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Guest-Induced Folding of the *N*-Benzyl Substituents in an Ammonium Resorcinarene Chloride and the Formation of a Halogen-Bonded Dimer of Capsules

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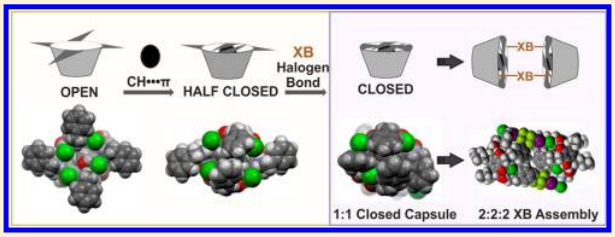
Supporting Information

ABSTRACT: In methanol, *N*-benzyl ammonium resorcinarene chloride (Bn-NARCl) crystallizes as a solvate with the benzyl groups oriented in an open flower-like manner parallel to the cation−anion seam. 1,4-Dioxane as guest triggers a "semi-closed" single-molecule capsule with two benzyl "arms" enclosing the guest. The introduction of halogen bond (XB) donor 1,4-diiodoperfluorobutane (1,4-DIOFB) additionally folds the remaining two benzyl arms thus resulting in a fully closed capsule. Two 1,4-DIOFB molecules bridge two such Bn-NARCl capsules, forming a 2:2:2 XB held dimeric assembly of single-molecule capsules. The peculiar behavior was not observed in the bromide analog under similar experimental conditions. The studies were performed in solid state by X-ray single crystal crystallography, and MM level theoretical calculations.



INTRODUCTION

Thermodynamically disfavored conformations play an important role in supramolecular self-assembly processes.[1−3] They are the foundation of its applications in many fields such as organic syntheses,[4,5] ion transport,[6,7] and materials science.[8,9] Since supramolecular self-assembly processes are supported mainly by weak noncovalent interactions that are sensitive to the environment, the precise control of the desired supramolecular aggregations is still a challenge.[10] Many external stimuli such as light, electrons, temperature, pH, and ions have been used to trigger molecular geometry changes.[11−13] Noncovalent interactions sometimes act as external stimuli in supramolecular self-assembly processes.[14−16] Molecular tweezers, first coined by Whitlock and Chen in the 1970s, usually consist of receptors with two binding sites, separated by a flexible spacer.[17] There are numerous receptors with tweezer-like behavior[18,19] and applications of molecular tweezers span chemistry, biology, and physics.[20,21]

Resorcinarenes in their C_{4v} conformation are receptors with concave cavities capable of binding small molecules.[22,23] The *N*-alkyl ammonium resorcinarene salts (NARXs) can act as receptors and/or molecular synthons for the design and construction of larger assemblies.[24−27] They possess a strong circular hydrogen bond (HB) seam $(\cdots NR'R''H_2^+\cdots X^-\cdots)_4$ between the ammonium cations and the halide anions. Previous studies show the NARXs to be versatile receptors for neutral and ionic guests as well as suitable multivalent halogen bond (XB) acceptors.[28−32]

The cavity size and complexation ability toward guests is largely influenced by the nature of the upper rim substituents.[28−32] The upper rim substituents also influence the halogen-bonded architectures.[28−32] The benzyl (Bn) group introduces a degree of flexibility to the upper rim of NARX receptors.[28,31,32] However, there has been no comparative study of the behavior of the flexible benzyl groups with different anions and/or guests. In principle, chloride and bromide are different in their abilities to participate in HBs and XBs. Generally, chloride is a better HB acceptor than bromide due to its stronger electronegativity; therefore, properties such as XB acceptor within the cation−anion seam are reduced by the relatively strong HBs making the bromide analogs of the NARXs better XB acceptors. In addition, the smaller size of the chloride coupled with the flexibility of the benzyl group could lead to potentially unpredictable properties.

In this contribution, we investigate the geometric features of the Bn-NARCls (**1a**, **1b**) in the presence of solvent and guest molecules. As a comparison, the structures of the Bn-NARBr **2** under similar conditions were also studied (Figure 1). In the few reported structures, the Bn-NARXs form open assemblies where the benzyl groups are oriented outward and parallel to the cation−anion seam in different solvents.[25,31,32] However, in the presence of 1,4-dioxane as a suitable guest, while the

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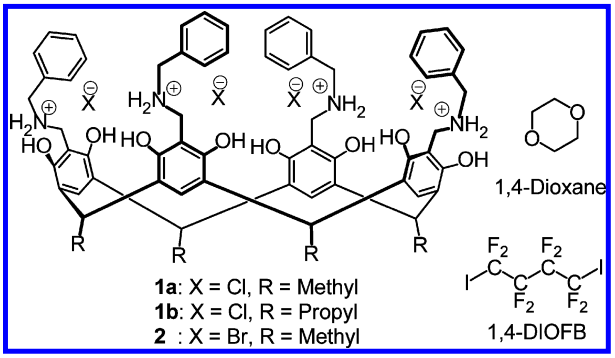

Figure 1. *N*-Benzyl ammonium resorcinarene halides (**1**,**2**), 1,4-dioxane as guest, and 1,4-diiodooctafluorobutane (1,4-DIOFB) as the divalent halogen bond donor.

bromide analog forms a 1:1 host−guest complex with the usual open skeleton, the chloride analog exhibits a tweezer-like behavior, whereby two of the four benzyl arms fold upward to completely enclose the guest resulting in a single-molecule host−guest capsule. The single-molecule host−guest capsule in the presence of 1,4-diiodoperfluorobutane (1,4-DIOFB), a divalent XB donor, forms an XB dimer of capsules. The results were analyzed by single crystal X-ray diffraction, and supported by MM level theoretical modeling.

RESULTS AND DISCUSSION

Structures of Bn-NARBr and Bn-NARCl with water or 1,2-dichloroethane and Bn-NARBr with 1,4-dioxane were previously reported.[25,31,32] In all the reported structures, the benzyl groups are oriented outward from the cavity parallel to the cation−anion seam resembling an open rose-flower with a broaden internal cavity. Intermolecular π-interactions between the phenyl groups from adjacent resorcinarenes or between the phenyl rings and the π-systems from the other components of the structure are generally responsible for the molecular aggregations.

Previously, the outward conformational orientation of the benzyl groups in Bn-NARXs was explained as a result of the flexible $-CH_2$ and packing in the solid state. A closer investigation reveals that, in addition to the above factors, the $-CH_2$ groups at the γ-position form intramolecular $-CH\cdots\pi$ interactions with the phenyl moiety when it folds down, thus pointing outward from the resorcinarene cavity (Figure S3). Single crystals for Bn-NARCl **1a** without 1,4-dioxane (Figure 2A) and Bn-NARBr **2** with 1,4-dioxane (Figure 2B) from methanolic solution were obtained via slow evaporation. The two compounds (MeOH@**1a** and 1,4-dioxane@**2**) crystallize with the Bn-NARX in the regular open conformation (Figure 2 and Figure S2). All the benzyl groups are oriented outward and parallel to the cation−anion seam with intramolecular γ-CH$\cdots\pi$ and intermolecular $\pi\cdots\pi$ interactions. The latter interactions further stabilize the structures extending the assembly into 1-D along the crystallographic *a* direction in MeOH@**1a** and the *c* direction in 1,4-dioxane@**2**.

Crystallization of **1a** in a mixture of MeOH and $CHCl_3$ with a few drops of 1,4-dioxane as the guest gave suitable single crystals. The compound crystallizes in monoclinic space group *C*2/*c*. A twofold axis runs through the center of the resorcinarene cavity, the 1,4-dioxane molecule, as well as the water molecule in between the methyl groups of the resorcinarene lower rim. The four OH···O hydrogen bonds between adjacent hydroxyl groups and circular $(H-N-H\cdots Cl^{-}\cdots H-N-H\cdots Cl^{-})_2$ hydrogen-bonded seam preserve the hereditary bowl shape of **1a** in this structure (Figure 3). Additionally, NH···O hydrogen bonds trap the 1,4-dioxane molecule into the cavity. Interestingly, and distinctly different from the previously observed conformation of the upper-rim benzyl groups, two of the four benzyl groups in this structure undergoes a 180° rotation around the N−C bonds, subsequently capping the cavity leading to a single-molecule host−guest capsule (Figure 3). Careful examination of the structure reveals short CH···benzyl contacts between the encapsulated 1,4-dioxane guest and the two folded benzyl groups (Figure 3). We propose weak $CH_{(1,4\text{-dioxane})}\cdots\pi_{(\text{upward-folded benzyl})}$ interactions between the guest and host to be responsible for this conformation. A water molecule sits in the center of the lower rim methyl groups of **1a** and interacts with two chloride anions of the adjacent host via hydrogen bonds, thus extending the assembly in *ab* plane (Figure S1b). An extra *exo*-cavity 1,4-dioxane and $CHCl_3$ molecules are also present in this structure thus completing the structural lattice. The other two benzyl groups are oriented outward and parallel to the cation−anion seam as in previously observed structures,[25,31,32] making the behavior of

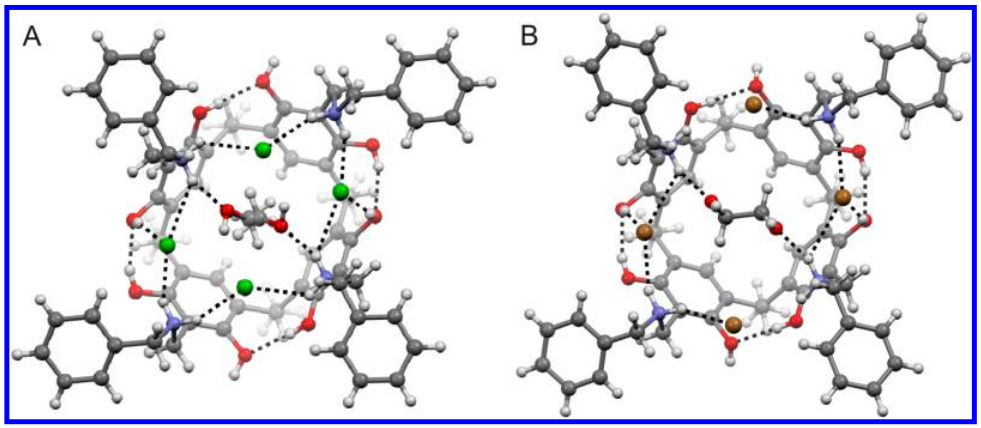

Figure 2. Ball-and-stick representation (top view) of the X-ray structure showing the "open" conformations of the Bn-NARCl in MeOH@**1a** (A) and Bn-NARBr in 1,4-dioxane@**2** (B). Hydrogen bonds are shown as dotted black lines.

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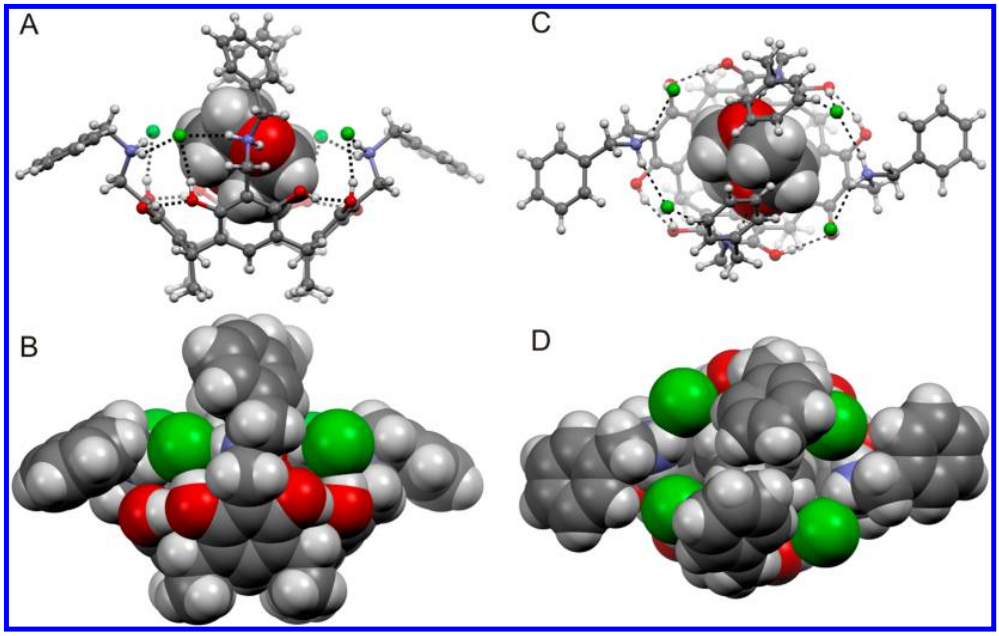

Figure 3. X-ray structure showing the "closed" conformation of Bn-NARCl in the single-molecule host–guest capsule 1,4-dioxane@**1a**. (A) Side view and (C) top view of the ball-and-stick representation with the guest in CPK mode. (B) Side view and (D) top view of the CPK representation of the capsule. Hydrogen bonds are shown as dotted black lines.

the two benzyl groups capping the capsule more surprising (Figure S1a).

The appearance of the unexpected conformer of the host in the structure of 1,4-dioxane@**1a** is somewhat surprising. Theoretical calculations were performed to examine the gas-phase energy of each equilibrium conformer. MM level[33] calculations with MMFF method showed the energy difference between the regular open conformer and the unexpected semiclosed conformer to be 34.4 kcal/mol in **1a**. This energy difference was also very large when adding one MeOH molecule into the cavity. However, it reduced to only 10.3 kcal/mol for 1,4-dioxane@**1a**. We propose that this is the result of the CH···π interactions between the 1,4-dioxane and the folded-up benzyl group. Accordingly, these calculations indicate that when one 1,4-dioxane molecule occupies the cavity and interacts with the folded-up benzyl groups, the unexpected folded conformation of **1a** is no longer thermodynamically unfavorable. The same modeling was also performed for the bromide receptor **2**. Although the results showed a similar trend, we found that in the case of 1,4-dioxane@**2**, the $CH_{(1,4\text{-dioxane})}\cdots\pi_{(\text{upward-folded benzyl})}$ contact is longer than in the chloride analog, and the energy difference between the open and semiclosed conformations in the bromide analog is also bigger than for the chloride receptor. All the numerical results have been documented in Table S2 (see Supporting Information). It should be noted that one cannot rely too much on the MM level calculations for the very weak intermolecular interactions analysis. However, in this particular case, they very well support the phenomena and our proposed explanations from the X-ray crystal structures. The combined analysis enabled us to conclude that the CH···π interactions between the encapsulated 1,4-dioxane guest and the benzyl groups play important roles in the formation of the unexpected folded conformer in 1,4-dioxane@**1a**.

The use of preorganized molecular entities to construct novel and desired architectures is one of the major aims of contemporary structural, supramolecular, and material chemistry. Recently, we reported a halogen-bonded dimeric capsule from *N*-cyclohexyl ammonium resorcinarene chloride and elemental I_2, with the encapsulation of three 1,4-dioxane molecules.[30] A series of halogen-bonded networks involving several *N*-alkyl ammonium resorcinarene halides and 1,4-DIOFB in the solid state and in solution were also recently reported.[32] Therein, the XB assembly between 1,4-DIOFB (1,4-diiodooctafluorobutane) and 1,4-dioxane@NARBr was studied, which showed an interesting "dumbbell"-like assembly with all the benzyl groups oriented outward and parallel to the cation–anion seam.[32]

Herein, the folded, single molecule capsule, 1,4-dioxane@**1b** as a unidirectional multivalent XB acceptor and 1,4-DIOFB as a divalent XB donor were utilized to construct a new XB assembly, and to probe how the XB donor (bromide or chloride) can affect the folding behavior of the benzyl groups. In the presence of the XB donor 1,4-DIOFB, the two 1,4-DIOFB molecules interact with two chlorides in each 1,4-dioxane@**1b** capsule resulting in an XB-linked dimer of host–guest capsules (1,4-dioxane@**1b**)·(1,4-DIOFB)$_2$·(1,4-dioxane@**1b**) (Figure 4), where the structure of the single molecule capsule 1,4-dioxane@**1b** is retained and acts as a part of the dimer (Figure 4).

The formation of the XB assembly also had an influence on the final host–guest complex. All four benzyl groups fold up resulting in a fully closed assembly (Figures 4 and 5). The folding of the remaining two benzyl groups could be a result of the steric hindrance and structural packing. Intramolecular CH···π interactions between the encapsulated 1,4-dioxane and two opposite benzyl rings are maintained in this XB assembly. Due to the asymmetrical geometry of the resorcinarene frame, the circular hydrogen-bonded cation–anion seam is broken with the breach compensated by the tilted benzyl group; thus, one of the $-NH_2$ hydrogen atoms points outward from the cavity. This out-of-seam chloride is also hydrogen-bonded to

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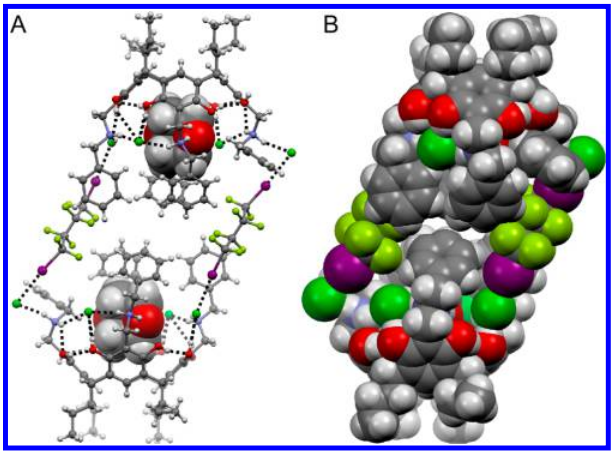

Figure 4. X-ray structure of halogen-bonded dimer of capsules (1,4-dioxane@**1b**)·(1,4-DIOFB)$_2$·(1,4-dioxane@**1b**) assembly showing the "closed" conformation of Bz-NARCl.

the hydroxyl group of the neighboring **1b**, thus connecting the assembly into a 1D polymer along the crystallographic [1 0 1] direction (Figure S4).

CONCLUSIONS

In conclusion, in the presence of 1,4-dioxane as a guest, two benzyl arms of Bn-NARCl **1**, undergo 180° folding around the N−C bonds in a tweezer-like manner to enclose the cavity of the receptor, resulting in a single-molecule host−guest capsule. This peculiar behavior is only realized with the chloride analog and only in the presence of 1,4-dioxane as the guest. The systematic investigation of the X-ray structures of 1,4-dioxane@**1a**, MeOH@**1a**, and 1,4-dioxane@**2** coupled with MM-level theoretical calculations explains the behavior of **1a** and **2** that present different conformers induced by guest molecules. The smaller size of the chloride anion, its stronger hydrogen bond affinity and the weak CH···π interactions observed between the encapsulated 1,4-dioxane and the folded-up benzyl rings manifest themselves as the driving force that overcomes the usual intramolecular γ-CH···π interactions in the regular "open" form. The divalent XB donor, 1,4-DIOFB, was used to connect the two single-molecule capsules into a 2:2:2 XB dimer. The introduction of the XB donors, leads to the transformation of the "semi-closed" host molecule **1a** to a "fully closed" form in the final XB assembly (Figure 5). Supramolecular chemistry is generally governed by thermodynamics. However, under certain conditions, molecules can distort into thermodynamically nonequilibrium conformations. It is therefore quite interesting to observe the uncommon folded conformation of the Bn-NARCl **1**. These CH···π and XB induced conformational changes could thus be added to the interactions tool box in host−guest chemistry and molecular devices.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.cgd.6b01454.

X-ray crystallography and geometry from modeling at MM level (PDF)

Accession Codes

CCDC 1488064−1488067 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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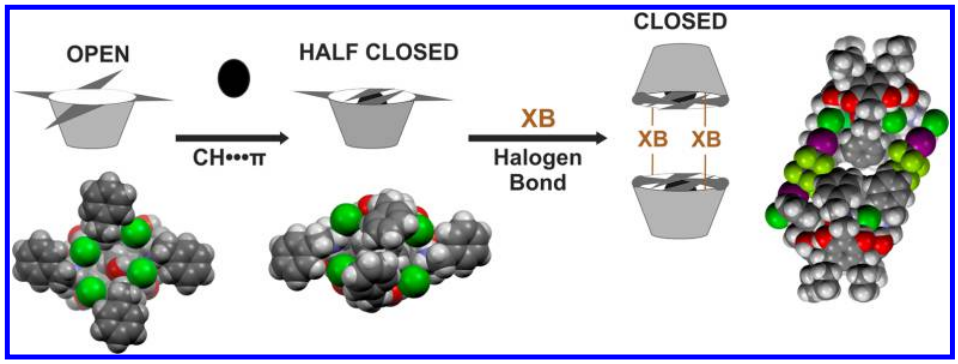

Figure 5. Overview of the process leading to the 1:1 single-molecule host−guest capsule and the 2:2:2 halogen-bonded dimer of single-molecule capsules.

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