCTION

Motivated by the selective processes that occur in highly organized biological assemblies, chemists have been interested in constructing smaller assemblies in the laboratory that exhibit similar unusual selective behavior.1−5 These smaller assemblies often known as “supramolecules” are made up of small molecules held together by weak interactions. Examples of these include weakly held micelles and liquid crystals,6,7 moderately held stoichiometric guest/host complexes,6,8−12 and strongly held structures such as crystals and zeolites.6,13−15 Our continued interest in supramolecular assemblies focuses on examining the excited-state chemistry and physics of guest molecules included within these assemblies.16−18 The host systems we have examined include crystals, zeolites, clay, silica, micelles, cyclodextrins (CD), cucurbiturils (CB), and calixarenes (CA).14−16,18,20 Whereas the first four solid assemblies are fairly rigid, the next four present in aqueous medium have a time-dependent structure. In order to fully predict the excited-state behavior of molecules included in such assemblies, one has to have an understanding of the time dependence (dynamics) of these structures. This report concerns probing the assembly−disassembly process of one such supramolecular structure (guest/host complex) by 1H NMR spectroscopy.21

Recently, we started exploring the value of a synthetic host known as octa acid (OA),22 that, depending on the guest, forms an open cavitandplex (one host and one or two guest molecules) or a closed capsuleplex (two hosts and one or two guest molecules). We use the terms cavitandplex and capsuleplex to mean open and closed complexes with the host.23 OA is established to include a large variety of organic molecules in borate buffer solution.18,24−28 An unusual feature of this host is that, unlike cavatids such as CD, CB, and CA, it forms a stable capsular assembly in the presence of a guest, especially hydrophobic ones. Such a capsular assembly provides a well-defined and a leak-proof confined space as the medium to explore the excited-state behavior of organic molecules. In addition, the interior of this water-soluble capsule that is present in water is hydrophobic and has micropolarity similar to that of benzene.25 The internal cavity offers a contrasting microenvironment (hydrophobic) to that of the external surrounding that is aqueous (hydrophilic). Because of the contrasting environment, hydrophobic guest molecules prefer to stay within the OA capsule, protecting their external surfaces from water. On the other hand, a molecule that has a hydrophobic body and hydrophilic head group forms an open cavitandplex, in which the body stays within the OA cavity and the head is exposed to water. Select hydrophilic guest molecules form both a cavitandplex and a capsuleplex.

Monitoring the excited-state quenching of encapsulated guests by oxygen, we inferred that the OA capsular assembly with hydrophobic guest molecules partially opens and closes (breathing motion) in a microsecond time scale.26 Recently,
pyrene-encapsulated OA capsules are shown to fully disassemble and assemble in 2.7 s. 31,32 Even stable OA capsules dissociate when the pH of the solution is lowered below 8.7. In fact, the assembly–disassembly of these capsules could be controlled by adjusting the pH between 8.7 and 6.5. 33 These observations led us to conclude that although the OA capsule remains intact during the lifetimes of excited singlet and triplet states of organic molecules (<µs), it is dynamic in a longer time scale. We anticipated that the dynamics of the cavitandplex and the capsuleplex would depend on the nature of the guest. This report deals with the dynamics of guest/host complexes wherein OA serves as the host and amphiphilic organic molecules serve as guests.

In terms of dynamics, we have shown previously that long-chain hydrocarbon guests undergo a tumbling motion (rotation around the short axis of the capsule) probably through coordinated flexible rotation of saturated (CH_2)_n units. However, when C=C double or triple bonds were introduced into the hydrocarbon chain, the tumbling motion was arrested. We found that two-dimensional NMR spectroscopy (ROSESY and NOESY) is a powerful technique to monitor this phenomenon. 21,54–36 The tumbling process averaged the magnetic anisotropy of the two OAs that form the capsule, resulting in NOESY correlations between the hydrogens of the two OA molecules. We believed that a similar correlation would result if the two cavitand OA molecules exchange their positions (top and bottom) while the guest remained stationary. To our knowledge, such a type of OA exchange has not been reported earlier. In this study, the focus is on qualitatively examining the mutual exchange of the two OA molecules that form a capsule, and their exchange with free uncomplexed OA molecules in solution. For this purpose, we have chosen rigid amphiphilic guest molecules that would not be able to tumble within the OA capsule. 37,38 We hypothesized that under conditions wherein the top and bottom OA molecules of a capsule exchange their positions, both molecules would experience a similar magnetic environment that would display an exchange in the NOESY and ROESY spectra.

To probe this phenomenon, we selected amphiphilic benzylidene-3-methylimidazolidinones ("BMIs") (Scheme 1)

Scheme 1. Chemical Structures of OA and Guests Studied

related to the green fluorescent protein chromophore as guests. 37–39 These molecules contain both hydrophobic (phenyl) and hydrophilic (imidazolidinone) parts. Based on the amphiphilic molecular skeleton, we expected them to form a 1:1 cavitandplex (hydrophilic part exposed to an aqueous exterior) as well as a 1:2 capsuleplex and thus would provide an opportunity to probe the dynamic exchange between the two types of complexes. Further, we expected that these unsymmetric guest molecules would provide different magnetic anisotropies to the two halves of the capsule, and thus the two parts of the capsule can be readily distinguished by the ^1H NMR signals of the host. We believed that this feature would allow us to monitor the exchange between the two OA molecules by NMR. Further, the tunable amphiphilic nature of these guest molecules provided an opportunity to probe which of the two, the hydrophobic or the hydrophilic part of the guest molecule, would bind to the OA strongly. Results of these experiments are discussed below. Of the six guest molecules, results of two (R_1−H and R_2 = Me and Pr) are discussed in detail. As all six molecules show a similar behavior, the results of the rest four are collected in the Supporting Information section. The goal of this investigation is to examine the occurrence of host exchange through intra- and inter-capsular processes, not through tumbling of the guest. Because of experimental limitations, quantitative rate parameters were not obtained. Results clearly showed that the two parts of the capsule exchange while the guest remain stationary.

**RESULT AND DISCUSSION**

**Labeling Host and Guest Hydrogens.** In the discussion below, one finds the guest and the host molecules to be present in different magnetic environments and because of this, similar hydrogens have different NMR chemical shifts. We have indicated similar hydrogens of the host and the guest with independent chemical shifts differently as elaborated below. First, the host OA molecule is present in three types of environments: free uncomplexed OA, OA that acts as a cavitand, OA that acts as a capsule. As the capsule accommodates an unsymmetric guest, the two OA molecules that form the capsule are not identical. Thus, in this presentation we come across four magnetically nonequivalent OA molecules. The hydrogens of OA are labeled in alphabets as indicated in Scheme 1. The hydrogens of the four magnetically nonequivalent OAs are labeled as illustrated in Figure 1, for example, as A, a, a′, and a″. As for the guest, there are at least three types: the free uncomplexed guest in water, the guest present as a cavitandplex, and the guest present as a capsuleplex. Figure 2 (top) makes the numbering clearer. The two types of guest hydrogens are labeled, for example, as 1 (complexed, present within OA) and 1′ (exposed to water). As in the cavitandplex, half the guest is exposed to water, hydrogens of the part of the molecule that is exposed to water have the same chemical shift as the uncomplexed molecule that is present in water. Also, the chemical shifts of the part of the molecule that is present within OA either as a cavitandplex or a capsuleplex are the same. Instead of assigning different numbers for the hydrogens present in similar magnetic environments, we assigned the same number for the ones present under a similar magnetic environment.

**Inclusion of Guests within OA.** An upfield shift of guest hydrogens in ^1H NMR has been established to be a signature of guest inclusion within OA. 24 In Figure 1, the spectra for all six guests (Scheme 1) in the presence of OA are shown. In all cases, the signals because of hydrogens present in the N-alkyl chain are shifted upfield, confirming their inclusion within OA. In order to infer the stoichiometry of the guest/host complex, 3H NMR titration experiments were carried out. Titrations were carried out by two independent methods: incremental addition of OA to the guest in water and incremental addition of guest to OA in water. Although the final results were the same, that is, formation of a stable 1:2 complex (host to guest),
Figure 1. $^1$H NMR spectra of capsular assemblies of guest@OA$_2$ ([OA] = 1 mM, guest/host = 1:2). Structures of guests provided above each trace. The signals of OA are indicated in Scheme 1 and that of guests in figures in the Supporting Information.

Figure 2. Top: structures of the guest, host/guest complexes, and numbering of various hydrogens. Bottom (i−vii): $^1$H NMR titration spectra of H/N−Me with OA. (i) Free OA (1 mM in 10 mM borate buffer solution in D$_2$O) (ii) free H/N−Me (1 mM in D$_2$O) (iii) guest/host = 1:0.05 (iv) guest/host = 1:0.1 (v) guest/host = 1:0.2 (vi) guest/host = 1:0.5 (vii) guest/host = 1:2. Three types of host signals are assigned with E and F corresponding to free OA; $e''$, $f''$ correspond to host signals from the 1:1 complex; $e$, $e'$, $f$, and $f'$ correspond to host signals from two halves of the 1:2 complex. The residual water signal is denoted by "•" and residual DMSO is denoted by "⧫". Structures of the tguest and he complexes are included at the top.
incremental addition of OA to the guest revealed the initial formation of a 1:1 cavitandplex. The final complex formed with guests H/N−Me and H/N−Pr were 1:2 (host to guest). Full and partial 1H NMR titration spectra in the case of H/N−Me and H−NPr are shown in Figures 2–4. Because of the unsymmetric nature of the guest, two OAs that form the capsule are magnetically nonequivalent. In Figure 1, these are clearly visible for b, c, f, and g protons of the host OA. These appear as two signals confirming that the hydrogens present in the two halves of the capsule experience different magnetic environments.

As illustrated in Figures 2–4, during the addition of OA to the guest, in the presence of less than 1 equivalent of OA, 1H NMR spectra reveal the presence of a 1:1 complex. Importantly, further addition of OA transforms the 1:1 complex (cavitandplex) to a 1:2 capsuleplex (guest/host).
For example, when OA was added to the solution of guest H/N–Me in D$_2$O, at a very low concentration of OA, one set of sharp signals (assigned as a’’ etc.) at δ different from that for free OA (assigned as A etc.) was observed (Figures 2 and 4a). These signals are attributable to the OA protons of the 1:1 complex in which the more hydrophobic aromatic moiety of the guest is included within OA. Upon increasing the OA concentration, two other sets of host signals because of the 1:2 complex (assigned as e and e’ etc.) gradually increased in intensity at the expense of signals because of the 1:1 complex. In the case of guest H/N–Pr, upon addition of OA in small increments, three sets of well-resolved signals because of OA were observed (assigned as e to g, e’ to g’, and e” to g’”) at δ different from that for the uncomplexed OA (assigned as A to G) (Figures 3 and 4b). We believe that these signals are consistent with the simultaneous presence of the 1:1 complex (assigned as a’” to g’”) and the 1:2 complex (assigned by e to g, and e’ to g’”). Similar results observed in the case of guests o-Me/N–Me and o-Me/N–Pr (Scheme 1, Figures S1 and S2) suggested that formation of the 1:1 complex at a lower concentration of OA and the 1:2 complex at a higher concentration of OA is a general phenomenon with BMI molecules. Thus, the titration wherein OA was added in small increments to the guest was valuable and revealed the sequence of formation of the guest/host complex, 1:1 to 1:2 (Scheme 2).

**Scheme 2. Cartoon Representation of the Mechanism of 1:2 Complex Formation of H/N–Me with OA**

The formation of the 1:1 complex at a lower concentration and the 1:2 complex at a higher concentration of OA was confirmed by measuring the diffusion constants of H/N–Me–OA complexes at various OA concentrations (Figure S3). Free H/N–Me and OA in D$_2$O showed diffusion constants of 4.7 × 10$^{-6}$ and 1.82 × 10$^{-6}$ m$^2$ s$^{-1}$, respectively. Upon addition of 0.05 equiv of OA to the solution of H/N–Me in D$_2$O, the diffusion constant for OA decreased to 1.68 × 10$^{-6}$ m$^2$ s$^{-1}$. This decrease in diffusion constant of OA compared to that of the free OA is expected only if a 1:1 complex is present in solution. The measured diffusion constant we believe is the average of free and 1:1 complexed OA. As would be seen later, there is an exchange between the 1:1 complex and free host and guest molecules within the NMR time scale. However, upon addition of 2 equiv of OA, the diffusion constants of both guest and host molecules were found to be 1.27 × 10$^{-6}$ m$^2$ s$^{-1}$. These values are consistent with literature reports for 1:2 complexes.

Between the two groups present in guest BMIs, preference for the more hydrophobic aromatic part over the hydrophilic imidazolidinone part of the BMI molecule for encapsulation within the OA cavity is evident from the $^1$H NMR spectrum shown in Figure 5 for p-Me/N–Me. In the case of p-Me/N–Me, there are three methyl groups, one on the aromatic group (p-Me) and two on the imidazolidinone moiety. Interestingly, at the initial stages of addition of OA, only the p-methyl group of the guest was upfield-shifted, whereas the signals because of other two methyl groups remained nearly at the same place (Figure 5(iii–v)). This suggests that in the case of the 1:1 complex, the p-methyl is anchored within OA, whereas the other two methlys are exposed to water (Figure 5). However, upon further addition of OA, all three methyl groups shifted upfield (Figure 5(vi,vii)), indicating the inclusion of all methyl groups within the OA capsular assembly of the 1:2 complex. Thus, analysis of the $^1$H NMR spectra recorded at various ratios of OA and the guest BMI revealed the mode of inclusion of guests within OA. Expectedly, the more hydrophobic part of a guest enters the capsule first to stay away from the aqueous exterior. Although this is intuitively expected, to our knowledge this has not been clearly established in the case of OA.

**Exchange between 1:1 and 1:2 Complexes.** Having established that amphiphilic BMIs form two types of complexes (1:1 cavitandplex and 1:2 capsuleplex), we were interested to examine the likelihood of exchange of OA between the two types of complexes. In Figure 6a, the visualized exchange is presented in a cartoon fashion. In this figure, three signals corresponding to proton E of OA of different complexes are marked (see above for details). To monitor the exchange, we carried out 2D ROESY NMR experiments. In the ROESY correlation spectrum, the diagonal and cross peaks because of dipolar relaxation have different signs independent of the molecular size. Further, the exchange EXSY and NOESY peaks are easily distinguished by their signs; the EXSY cross-peaks have the same sign as the diagonal peaks and different from NOESY peaks. To explore the dynamic behavior of the 1:1 and 1:2 complexes, a solution containing guest to host 1:0.2 ratio of OA and H/N–Pr was used (Figure 3v). $^1$H NMR spectrum of this solution showed it to contain a mixture of 1:1 and 1:2 complexes (Figure 4b(iv)). As discussed above, during the early stages of titration of OA into the guest solution, the presence of signals because of the 1:1 and 1:2 complexes is visible (Figures 3 and 4b). In Figure 4b, of the three signals because of H$_2$ two of them (e and e’) belong to the OA that form the capsuleplex whereas the one marked as e” belongs to the OA that form the cavitandplex. ROESY NMR experiments were performed with this solution employing spin locking time (also known as contact time, pulse length of spin lock, and mixing time) ranging between 300 and 50 ms. As shown in Figure 6b, OA signals of the 1:1 complex (e.g. e”) showed magnetization exchange with the OA that encapsulates the aromatic moiety (e’) of the 1:2 complex. The exchange that was strong at 300 ms contact time was negligible when the contact time was reduced to 50 ms. This confirms that in the 300 ms time scale the guest/host 1:1 and 1:2 complexes exchange the host OA. To establish the generality of this phenomenon, 2D ROESY NMR experiments with several guest/host complexes (Scheme 1) were carried out and the spectra are provided in the Supporting Information (Figures S4–S13). The results with all these systems were the same as with the guest H/N–Pr (Scheme 1). The fact that there are distinct signals in 1D NMR for the same protons from two or three OA molecules present in different magnetic environments suggests that there is no exchange between 1:1 and 1:2 complexes in the chemical shift time scale. From the above data, we conclude that both 1:1 and 1:2 complexes are labile in the time scale of 300 ms although stable in the NMR chemical shift time scale. This conclusion is important from the perspective of excited-state chemistry of encapsulated molecules, which is our main interest: the guest/host...
Figure 5. Top: structures of the guest, host/guest complexes, and numbering of various hydrogens. Bottom (i–vii): $^1$H NMR titration spectra of $p$-Me/N−Me with OA (i) free OA (1 mM in 10 mM borate buffer solution in D$_2$O) (ii) free $p$-Me/N−Me (1 mM in D$_2$O) (iii) guest/host = 1:0.05 (iv) guest/host = 1:0.1 (v) guest/host = 1:0.2 (vi) guest/host = 1:0.5 (vii) guest/host = 1:2. Three types of host signals are assigned with E and F that correspond to free OA; e″, f″ correspond to host signals from the 1:1 complex; e′, e′′, f′ and f′′ correspond to host signals from two halves of the 1:2 complex. The residual water signal is denoted by “•” and residual DMSO is denoted by “⧫”. Structures of the guest and host complexes are included at the top.

Figure 6. (a) Cartoon representation of exchange of cavitand between 1:1 and 1:2 complexes of H/N−Pr. (b) Partial 2D ROESY spectra of a solution containing 1:1 and 1:2 complexes of H/N−Pr with OA ([H/N−Pr] = 1 mM, guest/host = 1:0.1) with (i) 300 ms mixing time and (ii) 50 ms mixing time.
complexes are stable in the lifetime of excited states in solution (less than ms). Finally, a point to note is that the OA that caps the imidazolidinone part of the capsule is the one that exchanges between the 1:1 and 1:2 complex. One should also note that the exchange reported here is under the conditions wherein there is excess of guest and not enough host in solution. The dynamics is likely to be different when the ratio changes.

**Observations on Host and Guest Exchanges.** In this study, we have observed more than one type of exchange between 1:1 and 1:2 complexes occurring in different time scales. For example, (a) there is an exchange between the 1:1 and 1:2 complexes, (b) exchange of guest between the free and the 1:1 complex, (c) intra- and intercomplex exchange of OA in the 1:2 complex, and (d) exchange of free OA with the 1:2 complex. To understand the timings of various exchanges, we focus on Figures 4 and 5. As discussed in a section above, initially a free guest is complexed with OA to form a 1:1 complex, and with increasing concentrations of OA, 1:1 transforms to 1:2. The fact that the guest signal (e.g., 6' in Figure 5) continuously shifts with increasing concentration of OA suggests that there is a fast exchange of the guest between the free and the 1:1 complex in the chemical shift time scale. We recognize that under such conditions the recorded signal for guest hydrogens is an average of the chemical shift for the free and the 1:1 complexed guest. On the other hand, the fact that the above signal for the 1:2 complex does not change with the concentration of OA suggests that the guest exchange in this complex is slow on the chemical shift time scale. At the same time, one should note that at the initial stages of titration of OA into the guest solution, there is excess guest and little OA and exchange of OA is not expected although the guest exchanges between OA molecules. Appearance of three independent signals of OA in a mixture of 1:1 and 1:2 complexes suggests that the exchange of OA in these complexes is slow in the NMR chemical shift time scale. However, as discussed below, the exchange of OA occurs at a longer time scale (300 ms).

**Intracapsular Exchange of OA in the 1:2 Complex.** One of the interesting observations relates to the exchange of OA in the capsuleplex (Figure 7a). The 1:2 complex of BMI and OA consists of two OA molecules, one capping the aromatic and the other hosting the imidazolidinone part of the BMI. The exchange between the two was monitored by recording ROESY correlations at 300 ms contact time (mixing time). The concentrations of the guest to the host was maintained at 1:2. The full spectrum and the partial spectrum covering the host region are displayed in Figures 8 and 7b. A closer look at the signals of g and g' reveals that the two OA molecules that form the capsuleplex undergo exchange between each other (intramolecular) in the 300 ms timescale. Protons g and g' belonging to different OAs not only showed a ROESY correlation but also an NOE correlation with both e and e' protons (Figure 7). We believe that the NOE correlation of g with e' is aroused through exchange of e and e'. Similarly, other host signals also showed through space NOE correlation with both OA present in the capsuleplex, for example, e/e' and f/f'. These observations suggest that the capsuleplex disassembles in the 300 ms time scale and when it reassembles as illustrated in Figure 7a the two OA molecules exchange their position. A similar observation was made with o-Me/N−Me and p- Me/N− (Scheme 1), suggesting that this is a general phenomenon.

Perusal of Figure 8 reveals yet another feature that relates to the exchange of the guest between the 1:2 complex and the free ones. In a solution containing a 1:2 ratio of guest to host,
Figure 9. (a) Cartoon representation of exchange of cavitand between two unsymmetrical forms of the 1:2 complex, and with excess free OA present in the solution. (b) Partial 2D ROESY NMR (300 ms contact time) spectra of a solution of [H/N−Me] = 2.5 mM with (i) guest/host = 1:2, (ii) guest/host = 1:3, and (iii) guest/host = 1:7. Here, g and g’ correspond to two bound unsymmetrical cavitands from the 1:2 complex, and G represents the free cavitand.

Figure 10. (a) Cartoon representation of intramolecular host exchange. (b) Partial 2D ROESY (300 ms mixing time) spectra of a solution of [H/N−Me] = 2.5 mM with (i) guest/host = 1:2, (ii) guest/host = 1:7. Here, g and g’ correspond to two bound unsymmetrical cavitands from the 1:2 complex and G represents the unbound cavitand.
signals with a low intensity because of the unbound guest imidazolidinone moiety were observed (assigned as 1′ and 2′ in Figure 8). These signals are unlikely to be due to the 1:1 complex as no corresponding signals for OA were found. Focusing on signals because of methyl groups marked as 1, 1′, 2, and 2′, it is clear that the bound and free imidazolidinone moieties undergo exchange (interaction of 1 with 1′ and 2 with 2′ in Figure 8) in the 300 ms time scale. In this figure, note that the bound guest is marked 1 and 2 and the free guest is marked as 1′ and 2′.

**Exchange of OA between the 1:2 Complex and the Free OA.** Having established that the two OA molecules that form a capsule exchange their positions, we were curious to know whether such an exchange would take place with free OA. For this purpose, solutions containing more than a 1:2 ratio of the guest to the host were examined by ROESY experiments. Independent of the excess amount, the 1:2 complex was formed when more than 2 equiv of OA is added to 1 equiv of the guest. Partial ROESY correlation data for solutions containing 1:2, 1:3, and 1:7 guest (H/N−Me) to host (OA) solutions are presented in Figure 9. The spectra displayed for the host region clearly show that whereas the 1:2 sample contains only two signals, g and g′, when excess OA is present, an additional signal because of free OA (G) also appears. The ROESY experiments performed with an excess of OA (over 2 equiv) support the existence of the exchange process between free and bound counterparts (Figure 10(ii,iii)) in the 300 ms time scale. The smaller cross peak because of the mutual exchange of the bound OA in the presence of excess OA (>2 equiv) supports that in a solution there is a large excess of free OA compared to the amount that dissociates from the 1:2 complex. ROESY experiments revealed that in the solution containing 1:3 H/N−Me and OA, there is exchange between both the OAs of capsuleplex (e.g., notice signals g and g′) as well as with the free OA present in the solution (signal g′ and G). At higher concentrations of OA (1:7 H/N−Me and OA), the exchange between free OA and the two complexed OA of capsuleplex individually persisted but there was no exchange between g and g′. A comparison of the three correlations at three different ratios of the guest to the host in Figure 9 is striking: (a) When there is a lack of free OA, the two OAs of one capsuleplex assembly undergo exchange with each other. (b) When there is 1 equiv excess of OA (H/N−Me/OA = 1:3), the exchange is among all three types of OA molecules present in the solution. (c) In the presence of large excess of OA (H/N−Me/OA = 1:7), exchange takes place between free OA and individual OA molecules of the complex; intramolecular OA exchange is not seen in ROESY.

Consistent with the above conclusion, at 1:2 guest to host ratio, the −Me groups of the imidazolidinone moiety showed NOE correlation with the g proton of the OA that caps the imidazolidinone moiety, as well as with the g′ proton of the other OA that encloses the aromatic moiety (Figure 10). On the other hand, in the presence of excess OA at H/N−Me/OA = 1:7, as the exchange was only between free OA and OAs of each half of the capsuleplex, the −Me groups of the guest H/N−Me showed NOE correlation only with the g proton of the OA that caps the imidazolidinone moiety and with the G proton of the excess OA present in the solution, but there was no interaction with the g′ proton of the OA that encloses the aromatic moiety. The above studies with excess OA further confirm the dynamic nature of the OA complexes where even the free uncomplexed host participates in the assembly−disassembly process.

**Limitations of OA Exchange in the 1:2 Guest/Host Complex.** To probe the limitations of the above exchange process, we examined the exchange process with two guests H/N−Pr, o-Me/N−Pr that are more hydrophobic than H/N−Me. The observed ROESY correlations at the guest/host ratio of 1:2 at 300 ms contact time are presented in Figures 11 and 12. In both cases, at this concentration there was no exchange. Furthermore, as shown in Figure 13, no exchange was observed between the bound and the free OA in the presence of excess OA. This clearly indicates that the presence of two additional...
methylene groups in the alkyl chain of the guest results in a stronger complex and the guest has no tendency to leave the host. The results discussed above make it clear that OA capsules are capable of the assembly−disassembly process and

Figure 13. (a) Cartoon representation of the nonexchanging host of complex of H/N−Pr with OA between two unsymmetrical hosts of the 1:2 complex and with a free host present in the solution. (b) Partial 2D ROESY NMR spectra (300 ms mixing time) of H/N−Pr at (i) guest/host = 1:2, and (ii) guest/host = 1:3. ([OA] = 5 mM). Here, proton signals for free OA are assigned by G and from the 1:2 complex are assigned by g and g′.

Figure 14. Cartoon representation of (a) exchange between two types of OA of 1:2 complex with each other (k$_2$/k$_{-2}$) when OA/guest ≤ 1:2, (b) exchange among three types of OA, that is, two from the 1:2 complex and one unbound OA present in the solution when OA/guest = 3:1, (c) exchange between unbound OA and one of the bound OAs from the 1:2 complex separately when OA/guest ≈ 7:1.
the extent of it is controlled by the hydrophobicity of the guest molecule.

**Exchange Rate Constants.** The current study was undertaken to qualitatively probe the feasibility of host exchange in OA capsular complexes. Quantitative estimation of the rates of exchange was not pursued in detail. However, 2D ROESY experiments carried out at 300 ms and zero contact time enabled us to estimate the magnetization rate constants of exchange between two entities. In these experiments, the areas under cross and diagonal peaks were integrated for a particular set of protons that exchanged. Introduction of the integration values in the EKSY CALC program provided the magnetization rate constants of exchange that are related to the rate constants of exchange of two forms. Integration of cross and diagonal peaks of g and g’ protons of two OAs correspond to two halves of the 1:2 capsuleplex for H/N−Me. The rate constants of exchange of two OAs with each other, i.e., g to g’ (k1) and g’ to g (k−1) were estimated to be 4.5 s−1 (k1) and 4.5 s−1 (k−1), respectively (see Figure 9 for the definition of k1 and k−1). Whereas integration of cross and diagonal peaks of guest protons of H/ N−Me, that is, 2 and 2’, correspond to bound and free forms 1:2 capsuleplex H/N−Me, respectively, the rate constants of exchange for encapsulation (k1) and exclusion (k−2) of guests was obtained as 9.0 s−1 (k1) and 1.2 s−1 (k−2), respectively (see Figure 10 for the definition of k2 and k−2). It is important to note the relationship that exists between the exchange rate constant values that are extracted from the ROESY experiment and those corresponding to the rate constants of the formation and dissociation of the complex.

**CONCLUSIONS**

In this study, we have shown that amphiphilic guest molecules form both 1:1 and 1:2 (guest to host) complexes. As expected, in the case of the 1:1 complex a more hydrophobic part of the guest is encapsulated within OA. The most interesting aspect of the study relates to the dynamics of these complexes. 1H NMR correlation spectroscopic studies revealed that the complexes are not stable structures and they undergo an assembly–disassembly process in a 300 ms time scale. The host OA exchanges between the two parts of the capsule as well as with the free OA present in the solution. Our visualization of the exchange between various OA molecules is illustrated in Figure 14. As noted in the case of N−Pr benzylidinone systems, the dissociation depends on the hydrophobicity of the guest molecules. Clearly, the nature of the complex favored (1:1 or 1:2) and stability of the OA complex depend on the hydrophobicity of the guest. The hydrophobic guests form stable capsuleplexes with OA. The results presented support our general conclusion that the OA complexes are stable in the time scale of the excited singlet state lifetime of guest molecules and photochemistry and photophysics of encapsulated guests within the OA capsule.

**EXPERIMENTAL SECTION**

**Materials.** Synthesis and characterization of OA and various benzylidene-3-methylimidazolidinoines are reported elsewhere.11

**Methods.** 1D NMR, 2D COSY, NOESY, and ROESY experiments were performed on a 500 MHz NMR spectrometer at 25 °C. For the titration experiments, 600 µL of a 10 mM NaOD/D2O solution of host OA was taken in an NMR tube and to this guest aliquot in DMSO-d6 was added stepwise. The reverse titration of OA into the guest solution was also performed in a similar manner. The 1H NMR experiments were carried out after shaking the NMR tube for 5 min after each addition. Completion of complexation was monitored by the disappearance of the free host signals upon the addition of the guest.
Molecules by Suppressing Their Favorable Solution Pathways. Hydrophobicity of the Guest. Nonpolar Capsuleplex Dependent on the Molecular Size and Nature; Parthasarathy, A.; Ramamurthy, V. Cavitand Octa Acid Forms a Capsular Assembly. Photochemistry of Organic Molecules; University Science Books: Sausalito, CA, 2010. Ch. 13.

(24) Jayaraj, N.; Zhao, Y.; Parthasarathy, A.; Porel, M.; Choudhury, R.; Sundaresan, A. K.; Parthasarathy, A.; Ottaviani, M. F.; Jockusch, S.; Turro, N. J.; Ramamurthy, V. Guest Rotations within a Capsuleplex Probed by Nmr and Epr Techniques. Langmuir 2010, 26, 6943–6953.

(25) Porel, M.; Jayaraj, N.; Kaanumalle, L. S.; Maddipatla, M. V. S.; Yoshizawa, M.; Klosterman, J. K.; Fujita, M. Functional Molecular Flasks: New Properties and Reactions within Discrete, Self-Assembled Hosts. Angew. Chem., Int. Ed. 2009, 48, 3418–3438.

(26) Weiss, R. G.; Ramamurthy, V.; Hammond, G. S. Photochemistry in Organized and Confined Media: A Model. Acc. Chem. Res. 1993, 26, 530–536.

(27) Gibb, C. L. D.; Gibb, B. C. Activation of Fluorescent Protein Chromophores by Encapsulation. J. Am. Chem. Soc. 2010, 132, 1498–1499.

(28) Gunther, H. NMR Spectroscopy: John Wiley: Chichester, 1992. Photochemistry in Organized Media; VCH: New York, 1991.

(29) Choudhury, R.; Jayaraj, N.; Porel, M.; Choudhury, R.; Sundaresan, A. K.; Parthasarathy, A.; Ottaviani, M. F.; Jockusch, S.; Turro, N. J.; Ramamurthy, V. Guest Rotations within a Capsuleplex Probed by Nmr and Epr Techniques. Langmuir 2010, 26, 6943–6953.

(30) Jayaraj, N.; Jockusch, S.; Kaanumalle, L. S.; Turro, N. J.; Ramamurthy, V. Dynamics of Capsuleplex Formed between Octaacid Hydrocarbons Depending on the Chain Length and Head Group. Dynamics of a Supramolecular Capsule Assembly. Can. J. Chem. 2011, 89, 203–213.

(31) Tang, H.; de Oliveira, C. S.; Sonntag, G.; Gibb, C. L. D.; Gibb, B. C.; Bohne, C. Dynamics of a Supramolecular Capsule Assembly with Pyrene. J. Am. Chem. Soc. 2012, 134, 5544–5547.

(32) Thomas, S. S.; Tang, H.; Gaudes, A.; Bagsnes, S. B.; Gibb, C. L. D.; Gibb, B. C.; Bohne, C. Tuning the Binding Dynamics of a Guest-Octaacid Capsule through Non-Covalent Anchoring. J. Phys. Chem. Lett. 2017, 8, 2573–2578.

(33) Raj, A. M.; Talluri, S. G.; Dubus, M.; Gupta, S.; Mondal, B.; Ramamurthy, V. Probing the Ph Dependent Assembly-Disassembly of Water-Soluble Organic Capsules with Coumarins and Anthracenes. J. Photochem. Photobiol., A 2018, 355, 398–407.

(34) Keeler, J. Understanding NMR Spectroscopy; Wiley, 2005.

(35) Raj, A. M.; Talluri, S. G.; Dubus, M.; Gupta, S.; Mondal, B.; Ramamurthy, V. Probing the Ph Dependent Assembly-Disassembly of Water-Soluble Organic Capsules with Coumarins and Anthracenes. J. Photochem. Photobiol., A 2018, 355, 398–407.