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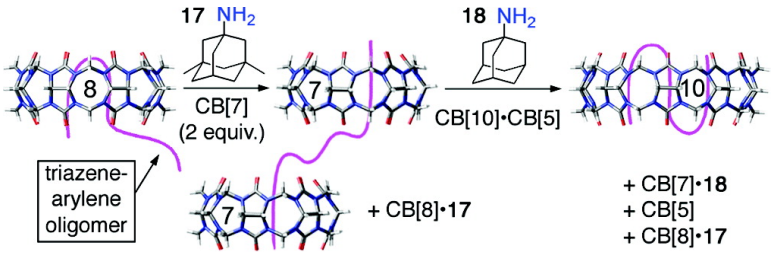

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Refolding Foldamers: Triazene-Arylene Oligomers That Change Shape with Chemical Stimuli

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Abstract: We describe the preparation of five triazene-arylene oligomers (**3**, **4**, **7**, **8**, and **11**) and investigations of their folding properties in aqueous solution. These oligomers contain four 2-fold rotors and populate a conformational ensemble comprising at least 10 states. Extensive 1D and 2D NMR studies as well as X-ray crystallography establish that the presence of three members of the cucurbit[*n*]uril family (CB[*n*]), CB[10], CB[7], and CB[8], results in the selective population of the (a,a,a,a)-, (a,s,s,a)-, and (a,a,a,s)-conformers. As a result of the high affinity and highly selective binding properties of the CB[*n*] family, it is possible to fold a single foldamer strand (**3**) into the CB[8]·(a,a,a,s)-**3** conformer by the addition of CB[8], then unfold and refold it into the CB[7]·(a,s,s,a)-**3**·CB[7] conformer by addition of CB[7] and 3,5-dimethylaminoadamantane (**17**), then unfold and refold it again into the CB[10]·(a,a,a,a)-**3** conformer by addition of CB[10]·CB[5] and aminoadamantane (**18**). The transformation of CB[8]·(a,a,a,s)-**3** into CB[7]·(a,s,s,a)-**3**·CB[7] proceeds through the intermediacy of CB [8]·(a,a,s,a)-**3**·CB[7], which enhances the rate of dissociation of strand **3** from CB[8].

Introduction

The unique functions of nature's oligomeric macromolecules, proteins and nucleic acids, depend on the constitution (e.g., sequence) of these oligomers and more importantly upon their precise three-dimensional folded conformations. Inspired by these natural systems, chemists have begun to design and study non-natural oligomers that fold into well-defined secondary, tertiary, or even quaternary structures driven by H-bonds as well as $\pi-\pi$ and electrostatic interactions.[1−3] Early examples of non-natural folding oligomers, foldamers, include the aromatic donor−acceptor stacks developed by Iverson,[4,5] Moore's phenyleneethynylene oligomers,[2,6] and the β-peptide system exploited by Seebach[7] and Gellman.[1,8] Of particular relevance to the triazene-arylene oligomers described in this Article are the folding preferences reported previously for oligo(amides), oligo(imides), oligo(ureas), and oligo(guanidines).[9,10] As the folding properties of non-natural oligomers have become better understood, the focus of research in the foldamer field has shifted toward the development of systems that are functional and conformationally switchable. For example, both the internal and the external surfaces of foldamers have been used to recognize the identity and chirality of suitable guests, to accelerate certain reactions, and to influence the behavior of their natural counterparts.[11] Foldamers that can switch between two or occasionally three different conformations in response to environmental stimuli (e.g., pH, light, chemical stimuli, metal ions, concentration, solvent) have been reported by a number of groups.[9,12]

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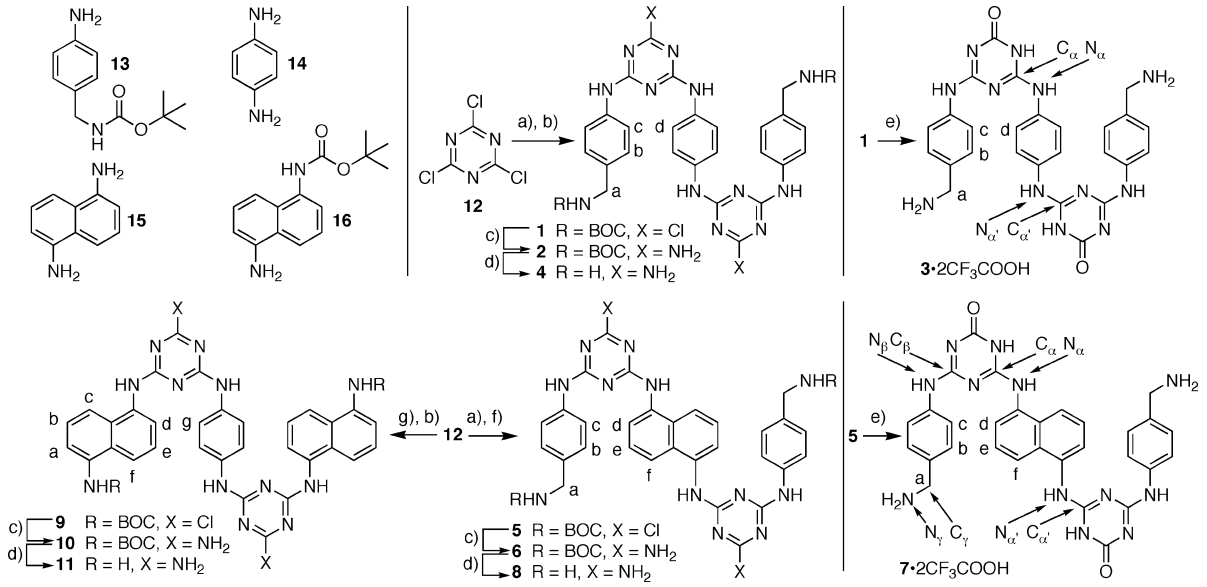
Scheme 1. Synthesis of Foldamers **3**, **4**, **7**, **8**, and **11**[a]



[a] Conditions: (a) **13**, THF, DIPEA, 0 °C, (b) **14**, room temperature, (c) NH_4OH, DMSO, 85 °C, (d) TFA, CH_2Cl_2, room temperature, (e) TFA, H_2O, reflux, (f) **15**, room temperature, (g) **16**, THF, DIPEA, 0 °C.

Although some proteins are capable of autonomously folding into their native conformations, many require the presence of chaperone proteins as molecular containers that promote folding into the native state by preventing trapping in kinetically stable misfolded or aggregated forms.[13] In contrast, for the majority of foldamers reported to date, the information that leads to well-defined folding processes is either encoded in the 1° structure of the oligomer itself or in combination with small molecule guests with convex binding sites. We wondered whether it would be possible to design foldamers with a large ensemble of nearly isoenergetic conformational states that could be accessed in a selective way by the presence of large synthetic molecular containers possessing concave recognition surfaces. In this manner, we thought it might be possible to switch between several folded states in response to the structure of the molecular container employed. Because molecular containers also respond to the presence of guests in their environment, we thought that it might be possible to change the shape of a given foldamer in response to suitable chemical stimuli. Last year, Fujita showed that concave bowl-shaped molecular containers are capable of inducing the folding of natural peptides in water.[14] A related approach was implemented by the Yashima group who reported an oligo(resorcinol) that forms a double helix in water but that unfolds in the presence of a β-cyclodextrin (β-CD) molecular container.[15] The double helical form is repopulated when β-CD is sequestered by the addition of suitable guest molecules. In this Article, we report the folding behavior of five triazene-arylene oligomers whose folding properties can be controlled by the presence of cucurbit[*n*]uril (CB[*n*]) molecular containers[16,17] and that also respond to the presence of competing chemical stimuli.

Results and Discussion

This section begins with a discussion of the rationale behind the design of triazene-arylene oligomers **1**−**11** (Scheme 1), the synthesis of water-soluble foldamers **3**, **4**, **7**, **8**, and **11**, and the enumeration of the conformational manifold open to **3**. This is

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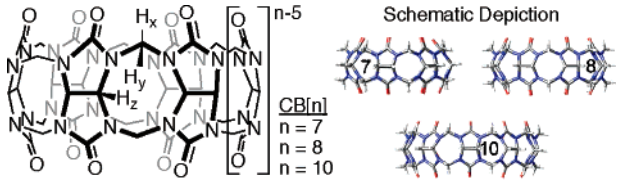
followed by the rationale for the selection of CB[*n*] molecular containers for this study. Last, we describe how CB[*n*] molecular containers can be used to control the conformations of foldamers **3**, **4**, **7**, **8**, and **11** and their response to suitable chemical stimuli.

Design and Synthesis of Triazene-Arylene Oligomers 1−11. To date, foldamer design has relied heavily on the introduction of intramolecular conformational biases (e.g., H-bonds and $\pi-\pi$ interactions) that shunt the conformational manifold toward a particular folded structure. We thought it would be interesting to design a system that exhibited a complex ensemble of nearly isoenergetic states from which individual folded conformations could be selected by interaction with molecular containers. For this purpose, we designed foldamers **3**, **4**, **7**, **8**, and **11** (Scheme 1), which contain two amino-substituted triazene rings linked by arylene units. It is well known that amino-substituents on triazene rings may adopt two conformations, unlike peptide bonds, of nearly equal energy.[18,19] Compounds **3**, **4**, **7**, **8**, and **11** with four such amino-triazene substituents were expected to exhibit a complex manifold of conformations with different shapes and H-bonding patterns.

We synthesized triazene-arylene oligomers **1**−**11** from cyanuric chloride (**12**) and building blocks **13**−**16** using well-established chemistry.[18,19] For example, **12** can be reacted with 1 equiv of **13** in the presence of diisopropylethylamine (DIPEA) followed by 0.5 equiv of **14** to yield **1** in 63% yield. Compound **1** can be transformed into **2** (87%) by heating with ammonium hydroxide in DMSO at 85 °C. Compound **2** can be deprotected by treatment with trifluoroacetic acid (TFA) to yield **4** (100%) as its trifluoroacetate salt. Compound **1** can also be transformed into **3** by heating at reflux in aqueous TFA (91%). Although we depict **3** as a single triazene−NH tautomer, it likely exists in aqueous solution as an equilibrating mixture of tautomers. Compounds **5**−**11** are prepared in an entirely analogous manner in very good yields. Compound pairs **3** and **4**, and **7** and **8** differ only in the nature of the third substituent (e.g., NH_2 or =O) on the two symmetry equivalent triazene rings. In this Article, we investigate the folding behavior of water-soluble compounds **3** and **4**, **7** and **8**, and **11** in the presence of CB[7], CB[8], and CB[10].

Selection of CB[*n*] Molecular Containers. Cucurbit[*n*]uril molecular containers comprise *n* glycoluril rings connected by pairs of CH_2-groups that define a hydrophobic cavity guarded by two ureidyl-carbonyl lined portals (Chart 1). A homologous series of CB[*n*] hosts (e.g., CB[*n*]; $n = 5, 6, 7, 8, 10$) are readily available in multigram quantities by the simple condensation of glycoluril and formaldehyde.[20,21] Individually, CB[*n*] compounds are well known for their high affinity toward cationic guests in water (e.g., K_a up to 10^{12} M^{-1}) and their high

Chart 1. Chemical Structures of CB[*n*]



selectivity (up to 10^6) based on subtle structural changes in their guests.[22−24] The well-defined recognition properties of individual CB[*n*] have been exploited in many applications including molecular shuttles, chemical sensors, drug delivery, supramolecular dye lasers, and supramolecular macromolecules.[25] Kim's group have used CB[8]-based folding processes to develop a variety of molecular machines including a molecular loop-lock.[26] Urbach has recently shown that CB[8] can be used for peptide recognition and dimerization in water.[27,28] We recently reported that the CB[*n*] family, which display high selectivity toward a common guest, collectively constitute a prime platform for the construction of the stimuli responsive systems.[23] For these reasons, we selected several members of the CB[*n*] family as the molecular containers to control the folding of the triazene-arylene oligomers (**3**, **4**, **7**, **8**, and **11**) described below.

Enumeration of the Conformational Manifold for 3. In our design of **3**, we sought to introduce a tractable level of conformational complexity that might be controlled by complexation with CB[7], CB[8], and CB[10]. It is well known that compounds containing triazene C−N bonds (Scheme 2, green arrows) may exist as two rotamers with intermediate exchange

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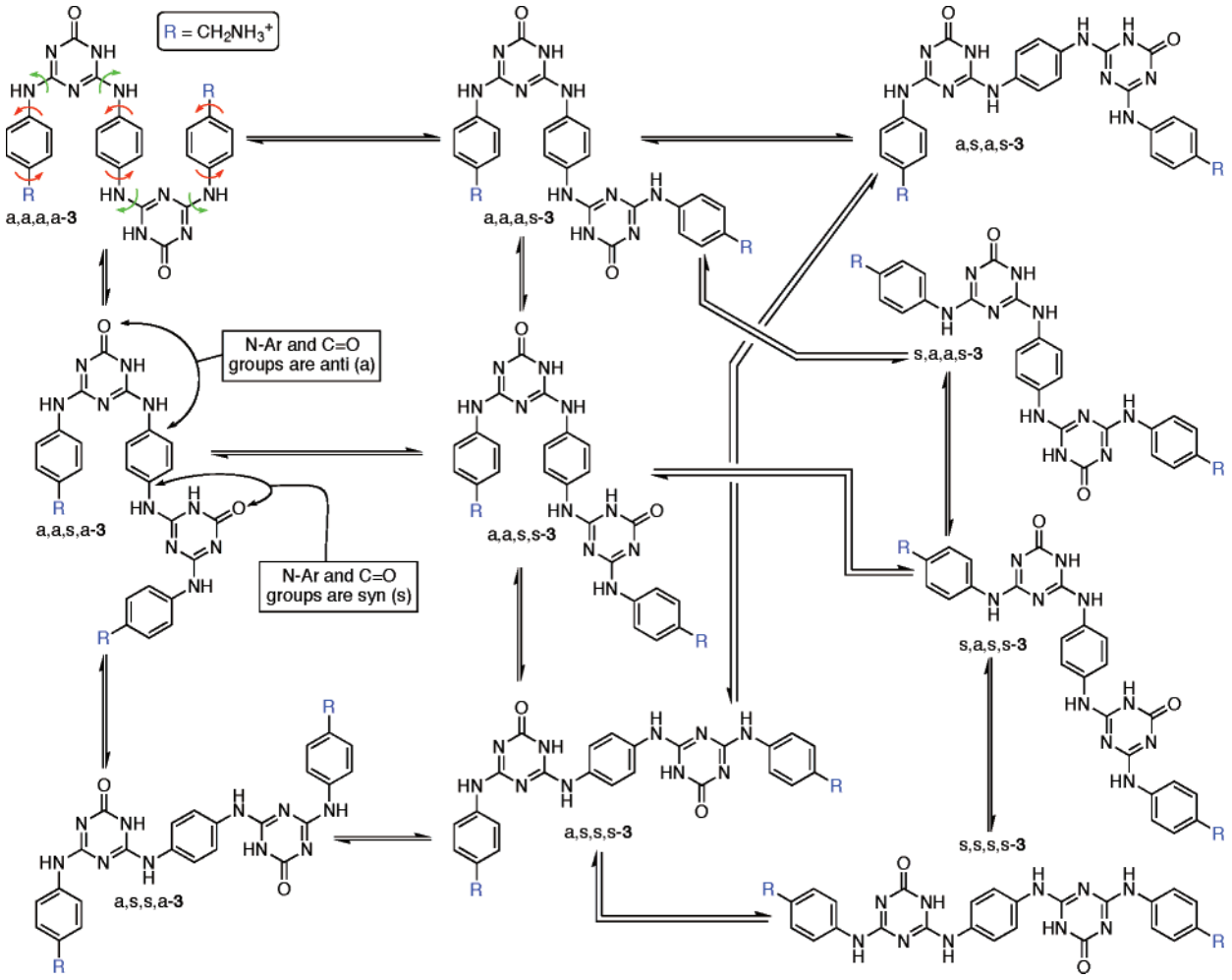
Scheme 2. Ten Distinct Conformations Are Available to **3** by Rotation around Triazene C−N Bonds



kinetics on the chemical shift time-scale.[18,19] For compounds like **3** that contain four such triazene C−N bonds, there are 2^4 (16) possible conformations of which 10 are unique (Scheme 2). To distinguish between these 10 conformations, we consider the orientation of the aryl-N group relative to the triazene C═O group and denote the two rotamers as either anti (a) or syn (s). In enumerating the 10 possible conformations of **3**, we consider each such aryl-N group sequentially to produce a unique identifier (e.g., a,a,a,a-**3**). In analogy to **3**, there are 10 possible conformations for compounds **4**, **7**, **8**, and **11**. In addition to these 10 rotamers involving the triazene C−N bonds, there are several Ar−N and Ar−C single bonds (Scheme 2, red arrows) that may exist in numerous possible conformations, which adds further complexity to the conformational manifold exhibited by **3**.

Compounds 3, 4, 7, 8, and 11 Do Not Exhibit a Preferred Conformation in Water. Before attempting to control the conformation of compounds **3**, **4**, **7**, **8**, and **11** through the application of CB[*n*] molecular containers, we sought to determine the innate conformational preferences of the oligomers themselves. Accordingly, we recorded the ^{1}H NMR spectra separately for all five water-soluble oligomers at room temperature (Supporting Information). The spectra are broad and featureless, which indicates that none of the oligomers adopts a dominant well-defined conformation in D_2O in the absence of CB[*n*] hosts.

In Their Complexes with CB[10], Compounds 3, 4, 7, 8, 11 Exclusively Populate the a,a,a,a-Conformer. Initially, we targeted the population of the a,a,a,a-conformer of the triazene-arylene oligomers because we hypothesized that this conformation might benefit from enhanced $\pi-\pi$ interactions driven by the hydrophobic effect in water. On the basis of our previous experience with the CB[*n*] family of molecular containers,[16,17] we selected CB[10],[21] with its spacious 870 Å^3 cavity, for this purpose. Experimentally, we found that CB[10] forms stable well-defined complexes with all five oligomers in D_2O. Figure 1 shows the ^{1}H NMR spectra recorded for CB[10]·**4**, CB[10]·**8**, and CB[10]·**11**. All three complexes exhibit a common spectral fingerprint: (1) a single set of upfield shifted resonances for the terminal and central arylene units of **4**, **8**, and **11**, (2) a single set of resonances for the CB[10] macrocycle, and (3) a pair of doublets for the terminal CH_2-group that are diastereotopic in the CB[10]·**4** and CB[10]·**8** complexes. In combination, these three spectral features uniquely identify the complexes as the CB[10]·a,a,a,a-**4**, CB[10]·a,a,a,a-**8**, and CB[10]·a,a,a,a-**11** conformers. For example, observation (1) eliminates the six unsymmetrical conformers (a,a,a,s-; a,a,s,a-; a,s,a,s-; a,a,s,s-; s,a,s,s-; a,s,s,s-) that would exhibit additional sets of resonances. Of the remaining four conformations (a,a,a,a-; s,a,a,s-; a,s,s,a-; and s,s,s,s-), only the a,a,a,a-conformer that positions all of the protons inside the shielding region of the cavity of CB[10] is consistent with the pattern of observed

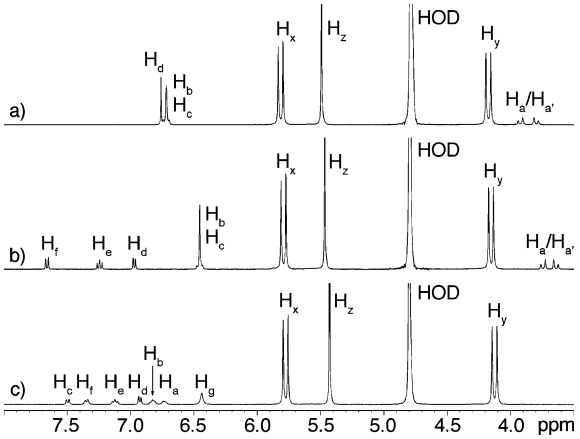


Figure 1. ^{1}H NMR spectra (400 MHz, D_2O, room temperature) recorded for: (a) CB[10]·**4**, (b) CB[10]·**8**, and (c) CB[10]·**11**.

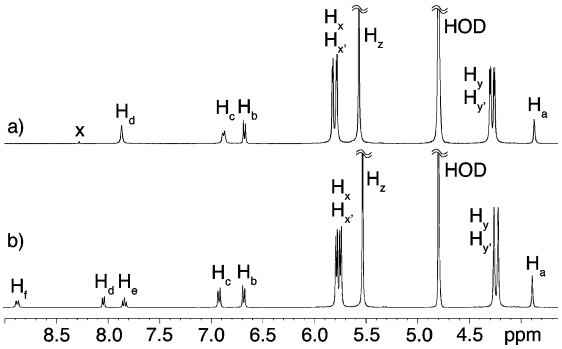


Figure 2. ^{1}H NMR spectra (400 MHz, D_2O, room temperature) recorded for: (a) CB[7]·**4**·CB[7] and (b) CB[7]·**7**·CB[7]. x = trace HCO_2H impurity.

upfield shifting. This conclusion is supported by the X-ray crystal structures of CB[10]·**3**, CB[10]·**4**, and CB[10]·**7** (vide infra). The detailed spectral assignment is based on the COSY and selective 1D ROESY experiments performed on the complexes (Supporting Information). Although the NMR experiments allow us to conclude that the a,a,a,a-conformer is dominant inside CB[10], it does not provide us with information regarding the $C_\alpha-N_\alpha-N_{\alpha'}-C_{\alpha'}$ and $C_\beta-N_\beta-C_\gamma-N_\gamma$ dihedral angles (Scheme 2, red arrows), which are needed to fully define the three-dimensional structure of the CB[10]·a,a,a,a-**4** (or **8** or **11**) complex.

In Their Complexes with CB[7], Compounds 3, 4, 7, 8, 11 Exclusively Populate the a,s,s,a-Conformer. Given the very encouraging results with the CB[10] complexes described above, we wondered whether it would be possible to selectively stabilize any of the other nine members of the conformational ensemble open to **3**, **4**, **7**, **8**, and **11**. For this purpose, we selected CB[7], which is a smaller member of the CB[*n*] family. CB[7] has an estimated cavity volume of 262 Å^3, similar to β-cyclodextrin, and easily binds to alkyl- and arylammonium ions including guests as large as adamantane. We envisioned that CB[7] would only be able to bind to the terminal regions of guests **3**, **4**, **7**, **8**, and **11** and might therefore stabilize different conformations than CB[10]. Figure 2 shows the ^{1}H NMR spectra recorded for mixtures of CB[7] (2 equiv) and **4** or **7**.[29] Similar to the CB[10] complexes described above, a single set of sharp

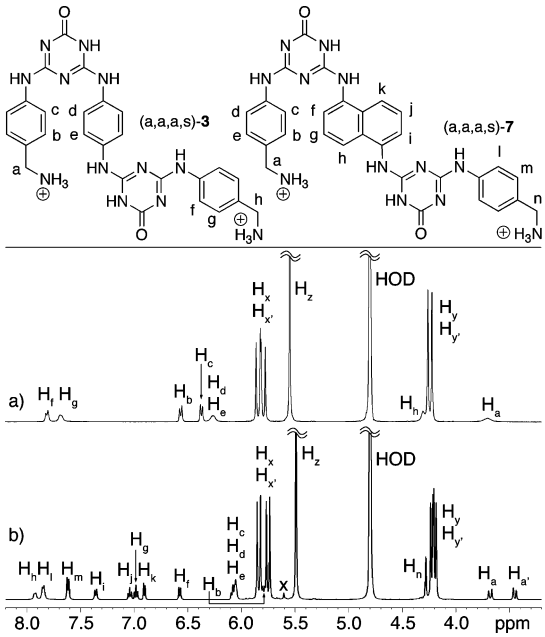


Figure 3. ^{1}H NMR spectra (400 MHz, D_2O, room temperature) recorded for: (a) CB[8]·(a,a,a,s)-**3** and (b) CB[8]·(a,a,a,s)-**7**.

resonances are observed for CB[7]·**3**·CB[7], CB[7]·**4**·CB[7], CB[7]·**7**·CB[7], and CB[7]·**8**·CB[7], which indicates a single well-defined conformation in D_2O. To determine the folded conformation of these CB[7]·guest·CB[7] complexes, we invoke symmetry considerations and chemical shift anisotropy arguments. For example, symmetry considerations rule out the six unsymmetrical conformers (a,a,a,s-; a,a,s,a-; a,s,a,s-; a,a,s,s-; s,a,s,s-; a,s,s,s-) that would display additional resonances. Unlike the CB[10] complexes whose guest resonances move uniformly upfield upon binding, the CB[7]·**4**·CB[7] and CB[7]·**7**·CB[7] complexes exhibit resonance(s) (**4**, H_d; **7**, H_d-H_f) that move significantly downfield.[30] On the basis of the well-established deshielding nature of the region just outside the ureidyl C=O portal of CB[*n*], we conclude that these protons are in the immediate vicinity of the portals.[16,22] This conclusion has been further confirmed by an observed ROESY interaction between H_d and H_x in the CB[7]·**4**·CB[7] complex. Of the remaining four conformations, only the a,s,s,a-conformer satisfies this distance constraint. Hence, we formulate the complex between CB[7] and **3**, **4**, **7**, and **8** as CB[7]·a,s,s,a-guest·CB[7]. Quite interestingly, but perhaps not surprisingly, CB[7] does not stabilize a distinct conformation of **11** because the terminal 1,5-diaminonaphthalene groups do not bind efficiently inside the cavity of CB[7].

In Their Complexes with CB[8], Compounds 3 and 7 Exclusively Populate the a,a,a,s-Conformer. Given the extremely well-defined folding preferences of the triazene-arylene oligomers in the presence of CB[10] and CB[7], we decided to investigate the influence of CB[8] on the conformational ensemble populated by **3** and **7**. We anticipated that CB[8], with its more spacious cavity (479 Å^3), would be able to bind to substantial portions but not all of **3** or **7**. Figure 3 shows the ^{1}H NMR spectra recorded for CB[8]·**3** and CB[8]·**7**. Unlike the cases described above with CB[10] or CB[7], two sets of resonances are observed upon complexation with CB[8]. For

(29) We also examined the influence of 1 equiv of CB[7] on the folding properties of **3**, **4**, **7**, and **8**. At this stoichiometry, a mixture of free guest, 1:1 complex, and 1:2 complex was observed, which made further analysis impractical.

(30) This downfield shifted resonance has been identified by a combination of COSY and selective 1D ROESY spectroscopy (Supporting Information).

example, (1) the terminal $-CH_2NH_3^+$ groups within CB[8]·**3** appear as two broadened resonances at 4.3 and 3.7 ppm, (2) the terminal phenylene rings display two pairs of doublets at 7.8 and 7.7 ppm as well as 6.6 and 6.4 ppm, and (3) a broadened resonance is displayed for the central arylene protons at 6.3 ppm. As described above, the observation of two sets of resonances eliminates the possibility of the four symmetric conformations, leaving only the six unsymmetric conformations (a,a,a,s-; a,a,s,a-; a,s,a,s-; a,a,s,s-; s,a,s,s-; a,s,s,s-) under consideration. The substantial upfield shifts observed for two of the three aromatic rings strongly suggest that the central arylene ring and one terminal arylene ring are inside the cavity of CB[8], which is only possible if the first two N-triazene bonds populate the a,a-conformer, which leaves only three possible conformations (a,a,a,s-; a,a,s,a-; and a,a,s,s-). The downfield chemical shifts observed for H_f in CB[8]·**3** suggested that H_f was just outside the ureidyl C═O portal of CB[8] within the complex. This conclusion was further substantiated by the observation of a ROESY cross-peak between H_f and H_x in the CB[8]·**3** complex. This distance constraint is only satisfied within the CB[8]·(a,a,a,s)-**3** complex. Figure 3b shows the ^{1}H NMR spectrum of CB[8]·**7**. Two interesting aspects of the ^{1}H NMR of CB[8]·(a,a,a,s)-**7** are the observation of: (1) a widely separated pair of doublets (H_a and $H_{a'}$) for the upfield shifted diastereotopic CH_2-group, and (2) four resonances for the bound terminal arylene rings (H_b, H_c, H_d, and H_e). Both observations indicate a well-defined conformational preference with restricted rotation around the terminal arylene ring relative to the central 1,5-diaminonaphthalene residue. Similar to the case of CB[8]·**3** described above, a combination of symmetry considerations and chemical shift analysis allows us to determine that the complex between CB[8] and **7** has the CB[8]·(a,a,a,s)-**7** folded conformation.

X-ray Crystal Structures of CB[10]·3, CB[10]·4, CB[10]·7, and CB[7]·7·CB[7]. Through a detailed analysis of their ^{1}H NMR and ROESY spectra, it was possible to assign the a,a,a,a-, a,s,s,a-, and a,a,a,s-conformers to the various triazene-arylene oligomers in the presence of CB[10], CB[7], and CB[8], respectively. It was not possible, however, to glean any information about the relative orientations (e.g., dihedral angles) of the various aromatic rings within the complex. A priori, one might postulate that maximization of favorable $\pi-\pi$ interactions between the various aromatic rings might drive the formation of a compact conformation in which as little hydrophobic surface area is exposed as possible. Conversely, in accord with the observations of Urbach on CB[8]·peptide complexes,[27] one might postulate that maximization of favorable N−H···O═C H-bonds and NH_3^+···O═C ion−dipole interactions would guide the folding process to its lowest energy conformer. Given the known very large binding constants for CB[*n*]·guest complexes (up to 10^{12} M^{-1})[23,24] and the fact that H-bonds or ion−dipole interactions individually enhance affinity by 10^1-10^3 M^{-1}, it was unclear to us which factor would dominate experimentally.

Fortunately, we were able to obtain X-ray crystal structures of CB[10]·(a,a,a,a)-**3**, CB[10]·(a,a,a,a)-**4**, CB[10]·(a,a,a,a)-**7**, and CB[7]·(a,s,s,a)-**7**·CB[7], which allows us to shed some light on these issues (Figure 4). Figure 4a and b shows the X-ray crystal structures of CB[10]·(a,a,a,a)-**3** and CB[10]·(a,a,a,a)-**4**, which are very closely related structurally. In both cases, foldamers **3** and **4** adopt conformations within CB[10] that benefit from

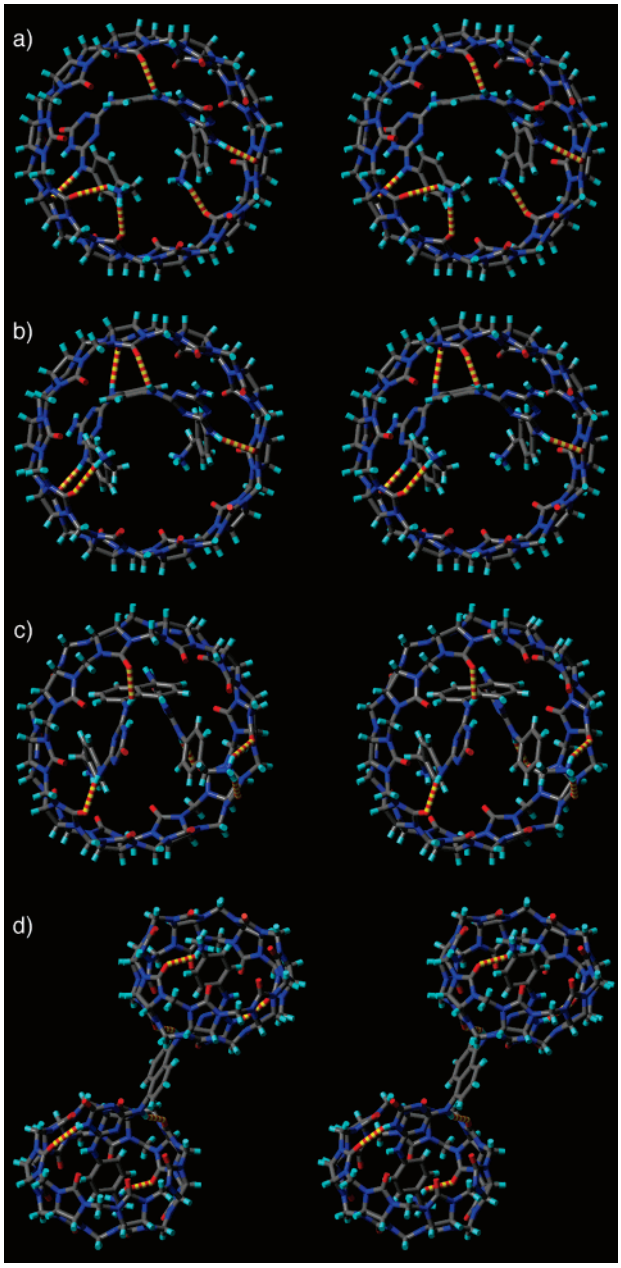
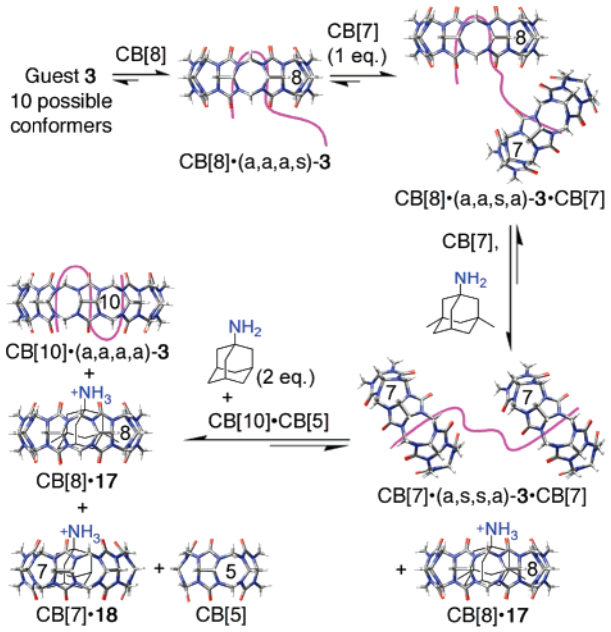


Figure 4. Cross-eyed stereoviews of the X-ray crystal structures of: (a) CB[10]·a,a,a,a-**3**, (b) CB[10]·a,a,a,a-**4**, (c) CB[10]·a,a,a,a-**7**, and (d) CB[7]·a,s,s,a-**7**·CB[7]. Color code: C, gray; H, aqua; N, blue; O, red; H-bonds, red−yellow striped.

multiple favorable N−H···O═C H-bonds and NH_3^+···O═C ion−dipole interactions. In contrast, a brief inspection of Figure 4a and b shows the arylene rings of **3** (**4**) do not benefit from any intramolecular $\pi-\pi$ interactions within CB[10]. The absence of such interactions is reflected in the observed $C_\alpha-N_\alpha-N_{\alpha'}-C_{\alpha'}$ (82° and 77°) dihedral angles, which splay the terminal arylene rings outward from the central arylene ring. Similarly, Figure 4c shows the structure of CB[10]·(a,a,a,a)-**7**, with its central 1,5-diaminonaphthalene ring, benefits from multiple N−H···O═C H-bonds and NH_3^+···O═C ion−dipole interactions but no intramolecular $\pi-\pi$ interactions. In this case, the larger 1,5-diaminonaphthalene spacer of **7** results in a smaller $C_\alpha-N_\alpha-N_{\alpha'}-C_{\alpha'}$ (59°) dihedral angle to accommodate the H-bonds and ion−dipole interactions. Although CB[10]·(a,a,a,a)-**7** displays $C_\beta-N_\beta-C_\gamma-N_\gamma$ dihedral angles of 104° and 123°

Scheme 3. Schematic Illustration of the Change of Conformation of **3** (Purple Strand) in Response to Chemical Stimuli



in the crystal, we do not expect this dihedral angle to display pronounced conformational preferences in water because several ureidyl carbonyl groups on the portals of CB[10] are available to satisfy the need for cation−dipole interactions.

Why do the constraints of H-bonds and ion−dipole interactions dominate the conformations of CB[*n*]•triazene-arylene oligomer complexes when the hydrophobic driving force for CB[*n*] complexes is known to be dominant? There appear to be several important factors. A major consideration is the sheer number of H-bond donating NH groups (four) and NH_3^+ groups (two) that need to be satisfied. Although individually weak, collectively these interactions are strong. A more subtle factor, but one that is presumably quite important, is differential aqueous solvation of free guest versus complexed guest. When free guest is transferred to the cavity of CB[10], it must shed a substantial portion of its solvating H_2O molecules regardless of the conformation assumed inside CB[10]. Once inside, where the guest experiences the low polarizability of the CB[*n*] cavity,[31] the guest is willing to trade the intramolecular $\pi-\pi$ interactions between the arylene rings for the interaction with the π-systems of the 20 ureidyl (N−C═O−N) groups that define the walls of CB[10] and the possibility to maximize the H-bonds and ion−dipole interactions. The message is clear and strikingly similar to those derived from studies of protein folding; although desolvation may provide the main thermodynamic driving force for folding, it is the more directional H-bonds and electrostatic interactions that dictate their precise three-dimensional folded structure.

Figure 4d shows the X-ray crystal structure of CB[7]•**7**•CB[7]. As expected on the basis of the NMR studies, **7** exclusively populates the (a,s,s,a)-**7** conformer in the crystal. Once again, the folding process appears to be controlled by the presence of multiple NH···O═C H-bonds and ion−dipole interactions. Interestingly, it is the ring NH group rather than the exocyclic NH group of the triazene that forms the H-bonds to the ureidyl C═O of CB[7]. In contrast to the structure of CB[10]•(a,a,a,a)-

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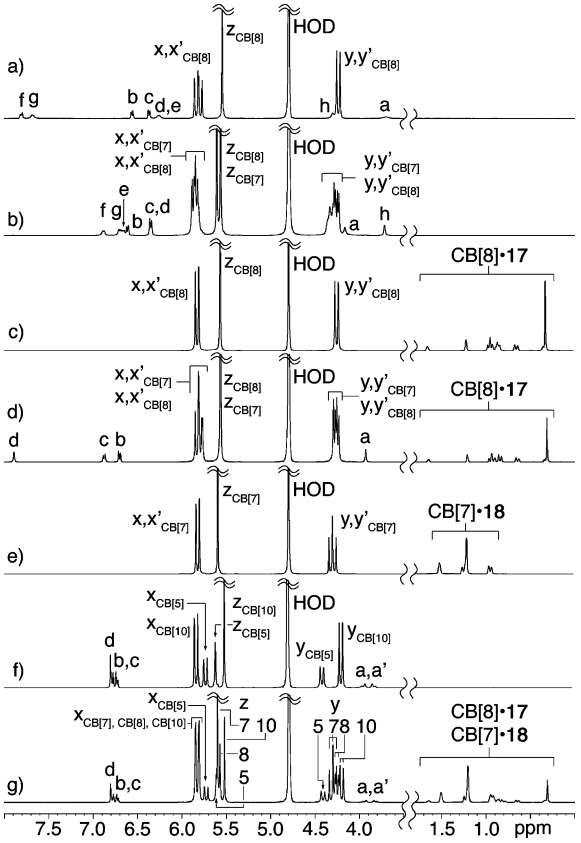

Figure 5. ^{1}H NMR spectra recorded (400 MHz, D_2O, room temperature) by sequential addition for: (a) CB[8]•(a,a,a,s)-**3**, (b) CB[8]•**3**•CB[7], (c) CB[8]•**17** (control spectrum), (d) CB[8]•**17** and CB[7]•(a,s,s,a)-**3**•CB[7], (e) CB[7]•**18** (control spectrum), (f) CB[10]•(a,a,a,a)-**3** and CB[5] (control spectrum), and (g) CB[10]•(a,a,a,a)-**3**, CB[8]•**17**, CB[7]•**18**, and CB[5].

7 where intracavity folding is important, the CB[7]•(a,s,s,a)-**7**•CB[7] conformation can be rationalized on the basis of the maximization of NH···O H-bonds elucidated by Urbach.[27]

Oligomer 3 Changes Shape in Response to Chemical Stimuli. Previously, we and others have shown that individual members of the CB[*n*] family (e.g., CB[6], CB[7], or CB[8]) display remarkable affinity toward their guests with high selectivities based on small structural changes.[22−24] We also showed that the various CB[*n*] (e.g., CB[6] vs CB[7] vs CB[8]) showed large differences in K_a (equivalent to $\Delta\Delta G$ driving force) toward a common guest and argued that these properties made the CB[*n*] family particularly well suited as a component of biomimetic self-sorting systems.[23] Given the separate ability of CB[10], CB[8], and CB[7] to control the folding of a non-natural oligomers, a biomimetic event, we wondered whether it would be possible to fold and refold a single triazene-arylene oligomer strand (e.g., **3**) in response to specific chemical stimuli (e.g., hosts and guests).

For this purpose, we prepared a solution containing **3** (Scheme 3 and Figure 5). As discussed above, **3** accesses a manifold of 10 possible conformations in the absence of CB[*n*] molecular containers. Upon addition of CB[8], **3** folds into the (a,a,a,s)-**3** conformation within the CB[8]•**3** complex. It is possible to unfold and then refold **3** by the addition of 2 equiv of CB[7] and 1 equiv of 3,5-dimethylaminoadamantane (**17**) to yield a well-defined state comprising CB[7]•(a,s,s,a)-**3**•CB[7] and CB[8]•**17**. The fidelity of the refolding process depends critically upon the addition of **17**; when **17** is omitted, a mixture of the

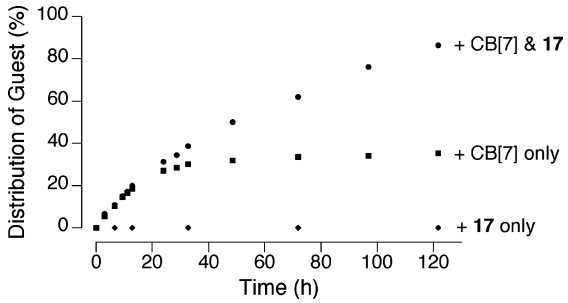

Figure 6. Plot of the release of guest **3** from the CB[8]·**3** complex as a function of time after addition of **17**, CB[7], or a mixture of **17** and CB[7]. ● = [CB[7]·**3**·CB[7]; ■ = [CB[7]·**3**·CB[7]; ◆ = CB[8]·**17**.

CB[7]·(a,s,s,a)-**3**·CB[7] and CB[8]·(a,a,a,s)-**3** is obtained. The addition of **17** provides a potent driving force for the equilibrium because **17** binds 10^7-fold[23] more tightly to CB[8] than to CB[7]. Next, it is possible to transform **3** into the (a,a,a,a)-**3** conformation by the addition of 2 equiv of 1-aminoadamantane (**18**) and 1 equiv of CB[10]·CB[5]. In this remarkable process, the 2 equiv of **18** with their high affinity for CB[7] ($K_a = 4.2 \times 10^{12}$ M^{-1})[23] release **3** to free solution where it displaces CB[5] from the CB[10]·CB[5] complex under formation of CB[10]·(a,a,a,a)-**3**. CB[5] remains in its free state because its cavity (82 Å^3) is too small to act as a molecular container. In theory, but not yet in practice, it should be possible to release free unfolded **3** into solution by the application of a guest that binds to CB[10] even more tightly than **3**. By the selection of components that provide sufficient driving force ($\Delta\Delta G$), it is possible to fold, unfold, and refold **3** into three distinct conformations under thermodynamic control.

CB[7] Enhances the Rate of Dissociation of the CB[8]·3 Complex. Given the slow rates observed for the unimolecular dissociation of some CB[*n*] complexes,[32] we were surprised that the transformation of CB[8]·(a,a,a,s)-**3** into CB[8]·**17** and CB[7]·(a,s,s,a)-**3**·CB[7] by the addition of **17** and CB[7] occurred so readily upon brief heating at 60 °C. We, therefore, decided to monitor the process by the addition of CB[7] and **17** alone and in combination by ^{1}H NMR at room temperature (Figure 6). For example, when we added **17** to CB[8]·(a,a,a,s)-**3** (Figure 6, + **17** only), we observed no change after 120 h (5 days). Conversely, when only CB[7] is added to CB[8]·(a,a,a,s)-**3** (Figure 6, + CB[7] only), an equilibrium mixture is established over the same time period. When both **17** and CB[7] are added, the system has largely transformed (~87%) to the thermodynamic state comprising CB[7]·(a,s,s,a)-**3**·CB[7] and CB[8]·**17** in 120 h. The addition of CB[7] either alone or in combination with **17** substantially enhances the rate of release of **3** from CB[8]·(a,a,a,s)-**3**! We can speculate as to the cause of the dramatic rate enhancement. When 1 equiv of CB[7] is added to CB[8]·(a,a,a,s)-**3**, a new species is formed within minutes (Figure 5b). On the basis of the upfield shifts observed for both the terminal arylene protons H_f (7.8 to 6.9) and H_g (7.7 to 6.7), we conclude that the "free" arm of CB[8]·(a,a,a,s)-**3** has become complexed to yield a new complex CB[8]·**3**·CB[7]. On the basis of the analysis of the anisotropic effects observed in the ^{1}H NMR spectrum and the above-described propensity of CB[8] to stabilize a,a-conformer units and CB[7] to stabilize s,a-conformer units, we formulate this complex as CB[8]·(a,a,s,a)-**3**·CB[7]. The rate of dissociation of **3** from CB[8]·(a,a,a,s)-**3** is enhanced by formation of termolecular complex CB[8]·(a,a,s,a)-**3**·CB[7] in which the terminal arylene unit is pulled away from CB[8] by complexation with CB[7]. Figure 7 shows schematic representations of CB[8]·(a,a,a,s)-**3** and CB[8]·(a,a,s,a)-**3**·CB[7] that illustrate the conformational change. In this manner, it is possible to access a fourth member of the 10-member conformational ensemble open to **3**.

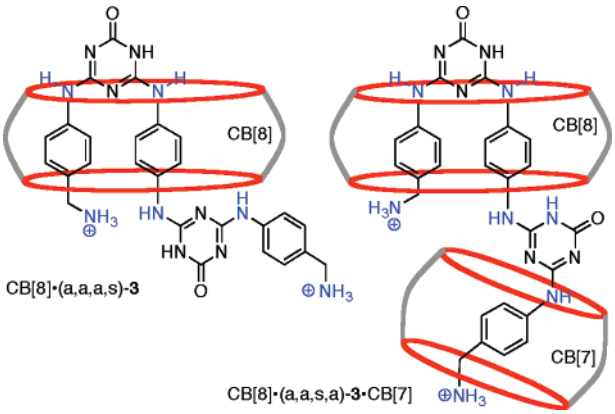

Figure 7. Representations of the proposed geometries of the CB[8]·(a,a,a,s)-**3** and CB[8]·(a,a,s,a)-**3**·CB[7] complexes.

Conclusions

We have described the synthesis of five water-soluble oligo(triazene-arylenes) containing two triazene and three aromatic rings (**3**, **4**, **7**, **8**, and **11**). These oligomers possess four 2-fold rotors and populate a conformational ensemble consisting of at least 10 distinct states of similar energy. We find that the presence of specific CB[*n*] molecular containers is capable of stabilizing a single member of this conformational ensemble. For example, CB[7] results in the population of the CB[7]·(a,s,s,a)-**3**·CB[7] conformer, CB[8] yields the unsymmetrical CB[8]·(a,a,a,s)-**3** complex, and the more spacious cavity of CB[10] stabilizes the most compact CB[10]·(a,a,a,a)-**3** conformer. Although the hydrophobic effect provides a potent driving force for inclusion of **3** in the various CB[*n*] molecular containers, it is the directionality inherent in the NH···O H-bonds and the need to satisfy cation−dipole interactions that dictate the specific member of the conformational ensemble that is expressed. Most interestingly, we found that foldamer **3** can be passed from CB[8] to CB[7] to CB[10] wherein the (a,a,a,s)-**3**, (a,s,s,a)-**3**, and (a,a,a,a)-**3** conformers are expressed in sequence in response to chemical stimuli (**17** and **18**). In this process, we observed that CB[7] is capable of catalyzing the dissociation of **3** from the CB[8]·(a,a,a,s)-**3** complex by transient stabilization of the CB[8]·(a,a,s,a)-**3**·CB[7] complex.

In addition to the system-specific observations described above, the study enables a series of more broadly applicable conclusions. First, the work represents a new direction in the foldamer field wherein intramolecular conformational biases are abandoned and replaced with a shallow conformation potential energy surface and a complex ensemble of conformations.[33] The ability to select a given member of that conformational ensemble in response to the presence of molecular containers (e.g.,

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CB[*n*]) makes the behavior of the system environmentally sensitive. Second, the ability to forcibly unfold and then refold the oligomer in response to chemical stimuli (e.g., **17** or **18**) provides a vivid illustration of the great potential of CB[*n*] molecular containers, with their high affinities, high selectivities, and therefore large $\Delta\Delta G$ driving forces, in the construction of complex self-sorting biomimetic systems.[23,34] A third goal that remains is the release of kinetically stable folded forms of these oligomers, just like natural chaperone proteins[13] do, from the molecular containers in which they fold. We believe this third goal may be accomplished upon progression to longer oligomers and those with backbone−backbone intramolecular contacts that are expected to exhibit higher kinetic barriers for the folded−unfolded transition.[5] Alternatively, it might be possible to employ covalent capture techniques[35] to stabilize and release such folded oligomers. When fully developed, the ability to fold, release, and recycle folded non-natural oligomers is expected to impact diverse areas of science including the development of supramolecular catalysts, synthetic multicomponent molecular machines, and enable the interfacing of supramolecular and biomolecular systems.

Experimental Section

General experimental details have been reported previously.[23] Compounds **13**[19] and **16**[36] were prepared by the literature procedures.

Compound 1. Cyanuric chloride (460 mg, 2.49 mmol) was dissolved in anhydrous THF (5.0 mL) at 0 °C, and 4-(*N*-*t*-butoxycarbonylaminomethyl)aniline (550 mg, 2.48 mmol) and *N*,*N*-diisopropylethylamine (1.00 mL, 6.05 mmol) in THF (5.0 mL) were added to the solution. The mixture was stirred at 0 °C for 30 min, and then for another 1 h at room temperature. After that, *p*-phenylenediamine (130 mg, 1.20 mmol) was added, and the reaction mixture was stirred at room temperature for 48 h. The precipitate was collected by filtration and washed with THF (5 mL) and cold water (20 mL). Compound **1** was obtained as a white solid after drying under high vacuum (590 mg, 0.760 mmol, 63%). Mp: > 300 °C. IR (KBr, cm^{-1}): 3281m, 2978m, 2932w, 1689s, 1579s, 1511s, 1417s, 1394s, 1244s, 1169m, 990s, 803m. ^{1}H NMR (500 MHz, DMSO, 70 °C): 9.94 (s, 4H), 7.65−7.55 (m, 8H), 7.18 (d, J = 7.7 Hz, 4H), 7.10−6.90 (br, 2H), 4.08 (d, J = 5.6 Hz, 4H), 1.38 (s, 18H). ^{13}C NMR (125 MHz, DMSO, 70 °C): 168.0, 163.6, 155.4, 136.7, 135.1, 133.8, 126.9, 121.2, 120.6, 77.4, 42.9, 27.9 (only 12 of the 13 expected resonances were observed). MS (ES): *m*/*z* 775.3 (15, $[M + H]^+$, $C_{36}H_{41}Cl_2N_{12}O_4$, calcd 775.2751).

Compound 2. Compound **1** (200 mg, 0.260 mmol) and ammonium hydroxide (1.80 g, 12.0 mmol) in DMSO (8.0 mL) were sealed in a 20 mL pressure tube, and the mixture was heated at 85 °C for 12 h. The reaction mixture was cooled to room temperature and poured into H_2O (40 mL). The precipitate was collected by centrifugation and dried under high vacuum. Flash chromatography (SiO_2, $CHCl_3$/CH_3OH/NH_4OH 9:1:0.05) gave compound **2** (165 mg, 0.220 mmol, 87%) as a white solid. TLC ($CHCl_3$/CH_3OH/NH_4OH 9:1:0.05): R_f 0.25. Mp: 163−166 °C. IR (KBr, cm^{-1}): 3396m, 2976w, 2928w, 1696s, 1603s, 1558s, 1500s, 1415s, 1366m, 1247m, 1166m, 810m. ^{1}H NMR (500 MHz, DMSO, 70 °C): 8.71 (s, 2H), 8.66 (s, 2H), 7.68 (d, J = 8.3 Hz, 4H), 7.61 (s, 4H), 7.12 (d, J = 8.3 Hz, 4H), 7.10−6.90 (br, 2H), 4.07 (d, J = 6.1 Hz, 4H), 1.40 (s, 18H). ^{13}C NMR (125 MHz, DMSO, 70 °C): 166.7, 164.3, 155.4, 138.7, 134.3, 133.0, 126.7, 120.2, 119.7, 77.4, 43.0, 28.0 (only 12 of the 13 expected resonances were observed). MS (ES): *m*/*z* 737.3 (100, $[M + H]^+$, $C_{36}H_{45}N_{14}O_4$, calcd 737.3748).

Compound 3. Compound **1** (170 mg, 0.220 mmol) was dissolved in a mixture of TFA (1.0 mL) and H_2O (1.0 mL) and heated at reflux for 10 h. The reaction mixture was cooled to room temperature, and precipitate was collected by filtration and dried on the frit for 3 d yielding **3** (150 mg, 0.200 mmol, 91%) as a white solid. Mp: > 300 °C. IR (KBr, cm^{-1}): 3037m, 2890m, 1740s, 1688s, 1595s, 1500s, 1365m, 1195s, 1146m, 841m, 724m. ^{1}H NMR (500 MHz, DMSO, 70 °C): 10.50 (br s, 4H), 8.19 (br s, 6H), 7.67 (d, J = 8.4 Hz, 4H), 7.59 (s, 4H), 7.18 (d, J = 8.4 Hz, 4H), 4.01 (s, 4H). ^{13}C NMR (125 MHz, DMSO, 70 °C): 158.9 (q, $^2J_{CF}$ = 34 Hz), 158.0, 152.5, 137.4, 133.6, 129.6, 129.0, 122.5, 121.4, 116.1 (q, $^1J_{CF}$ = 292 Hz), 41.8 (only 11 of the 12 expected resonances were observed). MS (ES): *m*/*z* 539.2 (100, $[M + H - 2TFA]^+$, $C_{26}H_{27}N_{12}O_2$, calcd 539.2380).

Compound 4. Compound **2** (120 mg, 0.160 mmol) was dissolved in a mixture of CH_2Cl_2 (1.2 mL) and TFA (1.2 mL) and stirred at room temperature for 2 h. The solvent was removed to give compound **4** (125 mg, 0.160 mmol, 100%) as a white salt. Mp: 106−109 °C. IR (KBr, cm^{-1}): 3122m, 2924m, 1682s, 1631s, 1508s, 1427s, 1204s, 1138s, 840m, 724m. ^{1}H NMR (500 MHz, DMSO, 70 °C): 9.50 (s, 2H), 9.44 (s, 2H), 8.19 (br s, 6H), 7.78 (d, J = 8.4 Hz, 4H), 7.64 (s, 4H), 7.37 (d, J = 8.4 Hz, 4H), 7.20−6.80 (br, 4H), 3.99 (s, 4H). ^{13}C NMR (125 MHz, DMSO, 70 °C): 163.1, 161.9, 161.6, 158.3 (q, $^2J_{CF}$ = 34 Hz), 139.3, 134.0, 128.8, 127.6, 121.3, 120.4, 116.2 (q, $^1J_{CF}$ = 292 Hz), 41.8. MS (ES): *m*/*z* 537.2 (25, $[M + H - 2TFA]^+$, $C_{26}H_{29}N_{14}$, calcd 537.2700).

Compound 5. Cyanuric chloride (735 mg, 3.96 mmol) was dissolved in anhydrous THF (15.0 mL) at 0 °C, and 4-(*N*-*t*-butoxycarbonylaminomethyl)aniline (900 mg, 4.05 mmol) and *N*,*N*-diisopropylethylamine (1.65 mL, 10.0 mmol) in THF (10.0 mL) were added to the solution. The mixture was stirred at 0 °C for 30 min, and then for another 1 h at room tempearture. After that, 1,5-diaminonaphthalene (290 mg, 1.83 mmol) was added, and the reaction mixture was stirred at room temperature for 72 h. The precipitate was collected by filtration and washed with THF (8.0 mL) and then cold water (25.0 mL). Compound **5** was obtained as a white solid after drying under high vacuum (870 mg, 1.05 mmol, 58%). Mp: > 300 °C. IR (KBr, cm^{-1}): 3282m, 2977m, 2928w, 1696m, 1573s, 1511s, 1392s, 1244m, 1167m, 994m, 803m. ^{1}H NMR (500 MHz, DMSO, 70 °C): 10.10 (s, 2H), 9.85 (s, 2H), 7.97 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 7.1 Hz, 2H), 7.57 (t, J = 7.9 Hz, 2H), 7.50−7.35 (br m, 4H), 7.20−6.90 (br m, 6H), 4.02 (s, 4H), 1.38 (s, 18H). ^{13}C NMR (125 MHz, DMSO, 70 °C): 168.2, 165.7, 163.5, 155.3, 136.8, 134.6, 133.5, 129.9, 126.7, 125.2, 124.0, 121.3, 120.0, 77.4, 42.9, 27.9. MS (ES): *m*/*z* 825.4 (100, $[M + H]^+$, $C_{40}H_{43}Cl_2N_{12}O_4$, calcd 825.2907).

Compound 6. Compound **5** (250 mg, 0.300 mmol) and ammonium hydroxide (2.00 g, 13.0 mmol) in DMSO (8.0 mL) were sealed in a 20 mL pressure tube, and the mixture was heated at 85 °C for 12 h. The reaction mixture was cooled to room temperature and poured into H_2O (40 mL). The precipitate was collected by centrifugation and dried under high vacuum. Flash chromatography (SiO_2, $CHCl_3$/CH_3OH/NH_4OH 9:1:0.05) gave compound **6** (195 mg, 0.24 mmol, 82%) as a white solid. TLC ($CHCl_3$/CH_3OH/NH_4OH 9:1:0.05): R_f 0.25. Mp: 165−169 °C. IR (KBr, cm^{-1}): 3396m, 3336m, 2977w, 2932w, 1696s, 1600s, 1570s, 1500s, 1411s, 1366m, 1166m, 811m. ^{1}H NMR (500 MHz, DMSO, 70 °C): 8.76 (s, 2H), 8.68 (s, 2H), 7.90 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 7.1 Hz, 2H), 7.60 (d, J = 8.3 Hz, 4H), 7.49 (t, J = 7.9 Hz, 2H), 7.04 (d, J = 8.3 Hz, 4H), 7.10−6.90 (br, 2H), 6.23 (s, 4H), 4.03 (d, J = 6.0 Hz, 4H), 1.39 (s, 18H). ^{13}C NMR (125 MHz, DMSO, 70 °C): 166.9, 166.1, 164.4, 155.4, 138.7, 134.9, 132.8, 130.2, 126.6, 124.8, 123.3, 120.2, 119.4, 77.4, 43.0, 28.0. MS (ES): *m*/*z* 787.3 (40, $[M + H]^+$, $C_{40}H_{47}N_{14}O_4$, calcd 787.3905).

Compound 7. Compound **5** (250 mg, 0.300 mmol) was dissolved in TFA (1.2 mL) and stirred for 1 h at room temperature. After H_2O (5.0 mL) was added, the solution was heated at reflux for 10 h. The

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reaction mixture was cooled to room temperature, and the precipitate was collected by filtration and dried on the frit for 3 d yielding **7** (185 mg, 0.230 mmol, 76%) as a white solid. Mp: > 300 °C. IR (KBr, cm^{-1}): 3440m, 3037m, 2885m, 1757s, 1684s, 1628s, 1600s, 1509m, 1204s, 1142m, 840m, 724m. ^{1}H NMR (500 MHz, DMSO, 70 °C): 10.80−10.20 (br, 2H), 9.20−8.40 (br, 2H), 8.12 (s, 6H), 8.05 (d, J = 8.4 Hz, 2H), 7.75 (d, J = 7.1 Hz, 2H), 7.65 (t, J = 7.9 Hz, 2H), 7.42 (br, 4H), 7.21 (br, 4H), 3.92 (s, 4H). ^{13}C NMR (125 MHz, DMSO, 70 °C): 159.2 (q, $^2J_{CF}$ = 34 Hz), 157.3, 151.6, 137.3, 132.3, 129.7, 129.2, 128.8, 125.7, 124.5, 121.7, 120.8, 116.1 (q, $^1J_{CF}$ = 292 Hz), 41.6 (only 14 of the 15 expected resonances were observed). MS (ES): *m*/*z* 589.2 (100, $[M + H - 2TFA]^+$, $C_{30}H_{29}N_{12}O_2$, calcd 589.2536).

Compound 8. Compound **6** (90 mg, 0.11 mmol) was dissolved in a mixture of CH_2Cl_2 (1.0 mL) and TFA (1.0 mL) and stirred at room temperature for 2 h. The solvent was removed to give compound **8** (95 mg, 0.11 mmol, 100%) as a white salt. Mp: 233−236 °C. IR (KBr, cm^{-1}): 3374m, 3125m, 2920m, 1685s, 1631s, 1608s, 1513s, 1429s, 1380m, 1198s, 1143s, 840m, 798m, 724m. ^{1}H NMR (500 MHz, DMSO, 70 °C): 9.55 (s, 2H), 9.41(s, 2H), 8.12 (s, 6H), 7.97 (d, J = 8.4 Hz, 2H), 7.75−7.65 (m, 6H), 7.57 (t, J = 7.9 Hz, 2H), 7.26 (d, J = 8.3 Hz, 4H), 7.20−6.80 (br, 4H), 3.95 (s, 4H). ^{13}C NMR (125 MHz, DMSO, 70 °C): 163.3, 162.2, 158.1 (q, $^2J_{CF}$ = 34 Hz), 139.3, 133.8, 130.2, 128.7, 127.3, 125.2, 124.0, 120.9, 120.0, 116.2 (q, $^1J_{CF}$ = 292 Hz), 41.8 (only 14 of the 15 expected resonances were observed). MS (ES): *m*/*z* 587.2 (20, $[M + H - 2TFA]^+$, $C_{30}H_{31}N_{14}$, calcd 587.2856).

Compound 9. After cyanuric chloride (228 mg, 1.24 mmol) was dissolved in anhydrous THF (15.0 mL) at 0 °C, mono-BOC-protected 1,5-diaminonaphthalene (320 mg, 1.24 mmol) and *N*,*N*-diisopropylethylamine (0.55 mL, 3.30 mmol) were added to the solution. The mixture was stirred at 0 °C for 30 min, and then for another 1 h at room temperature. After that, *p*-phenylenediamine (62 mg, 0.56 mmol) was added, and the reaction mixture was stirred at room temperature for 72 h. The precipitate was collected by filtration and washed with THF (5 mL) and then cold water (20 mL). Compound **9** was obtained as a white solid after dried under high vacuum (254 mg, 0.300 mmol, 53%). Mp: 290 °C (dec). IR (KBr, cm^{-1}): 3395m, 3282m, 2978w, 2928w, 1699m, 1560s, 1497s, 1409s, 1368m, 1239m, 1159m, 988m, 782m. ^{1}H NMR (500 MHz, DMSO, 70 °C): 10.10−9.90 (br s, 2H), 9.75−9.60 (br s, 2H), 9.01 (s, 2H), 7.99 (d, J = 8.4 Hz, 2H), 7.81 (d, J = 8.4 Hz, 2H), 7.70−7.40 (m, 8H), 7.35−7.15 (br. s, 4H), 1.51 (s, 18H). ^{13}C NMR (125 MHz, DMSO, 70 °C): 168.2, 165.7, 163.4, 153.8, 134.2, 133.5, 133.4, 129.9, 128.9, 125.3, 124.7, 123.8, 121.4, 121.2, 120.4, 119.8, 78.7, 27.9. MS (ES): *m*/*z* 847.3 (45, $[M + H]^+$, $C_{42}H_{41}Cl_2N_{12}O_4$, calcd 847.2751).

Compound 10. A solution of compound **9** (200 mg, 0.240 mmol) and ammonium hydroxide (1.8 g, 12 mmol) in DMSO (8 mL) was sealed in a 20 mL pressure tube. The mixture was heated at 85 °C for 12 h. The reaction mixture was cooled to room temperature and poured into H_2O (40 mL). The precipitate was collected by centrifugation and dried under high vacuum. Flash chromatography (SiO_2, $CHCl_3/CH_3OH/NH_4OH$ 9:1:0.05) gave compound **10** (130 mg, 0.160 mmol, 65%) as a pale-yellow solid. TLC ($CHCl_3/CH_3OH/NH_4OH$ 9:1:0.05): R_f 0.23. Mp: 171−173 °C. IR (KBr, cm^{-1}): 3394m, 3324m, 3227m, 2977w, 2932w, 1707m, 1600s, 1545s, 1495s, 1407s, 1367m, 1243m, 1161m, 1024m, 811m, 785m. ^{1}H NMR (500 MHz, DMSO, 70 °C): 8.97 (s, 2H), 8.68 (s, 2H), 8.51 (s, 2H), 7.89 (d, J = 8.4 Hz, 2H), 7.85 (d, J = 8.4 Hz, 2H), 7.63 (d, J = 7.2 Hz, 2H), 7.53 (d, J = 7.2 Hz, 2H), 7.50 (t, J = 7.2 Hz, 2H), 7.50−7.35 (m, 2H), 7.40 (s, 4H), 6.19 (s, 4H), 1.51 (s, 18H). ^{13}C NMR (125 MHz, DMSO, 70 °C): 166.9, 166.1, 164.3, 153.9, 135.1, 134.1, 133.9, 130.3, 129.0, 124.8, 124.7, 123.3, 121.3, 120.2, 119.8, 78.6, 27.9 (only 17 of the 18 expected resonances were observed). MS (ES): *m*/*z* 809.3 (100, $[M + H]^+$, $C_{42}H_{45}N_{14}O_4$, calcd 809.3748).

Compound 11. Compound **10** (100 mg, 0.120 mmol) was dissolved in a mixture of CH_2Cl_2 (1.0 mL) and TFA (1.0 mL) and stirred at room temperature for 2 h. The solvent was removed to give compound **11** (105 mg, 0.120 mmol, 100%) as a pale-yellow salt. Mp: 208−211 °C. IR (KBr, cm^{-1}): 3359m, 3171m, 3107m, 2917m, 1682s, 1616s, 1565s, 1507s, 1415s, 1356m, 1204s, 1137s, 841m, 785m, 724m. ^{1}H NMR (500 MHz, DMSO, 70 °C): 10.15−10.00 (br s, 2H), 9.90 (s, 2H), 8.06 (d, J = 8.4 Hz, 2H), 7.90−7.20 (br, 10H), 7.58 (d, J = 7.2 Hz, 2H), 7.50−7.40 (m, 4H), 7.35−7.25 (m, 6H), 6.88 (d, J = 7.2 Hz, 2H). ^{13}C NMR (125 MHz, DMSO, 70 °C): 159.6, 158.8, 158.2 (q, $^2J_{CF}$ = 34 Hz), 142.7, 133.6, 131.8, 130.3, 126.9, 124.2, 123.9, 123.2, 121.7, 121.3, 115.8 (q, $^1J_{CF}$ = 292 Hz), 111.6, 109.6 (only 16 of the 17 expected resonances were observed). MS (ES): *m*/*z* 609.2 (100, $[M + H - 2TFA]^+$, $C_{32}H_{29}N_{14}$, calcd 609.2700).

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Supporting Information Available: Selected NMR spectra for CB[*n*]·foldamer complexes, ^{1}H and ^{13}C NMR spectra for all new compounds, and details of the X-ray structures of CB[10]·**3**, CB[10]·**4**, CB[10]·**7**, and CB[7]·**7**·CB[7] (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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