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Halide Functionality Dependent Formation of Molecular Receptors and Their Ion Recognition Properties

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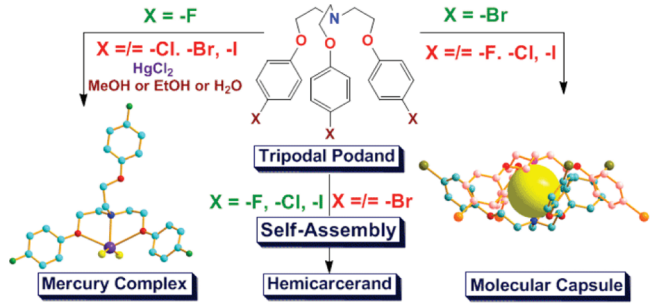
ABSTRACT



The halide functionality on *N*-bridged tripodal receptors has shown a distinct behavior on their self-assembly structures and binding ability toward $HgCl_2$ and ClO_4^- anions. The receptors containing fluoro, chloro, and iodo groups crystallized to form hemicarcerands in the solid state, whereas the receptor with a bromo group forms a molecular capsule via C−H···Br and C−H···π interactions. The cavity of the molecular capsule is tunable and is capable of reversible encapsulating-releasing the guest molecules by pH modulation.

Self-assembly is the fundamental feature of natural and biological processes with noncovalent interactions acting as tools to accomplish these tasks. Inspired by this biological phenomenon, self-assembly has become a key step for miniaturization of functional devices and the development of future nanotechnology.[1,2] The properties of a self-assembled "superstructure" depend upon the information encoded in individual components such as charge, magnetic dipole, polarizability, size, shape, and surface properties, etc. These characteristics determine the interactions among the components to accomplish such self-assembly processes and final products.

Podands, cavitands, hemicarcerands, and capsules are interesting members of the receptor family,[3] where the confined interior space (or cavity) formed either by self-assembly of the monomeric unit through noncovalent interactions or by the metal−ligand coordination bond has

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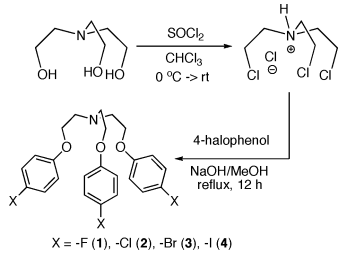
been employed for various applications.[4] The dynamic nature of self-assembled molecular receptors has also been studied in depth for its potential applications, such as molecular or drug delivery[5] and molecular catalysis.[6]

Mercury and its salts (such as $HgCl_2$) are highly toxic and environmentally hazardous pollutants because of their physical existence in all three forms (solid, soluble in water, and gaseous state) and readiness to release into biological cycles.[7] During the course of searching for effective ion recognition receptors, we have synthesized a series of podands bearing different halide functionality (Scheme 1). We envisioned that

Scheme 1. Synthesis of Tripodal Podands



incorporating various halides to the framework of a tripodal podand would modulate the binding angle toward Hg(II) via the inductive effect exerted by the halides with different degrees of electronegativity. The different sizes of the halides are expected to impart a steric requirement during the crystallization and result in different macroscopic packing outcomes. Moreover, the flexible nature of the podand structure also increases the possibility of modulating the guest binding with external stimuli such as pH. Herein, we report the synthesis and the effect of halide substitution at the para postion of aromatic rings of a *N*-bridged tripodal podand on the self-assembly process and its binding ability for $HgCl_2$ and the unexpected discovery of proton-assisted binding for ClO_4^- anions.

The studied podands were synthesized by simple S_N2 substitution of their corresponding phenols on tris(2-chloroethyl)amine hydrochloride, obtained by condensation of commercially available triethanolamine with $SOCl_2$. These receptors have been fully characterized by ^1H NMR, ^{13}C NMR, high-resolution mass spectrometry, and single-crystal X-ray diffraction. The single crystals of these receptors suitable for X-ray diffraction studies were obtained by slow evaporation of their methanolic solution at room temperature over a period of 1−2 days.

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Receptors **1**, **2**, and **4** crystallized with rhombohedral symmetry, forming hemicarcerands through self-assembly in the solid state. Their patterns of intermolecular interactions, however, are different. The crystal packing diagram of receptor **1** shows that the structures are stabilized through weak C−H···O interactions ($d_{C-H\cdots O}$ 2.52 Å). In receptor **2**, molecules are stabilized through C−H···Cl and C−H···π interactions, respectively. Each arm of the tripodal unit is linked with its neighboring unit by aliphatic C−H···Cl interactions ($d_{C-H\cdots Cl}$ 2.90 and 3.03 Å) in the same plane and through aromatic C−H···Cl interactions ($d_{C-H\cdots Cl}$ 2.91 Å) with molecules in the adjacent plane.[8] In receptor **4**, molecules are stabilized through aliphatic and aromatic C−H···π interactions (Figure 1). In all three receptors (**1**, **2**, and **4**),

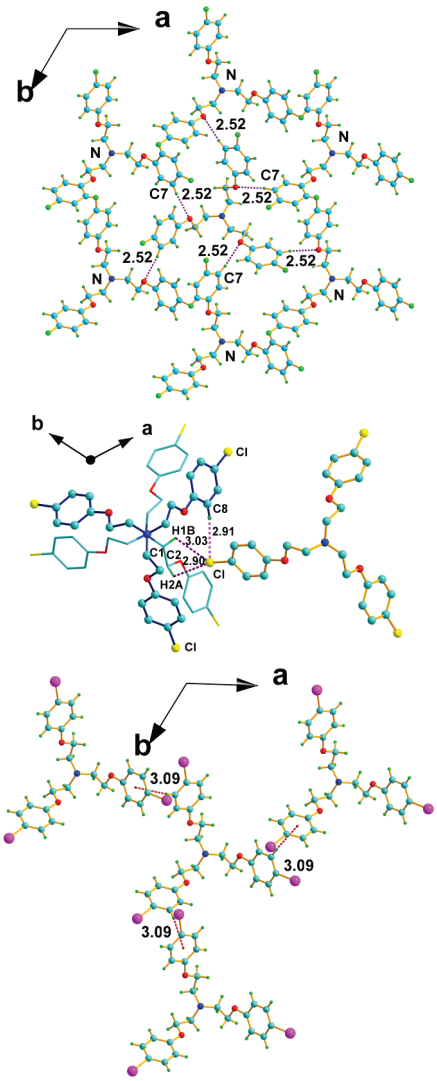

Figure 1. Crystal structure of **1** (top), **2** (middle), and **4** (bottom), showing pattern of intermolecular noncovalent interactions in their crystal packings.

each tripodal unit is surrounded by six other ligands (see the Supporting Information) occupying a chair conformation. The shortest N···N distance in the 1D plane (along *c*-axis) is

11.06, 13.32, and 12.85 Å in the crystal structures of **1**, **2**, and **4**, respectively.

In crystal structure **3**, however, two tripodal units self-assemble to form a molecular capsule ($\mathbf{3}_2$) via intermolecular C−H···π and C−H···Br interactions. Like receptors **1**, **2**, and **4**, each tripodal unit of **3** is hexagonally surrounded by six other ligands forming a chair conformation (Supporting Information). Each of the two molecules of **3** in the crystal structure is stabilized in a staggered conformation. Two units of **3** are flipped inward toward each other in a face-to-face fashion ($d_{N1\cdots N1}$ 4.17 Å) and held together via C−H···π interactions ($d_{C-H\cdots\pi}$ 3.27 Å, Figure 2b) from the ortho C−H

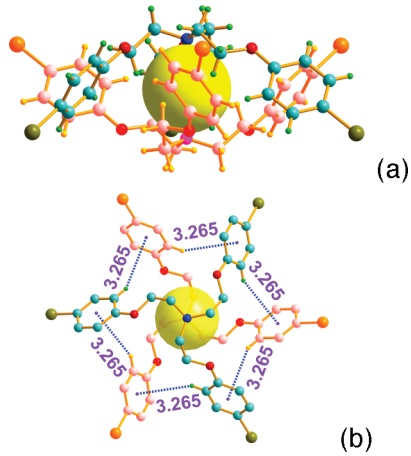

Figure 2. Illustration of the crystal structure of molecular capsule $\mathbf{3}_2$. (a) Lateral view of molecular capsule (each half of capsule is shown by different color) and (b) front view of molecular capsule showing each arm of capsule is in staggered form to each other.

of the aromatic ring, creating a cavity inside the capsule. Three types of interactions are present in the crystal packing: (a) C−H···π interactions, (b) C−H···Br interactions, and (c) π···π interactions. One arm of each half of molecular capsule is linked with that of a neighboring capsule (through π···π stacking, $d_{\pi\cdots\pi}$ 3.72 Å) to form a 1D helical chain, and the remaining two arms of each half are linked with a lateral neighboring capsule to form an overall 3D network. The molecular capsule is stable in MeCN solution as confirmed by the ESI-mass spectrum (*m*/*z* 1228.86) and ^{1}H NMR spectrum. Figure 3 shows the ^{1}H NMR spectrum recorded after 10 h of dissolving the crystals of $\mathbf{3}_2$ (molecular capsule form) in CD_3CN at 293 K. It is clear to see that an equilibrium was established between the capsule form and the monomeric form with a dissociation constant of ca. 8.8 M at 293 K.

The binding ability of these tripodal receptors has been explored for Hg(II) and $HgCl_2$. Interestingly, only the podand having a fluoro functional group (**1**) was found to bind with $HgCl_2$ to form a mercury complex (**1a**) (Figure 4). Other receptors (**2**, **3**, and **4**) in the presence of $HgCl_2$ only crystallized to give **2**, **3**, and **4**, respectively. The excellent solubility of the mercury complex (**1a**) in MeCN (insoluble in $CHCl_3$, MeOH, and acetone) allowed us to perform ^{1}H

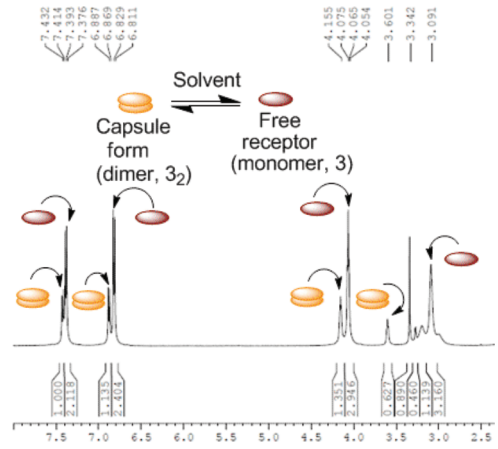

Figure 3. ^{1}H NMR spectrum (400 MHz) recorded after 10 h of dissolving crystals of the molecular capsule ($\mathbf{3}_2$, 3.18 × 10^{-2} M) in CD_3CN at 293 K. The orange circles represent the peaks from the molecular capsule ($\mathbf{3}_2$) and the brown circles represent the peaks from the open form (free receptor **3**).

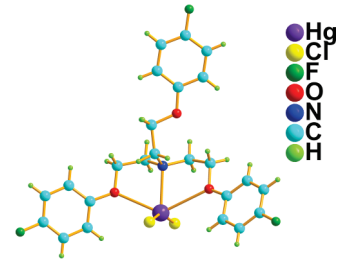

Figure 4. Crystal structure of mercury complex (**1a**) obtained after complexation of receptor **1** with $HgCl_2$.

NMR titrations (Figure 5). The titration results showed that receptor **1** selectively associated with $HgCl_2$ with an association constant of 35 M^{-1} at 293 K. Although receptor **1** also interacted with Cd(II) and Zn(II), the Cd(II) and Zn(II) ions exhibited tendency to bind with water present in deuterated solvent and these complexes were not stable in solution (see the Supporting Information).

^{1}H NMR titration of receptor **3** with $HgCl_2$ showed surprising results. After addition of 0.3 equiv of $HgCl_2$ to **3** in CD_3CN, each peak shifted slightly downfield to peaks in the aromatic region as well as in the aliphatic region (Figure 5, top) along with the appearance of small new peaks in the downfield positions next to the major peaks. Although the pattern of peak shifting in the aliphatic region was similar to the titration studies of **1** with $HgCl_2$, the peak near 3.0 ppm became broad with increasing equivalents of $HgCl_2$. The new peaks in the aromatic and aliphatic regions are similar to the spectrum corresponding to the molecular capsule form, as shown in Figure 3, that was acquired by directly dissolving crystals of $\mathbf{3}_2$ (molecular capsule) in CD_3CN. This result indicates that three species (**3**, $HgCl_2$ adduct of **3** and molecular capsule, $\mathbf{3}_2$) were in equilibria during the course of ^{1}H NMR titrations. This result also

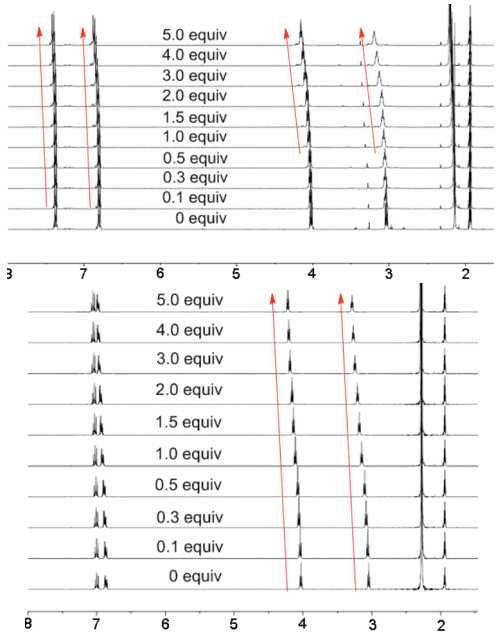

Figure 5. ^{1}H NMR spectra (400 MHz) of tripodal podand **3** (1.59×10^{-2} M, top) and **1** (1.27×10^{-2} M, bottom) titrated with solution of $HgCl_2$ in CD_3CN at 293 K.

signifies that the rate of capsule formation is in competition to the complexation of **3** with $HgCl_2$. Perhaps this is the reason why only crystals of the molecular capsule ($\mathbf{3}_2$) were obtained during the crystallization of **3** with $HgCl_2$.

The binding ability of molecular capsule ($\mathbf{3}_2$) toward environmentally hazardous perchlorate anion has also been studied in the solid state. The crystal of the anionic complex (**3a**), suitable for single X-ray diffraction, was obtained by slow evaporation of $CHCl_3$ layer of molecular capsule ($\mathbf{3}_2$) after extraction with dilute perchloric acid. Single crystal analysis showed that the centrally bridged *N*-atoms of **3** were protonated and the two perchlorate anions were sandwiched between them (Figure 6) via electrostatic interactions.[9] The

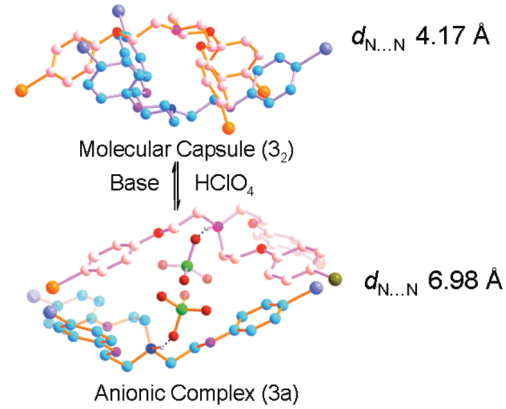

Figure 6. pH-modulated reversible exchange between molecular capsule $\mathbf{3}_2$ (top) and its anion complex **3a** (bottom). Each half is shown by a different color, and all H-atoms (except for N···H) have been removed for clarity.

distance between the centrally bridged *N*-atoms in anionic complex (**3a**) is 6.98 Å. The crystal of molecular capsule ($\mathbf{3}_2$) was recovered by slow evaporation of a $CHCl_3$ layer of anionic complex (**3a**) after washing with H_2O/Et_3N solution.

In conclusion, we have demonstrated that the formation of molecular receptors of different topology can be manipulated by simply varying the halide substitution on the *N*-bridged tripodal podand. We have also introduced a simple strategy to assemble a molecular capsule with an interior hydrophobic cavity based on arrays of C−H···π and C−H···Br interactions. The aliphatic chain and tertiary *N*-atom provide opportunities to modulate the cavity size of the capsule, and it is also possible to make it water soluble by incorporating suitable functionality. Further research working to explore applications of molecular capsules of this kind is in progress.

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Supporting Information Available: Detailed experimental procedures, spectra, and single-crystal X-ray crystallographic files (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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