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ARTICLE *in* THE JOURNAL OF PHYSICAL CHEMISTRY A · APRIL 2013

Impact Factor: 2.69 · DOI: 10.1021/jp3113478 · Source: PubMed

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Anion-Binding Properties of π-Electron Deficient Cavities in Bis(tetraoxacalix[2]arene[2]triazine): A Theoretical Study

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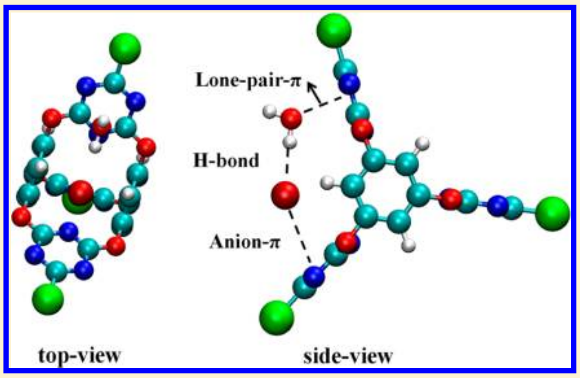
Supporting Information

ABSTRACT: The anion recognition by synthetic host molecules is an important theme in supramolecular chemistry. Bis(tetraoxacalix[2]arene[2]triazine) is a conformationally rigid cage molecule with three V-shaped clefts, each constituted by two electron-deficient triazine rings and two aryl C−H moieties. Its halide-binding properties are investigated in this work by quantum chemistry methods. The calculated Gibbs free energies display similar trends as the experimental observations. It has been shown that different types of noncovalent interactions including H-bond, anion−π, and lone-pair−π interactions are concurrent, leading to a cooperative effect. The respective contributions of the interactions to the overall stability are evaluated by using appropriate reference systems, with the anion−π interactions found to be as significant as the hydrogen bond interactions. In addition, in the presence of a water molecule, the stability of the ternary complexes has enhanced greatly in comparison with the binary complexes. Investigations of the solvent effect by the continuum solvent model show that the anion binding energies decrease with increasing solvent polarities. The weak halide binding energies in solution indicate that the reversible binding interactions with bis(tetraoxacalix[2]arene[2]triazine) can offer potential applications for anion transport in the membrane environment.



1. INTRODUCTION

Anion recognition by synthetic electron-deficient aromatic molecules has attracted renewed interests due to the key roles anions play in many chemical and biological processes,[1−7] and the involvement of aromatic rings in anion binding and transport in highly selective anion receptors and channels.[8] One of the biggest challenges in this regard is to design hosts that recognize specific anions. Various types of noncovalent interactions including hydrogen bond interactions, electrostatic interactions, and metal ion coordination, have been utilized over the years to establish anion recognition systems. In close analogy to the widely studied cation-π interaction,[9] noncovalent forces between anions and electron-deficient aromatic rings with positive quadrupole moments, designated as "anion−π" interaction,[10] are unearthed.[8,10−22] This noncovalent force, which is dominated by the electrostatic interaction and the anion-induced polarization,[10,13,23,24] has been shown to be energetically favorable by numerous theoretical[11,13,14,24−27] and experimental studies.[11,28−34]

Evaluation of the crystal structures of anion-arene adducts, high-level electronic structure calculations, as well as experimental evidence have revealed four distinct binding modes of anions to multiple arene bonding motifs: (i) strong σ-type interaction in which the anion attacks a partially positive aromatic carbon, changing the hybridization of arene-C to sp^3; (ii) weak σ-type interaction, where the anion is located over the periphery of the aromatic ring, and the charge transfer between the anion and the aromatic ring exists; (iii) anion−π interaction, involving primarily the electrostatic interaction between the anion and the positive quadrupole moment of the electron-deficient arene, and the anion-induced polarization of the arene; and (iv) hydrogen bond (H-bond) interaction between the aryl C−H donor and the anion.[18,35−37] To judge whether it is anion−π or weak σ-type interaction, we need a criterion other than geometry to distinguish the type of interactions. From the electronic structure calculations it is possible to render electron density isosurfaces, which can serve to locate atoms, delineate covalent bonds, or indicate overall molecular size and shape.[38] Hay et al.[18] proposed that the maximum electron density in the region between the anion and the aromatic ring ρ_{max} can serve as a measure of the degree of covalency: ρ_{max} is <0.012 e Å^{-3} for noncovalent anion−π interaction, 0.012 e Å^{-3} < ρ_{max} < 0.1 e Å^{-3} for weakly covalent σ interaction, and ρ_{max} > 0.1 e Å^{-3} for strongly covalent σ interaction. The aryl C−H groups can serve as hydrogen bond donors, and it is generally believed that C−H groups form much weaker hydrogen bonds than conventional donor groups such as O−H and N−H. However, both theory and experiment

Received: November 16, 2012
Revised: April 11, 2013
Published: April 11, 2013

show that aryl C−H groups form moderate to strong hydrogen bonds with anions, suggesting that these interactions play an important role in anion recognition. An experimental study shows that anions prefer to hydrogen bond to the remaining H atoms in $C_6F_nH_{6-n}$,[22] rather than bind to the positively charged ring. And bifurcated hydrogen bonds to two neighboring C−H groups are energetically favored over the linear hydrogen bond to a single C−H group.

Interactions of the electron-deficient neutral arenes with anions, including 1,3,5-triazine, hexafluorobenzene, 1,3,5-tricyanobenzene, and 1,2,4,5-tetracyanobenzene have been characterized. Charge distribution in these model systems is tuned by substitution of the aryl H atoms with electron-withdrawing groups, and positive partial charges on the carbon atoms can be achieved. On top of that, new host architectures tailered for specific guests are designed and synthesized. Among these, heteroatom-bridged heteroaromatic calixarenes that contain oxygen-bridged electron-deficient triazine rings, represent a novel type of macrocyclic molecules with emerging importance in the field of supramolecular chemistry.[8] These calixarenes exhibited unique electronic properties, and adopted different conformations to show varying degrees of conjugation with adjacent heteroaromatic rings, resulting in heteroaromatic calixarenes with dimensions, conformations and sizes different from conventional calixarenes. Recent theoretical studies have reported anion binding by calixarenes in gas phase[37] and in CH_2Cl_2.[39] Wang et al.[40] devised a conformationally rigid macrocyclic molecule containing three electron-deficient V-shaped clefts and explored its interactions with halides. They observed multitypes of noncovalent interactions in the solid state, and a formation of 1:1 complexes with halides in acetonitrile. Due to weak anion binding energies in solution,[16] it is challenging to accurately quantify these interactions either experimentally or theoretically. Because different types of noncovalent interactions coexist in neutral host−guest systems, the strength of anion−π interactions is usually indirectly detected as a modulation of the stronger hydrogen bond interactions. In this work, we present a theoretical study on bis(tetraoxacalix[2]arene[2]triazine) (**1**)[40] (Figure 1) to address its halide binding properties and selectivity by considering geometries and energies of $1/X^-$ and $1/(X^-{\bullet}H_2O)$ (X^- = F^-, Cl^-, and Br^-) in the gas phase and in solution. The solvent effect on the stability of the host−guest systems is examined by considering four solvents of different polarities: $CHCl_3$, CH_3COCH_3, CH_3CN and H_2O. With the help of electronic structure calculations, the ambiguity in distinguishing between different types of interactions is resolved, and new insight into the interplay between the noncovalent interactions has been gained.

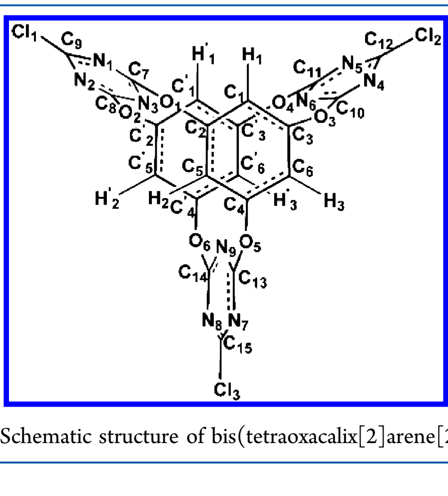


Figure 1. Schematic structure of bis(tetraoxacalix[2]arene[2]triazine).

2. COMPUTATIONAL DETAILS

The electronic structure calculations in this work were mainly carried out by the *Gaussian 09* package.[41] The characterization of weak noncovalent interactions is a challenging task. The long-range corrected hybrid density functionals have been shown to be accurate in characterizing noncovalent interactions, when compared with conventional hybrid density functionals. The recently developed ωB97XD functional with long-range correlation[42,43] was used in conjunction with the 6-31++G** basis set for full geometry optimizations without any symmetry constraints. Normal modes analysis were performed at the same level of theory to ensure that the optimized structures correspond to a true minimum (see the Supporting Information). To reinforce the results calculated by the ωB97XD/6-31++G** method, the second-order Möller-Plesset perturbation theory within the approximation resolution of identity (RI-MP2)[44] implemented in the Turbomole package (version 6.3)[45] and the correlation consistent double-ζ basis set (cc-pVDZ)[46] were also applied for geometry optimizations and binding energy calculations. In order to ascertain the effect of the incompleteness of the basis set on interaction energies, the basis set superposition error (BSSE) is usually corrected for by the counterpoise method of Boys and Bernadi.[47] The counterpoise correction, however, is known to often overestimate the error for finite basis set.[48] Since the benefit of the counterpoise correction in calculating interaction energies is controversial, the thermodynamic functions at 298 K, including the thermal energies, the enthalpies, and the Gibbs free energies, were reported both with and without BSSE corrections. To clarify the nature of various noncovalent interactions, the redistribution of electron density in different bonding and antibonding orbitals and the second-order perturbation stabilization energies E_2 have been calculated by the natural bond orbital (NBO) analysis method.[49−52] The anion binding free energies in solution were calculated by using the polarizable continuum model (PCM)[53] in four solvents: $CHCl_3$, CH_3COCH_3, CH_3CN, and H_2O with the dielectric constant of 4.71, 20.49, 35.69, and 78.36, respectively.

3. RESULTS AND DISCUSSION

Binding Geometries and Energies of Binary Complexes. The optimized structures and electron density isosurfaces of $1/X^-$ (X^- = F^-, Cl^-, and Br^-) calculated by the ωB97XD/6-31++G** method were provided in Figure 2. Those calculated by the RI-MP2/cc-pVDZ method were provided in the Supporting Information (Figure S1).

For $1/F^-$, F^- attacks the aryl C_7 atom of one triazine ring to form a strongly covalent σ complex. The interatomic distance for F−C_7 is 1.432 Å, close to the average F−C (sp^3) distance found in the Cambridge Structural Database (1.46 ± 0.02 Å). The aryl carbon C_7 under attack has rehybridized to exhibit a tetrahedral rather than a planar geometry. The Cl_1−Cl_2 distance $d_{Cl1-Cl2}$ of the two triazine rings increases from 12.179 Å in the parent host molecule to 12.342 Å in the complex due to strong covalent σ interactions. Considerable second-order perturbation stabilization energies E_2 contributed by charge transfers LP $O_1 \rightarrow \sigma^*$ C_7−F, LP F $\rightarrow \sigma^*$ C_7−N_3, LP F $\rightarrow \sigma^*$ C_7−O_1, and LP F $\rightarrow \sigma^*$ C_7−N_1 (79.04, 53.98, 34.65,

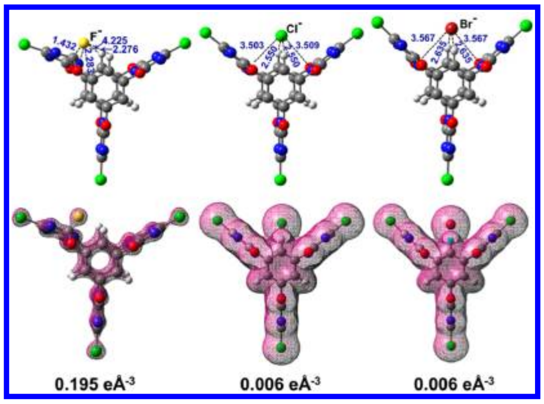


Figure 2. The optimized structures and the maximum electron density isosurfaces ρ_{max} in the region between the triazine rings and anions (isovalues in e Å^{-3}) for **1**/X$^-$ (X$^-$ = F$^-$, Cl$^-$, and Br$^-$) calculated by the ωB97XD/6-31++G** method. The representative structural parameters and the isovalues of ρ_{max} are provided.

and 33.05 kJ/mol) also support the formation of a strong σ complex. Our results are consistent with prior gas phase experiments[54,55] and theoretical studies[11,13,14,18,54,56,57] in that fluoride always undergoes a nucleophilic attack on the ring carbon atom of electron-deficient arenes, leading to a strong σ complex. A recent theoretical study at the RI-MP2 level of theory[37] seemed to suggest that F$^-$ complexes with tetraoxacalix[2]arene[2]triazine, a macrocyclic molecule with one V-shaped cleft, by H-bond and anion−π interactions, which is obviously different from our observations here. The maximum electron density ρ_{max} in the region between fluoride and the triazine ring is 0.195 e Å^{-3}, which is also an indication of forming strongly covalent σ interactions according to Hay et al.[18] The H-bond interaction in **1**/F$^-$ is very weak, characterized by E_2 of 5.19 kJ/mol contributed by charge transfer LP F → σ* C_1−H_1.

In **1**/Cl$^-$ and **1**/Br$^-$, anions are located in the middle of the V-shaped cleft and at a large offset distance to the center of π-electron deficient triazine rings, so anions are not able to interact with the triazine rings efficiently. The corresponding Cl_1−Cl_2 distances $d_{Cl1-Cl2}$ of the two triazine rings interacting with the halides decrease from 12.179 Å in the parent molecule to 11.343 Å and 10.947 Å respectively to maximize the anion−π interactions. The other noncovalent interaction contributing to the stabilization of **1**/Cl$^-$ and **1**/Br$^-$, is the bifurcated H-bonds between two aryl C−Hs of benzene rings and anions. The hydrogen atoms are separated from Cl$^-$ and Br$^-$ by 2.550 and 2.635 Å, respectively. These distances are longer than a single anion-arene H-bond distance,[18] indicating a weaker interaction. The second-order perturbation stabilization energies E_2 for Cl$^-$ and Br$^-$ are 26.44 and 29.92 kJ/mol, respectively, which suggests the existence of moderate H-bond interactions. Our results of calculation show that H-bond interactions play a significant role in the stabilization of complexes. For **1**/Cl$^-$ and **1**/Br$^-$, the ρ_{max} values are both 0.006 e Å^{-3}, which also indicates the absence of covalent bond interactions, instead the existence of weak anion−π interactions.

The thermodynamic functions of **1**/X$^-$ (X$^-$ = F$^-$, Cl$^-$, and Br$^-$) calculated at the ωB97XD/6-31++G** and RI-MP2/cc-pVDZ levels of theory at 298 K are summarized in Table 1. The significantly negative Gibbs free energy changes indicate that bis(tetraoxacalix[2]arene[2]triazine) can act as a neutral receptor of halides in the gas phase. The BSSE corrected Gibbs free energies calculated by the ωB97XD/6-31++G** method, as well as both BSSE corrected and uncorrected Gibbs free energies calculated by the RI-MP2/cc-pVDZ method display similar trends as the experimental results, i.e., the binding strength is in the sequence of F$^-$ > Cl$^-$ > Br$^-$.

Interplay between Noncovalent Interactions. There exist concurrent noncovalent interactions, i.e., H-bond and anion−π interactions between the host receptor and the halides in **1**/Cl$^-$ and **1**/Br$^-$. Their respective contributions to the overall stability is not clear. In order to study the interplay between the anion−π and H-bond interactions, we separate the two types of interactions contributing to the global stability, estimate their relative importance, and show that mutual influence between them leads to a cooperative effect. We separate the entire system into two subsystems, one is the H-bond subsystem consisting of two facing benzenes and an anion, the other is the anion−π subsystem including two 2-chloro-4,6-methoxytriazines and an anion. At the first glance, 1,3,5-methoxybenzene is a better H-bond model than benzene since it more closely mimics the electronic character in the actual receptor. However, 1,3,5-methoxybenzene turns out to be not a good H-bond model of the actual receptor since its methoxyl hydrogens, in addition to the aryl C-Hs, also interact with the anion. Besides, the aryl C−H of 1,3,5-methoxybenzene is much more acidic than that of the actual receptor. The atomic charges obtained by the CHELPG scheme via the electrostatic potential fitting are compared among the actual receptor, benzene, and 1,3,5-methoxybenzene (see Figure S2 in the Supporting Information). The aryl C−H of benzene has a partial charge apparently closer to the actual receptor than 1,3,5-methoxybenzene does. The geometries of subsystems shown in Figure 3 are extracted from the optimized structures of **1**/Cl$^-$ and **1**/Br$^-$.

The cooperative energy ΔE_{coop} is defined as the binding energy of **1**/X$^-$ subtracted by the binding energies of two subsystems under the same geometry. The binding energies of both subsystems and the cooperative effects without and with

Table 1. Thermal Energies (ΔE), Enthalpies (ΔH), and Gibbs Free Energies (ΔG) of 1/X$^-$ (X$^-$ = F$^-$, Cl$^-$, and Br$^-$) Calculated at the ωB97XD/6-31++G and RI-MP2/cc-pVDZ Levels of Theory at 298 K without and with the BSSE Corrections**

	ωB97XD/6-31++G**			RI-MP2/cc-pVDZ		
energies (kJ/mol)	**1**/F$^-$	**1**/Cl$^-$	**1**/Br$^-$	**1**/F$^-$	**1**/Cl$^-$	**1**/Br$^-$
ΔE	−241.63	−135.58	−184.30	−401.70	−164.14	−152.90
ΔE^{cp}	−231.55	−133.19	−123.02	−228.56	−113.84	−107.72
ΔH	−243.99	−137.95	−186.67	−404.18	−166.62	−155.38
ΔH^{cp}	−233.91	−135.22	−125.38	−231.04	−116.32	−110.20
ΔG	−208.55	−110.06	−158.71	−366.04	−134.87	−123.21
ΔG^{cp}	−198.48	−107.67	−97.43	−192.90	−84.57	−78.02

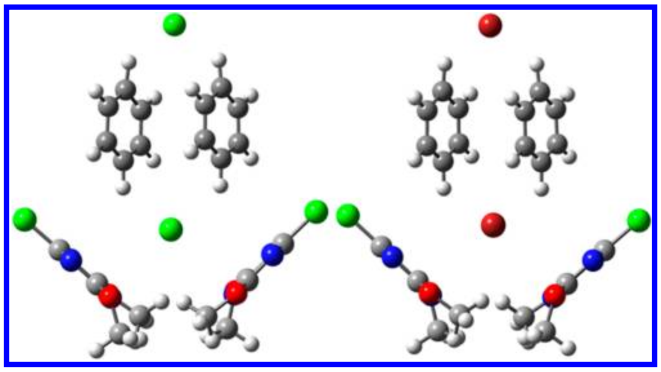


Figure 3. Model subsystems used to separate the H-bond interactions (upper panel) and the anion−π interactions (lower panel).

the BSSE corrections are listed in Table 2. The BSSE corrected stabilization energies of anion−π interactions are estimated to be −73.47 for Cl^- and −70.02 kJ/mol for Br^-, which are almost twice as much as the corresponding stabilization energies of H-bond interactions, −36.55 and −29.13 kJ/mol respectively. So it is inferred that anion−π interactions between X^- and two triazine rings contribute more to the global stability of **1**/X^- than the H-bond interactions between X^- and two aryl C-Hs of benzene. A recent experiment reported that H-bond interactions are favored over anion−π interactions when anions Cl^-, I^-, and SF_6^- complex with $C_6F_nH_{6\text{-}n}$.[22] This is actually not in contradiction with our observation for the following reasons. First, there exist multiple arene binding motifs in $C_6F_nH_{6\text{-}n}$, but only one binding mode is possible, either H-bond or anion−π interactions. In contrast, due to the unique conformations that calixarenes adopt, various noncovalent interactions are concurrent in **1**/X^-, where the anion interacts with two triazine rings via anion−π interactions and two benzene rings via bifurcated H-bonds simultaneously. Second, theoretical studies have shown that anion−π interactions are additive in terms of both geometries and binding energies.[58] Therefore the stabilization energies contributed by each triazene ring in **1**/Cl^- and **1**/Br^- are −36.74 and −35.01 kJ/mol, respectively, which are comparable to the H-bond strengths of −36.55 and −29.13 kJ/mol. Third, both experimental[22,59] and theoretical[18] studies have shown that bifurcated hydrogen bonds to two neighboring C−H groups are energetically favored over the linear hydrogen bond to a single C−H group. However, unlike anion−π interactions, the binding energy of bifurcated hydrogen bonds is not twice that of a linear hydrogen bond due to the directionality of H-bond interactions, with the former only a few kJ/mol negative than the latter. The reasonings above can explain why anion−π interactions contribute more to the global stability of **1**/X^- than H-bond interactions. The negative values of ΔE_{coop} indicate a favorable cooperativity between anion−π and H-bond interactions. Similar analysis of the synergetic effect between different types of noncovalent interactions have been reported in the literature.[37,60]

Table 2. Binding Energies without and with the BSSE Corrections for Both H-Bond and Anion-π Subsystems as well as 1/X^- (X^- = Cl^- and Br^-) Calculated by the ωB97XD/6-31++G Method[a]**

	kJ/mol	H-bond	anion−π	**1**/X^-	ΔE_{coop}
Cl^-	ΔE	−37.36	−75.46	−141.84	−29.02
	ΔE^{cp}	−36.55	−73.47	−139.44	−29.42
Br^-	ΔE	−57.09	−117.70	−190.03	−15.24
	ΔE^{cp}	−29.13	−70.02	−128.73	−29.58

[a]The cooperative energy (ΔE_{coop}) is defined as ΔE (**1**/X^-) − ΔE (H-bond) − ΔE (anion−π).

Binding Geometries and Energies of Ternary Complexes. The calculations and analysis above have established significant attractions between anions and the host receptor **1** in the gas phase. However, the anions are not alone, they are accompanied by cations and the corresponding dissociating media, usually water. The water molecules played an important role in the anion binding in the solid state as revealed by the X-ray crystallography and should be explicitly included in the models of calculations. The structures of ternary complexes **1**/($X^-\cdot H_2O$) (X^- = F^-, Cl^-, and Br^-) optimized at the ωB97XD/6-311++G** level of theory are shown in Figure 4. The corresponding structures optimized by the RI-MP2/cc-pVDZ method are provided in the Supporting Information.

As **1**/F^-, **1**/($F^-\cdot H_2O$) involves strong σ interactions between the aryl-C of one triazine ring and F^-, as evidenced by the short interatomic distance of 1.425 Å for F−C_7 and considerable second-order perturbation stabilization energies E_2 contributed by LP F → σ* C_7−O_1, LP F → σ* C_7−N_1, and LP F → σ* C_7−N_3 (54.06, 35.19, and 31.88 kJ/mol, respectively). The carbon atom under attack has rehybridized to exhibit a tetrahedral geometry, so that the V-shaped cleft with F^- and H_2O in it has a wider opening than the host molecule. In addition to the covalent interactions, the water molecule as a hydrogen donor forms a moderate H-bond with the nitrogen atom in the triazine ring, which is characterized by the stabilization energy E_2 of 53.30 kJ/mol, and as a hydrogen acceptor a weak H-bond with the aryl C−H of benzene, which is characterized by the stabilization energy of 10.71 kJ/mol. Regarding **1**/($Cl^-\cdot H_2O$), the chloride ion is located above the

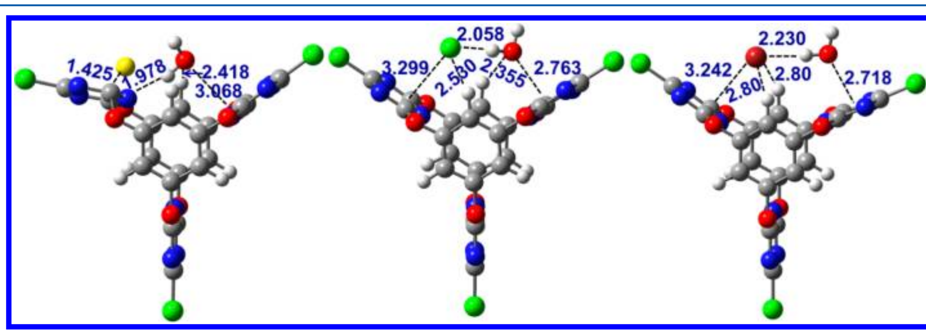


Figure 4. Structures of **1**/($X^-\cdot H_2O$) (X^- = F^-, Cl^-, and Br^-) optimized by the ωB97XD/6-31++G** method. The representative structural parameters are labled in the structures.

Table 3. Thermal Energies (ΔE), Enthalpies (ΔH), and Gibbs Free Energies (ΔG) of 1/($X^-\cdot H_2O$) (X^- = F^-, Cl^-, and Br^-) Calculated at the ωB97XD/6-31++G and RI-MP2/cc-pVDZ Levels of Theory at 298 K without and with the BSSE Corrections**

	ωB97XD/6-31++G**			RI-MP2/cc-pVDZ		
energies (kJ/mol)	1/($F^-\cdot H_2O$)	1/($Cl^-\cdot H_2O$)	1/($Br^-\cdot H_2O$)	1/($F^-\cdot H_2O$)	1/($Cl^-\cdot H_2O$)	1/($Br^-\cdot H_2O$)
ΔE	−294.24	−192.38	−231.45	−463.01	−235.61	−215.10
ΔE^{cp}	−282.29	−184.90	−173.39	−283.93	−170.71	−154.22
ΔH	−299.08	−197.22	−236.29	−467.97	−240.57	−220.06
ΔH^{cp}	−287.13	−189.74	−178.24	−288.88	−175.67	−159.18
ΔG	−221.36	−125.31	−164.81	−382.34	−161.79	−141.59
ΔG^{cp}	−209.41	−117.84	−106.76	−203.25	−96.90	−80.71

aryl carbon C_7 of one triazine ring and is in close vicinity to the aryl C_1−H_1 of one benzene ring, whereas the water molecule is located above the aryl carbon C_{11} of the other triazine ring and is close to the aryl C_1'−H_1' of the other benzene ring. The concurrent noncovalent interactions between the host and guest species in the V-shaped cleft are intriguing: (i) Cl^- and H_2O (its oxygen and hydrogen atoms are represented by $O_{(1)}$, $H_{(1)}$, and $H_{(2)}$ respectively) form a strong H-bond with a Cl−$H_{(1)}$ distance of 2.058 Å and a stabilization energy E_2 of 143.60 kJ/mol; (ii) Cl^- is located above the aryl C_7 of one triazine ring with an interatomic distance Cl−C_7 of 3.299 Å forming anion−π interactions, and water is located above the aryl C_{11} of the other triazine ring with an interatomic distance $O_{(1)}$−C_{11} of 2.763 Å forming lone-pair-π interactions.[61] The distance between Cl^- and one triazine ring is shorter than that in 1/Cl^-, suggesting a strengthened anion−π interaction; (iii) The interatomic distances of Cl−H_1 and $O_{(1)}$−H_1' (2.530 and 2.355 Å) and the corresponding stabilization energies E_2 LP Cl → σ^* C_1−H_1 and LP $O_{(1)}$ → σ^* C_1'−H_1' (35.61 and 14.48 kJ/mol) indicate a moderate and a weak H-bond, respectively.

In 1/($Br^-\cdot H_2O$), Br^- and H_2O are located in the same plane, each interacting with a triazine ring. In contrast to 1/($Cl^-\cdot H_2O$), Br^- is located in the cleft with an equal distance to the aryl C−H of two benzene rings, due to the larger radius of Br^-, and the stronger H-bond of aryl C−H donors with anion acceptors. One of representative noncovalent interactions contributing to the stability of 1/($Br^-\cdot H_2O$) is bifurcated H-bond between the aryl C−Hs of the host molecule and Br^-. H_1 and H_1' atoms are separated from Br^- with the same interatomic distance of 2.80 Å, and the corresponding stabilization energy is 38.29 kJ/mol. This hydrogen bond is weaker than the one in 1/Br^-, where the Br−H_1(H_1') distance is shorter (2.635 Å) and Br^- is right in the middle of the V-shaped cleft. The distance between Br^- and one triazine plane is 3.242 Å, shorter than that in 1/Br^-, so the existence of a water molecule allows Br^- to be optimally positioned to maximize its interactions with the triazine ring. At the same time, H_2O interacts with the other triazine ring with a perpendicular distance of 2.718 Å, so anion−π and lone-pair-π[61] interactions coexist in 1/($Br^-\cdot H_2O$). Besides, there is a strong H-bond established between the water molecule and Br^-, with an interatomic distance Br^--$H_{(1)}$ of 2.230 Å and a stabilization energy of 107.61 kJ/mol.

The existence of anion−π and lone-pair-π interactions in 1/($Cl^-\cdot H_2O$) and 1/($Br^-\cdot H_2O$) is also confirmed by the electron density isosurfaces. The maximum eletron density isosurfaces in the region between anions and one triazine ring, as well as in the region between H_2O and the other triazine ring are provided in Figure S4 (see the Supporting Information). The isovalues ρ_{max} of 0.2, 0.009, and 0.010 e Å^{-3} respectively in the region between F^-, Cl^-, and Br^- and one triazine ring suggest the existence of strong-σ interactions in 1/($F^-\cdot H_2O$) and anion−π interactions in 1/($Cl^-\cdot H_2O$) and 1/($Br^-\cdot H_2O$). All of the interactions are strengthened when compared with 1/X^-, where ρ_{max} of 0.195, 0.006, and 0.006 e Å^{-3} are observed. The isovalues of 0.009, 0.013, and 0.010 e Å^{-3} in the region between water and the other triazine ring also suggest the existence of lone-pair−π interactions in 1/($X^-\cdot H_2O$) (X^- = F^-, Cl^-, and Br^-).

The thermodynamic functions of 1/($X^-\cdot H_2O$) (X^- = F^-, Cl^-, and Br^-) calculated at the ωB97XD/6-31++G** and RI-MP2/cc-pVDZ levels of theory at 298 K are reported in Table 3. All of the BSSE corrected thermal energy, enthalpy, and Gibbs free energy changes are negative, and the stabilization of 1/($X^-\cdot H_2O$) (X^- = F^-, Cl^-, and Br^-) decreases as the size of halides increases. The thermodynamic functions of 1/($X^-\cdot H_2O$) are more negative than those of corresponding 1/X^-. The water molecule not only allows the halide to be optimally oriented to maximize its interactions with one triazine ring, but also interacts with the other triazine ring and at the same time establishes a strong hydrogen bond with the halide. The presence of a water molecule leads to a remarkable increase in the stability, due to the concurrent noncovalent interactions and the cooperative effect.

Solvent Effect. Researchers usually have no doubt about the existence of anion−π interactions in the gas phase and in the solid state, but few examples of attractive anion−π interactions in solution have been reported. As mentioned in the Introduction, the renewed interest in anion−π interactions arises from their biological relevance, with the expectation to utilize the noncovalent interactions for the design of novel hosts, carriers, catalysts, and materials. However, the detailed and accurate thermodynamic characterization of anion−π interactions in solution has not been achieved yet. Studies show that the free energy of binding estimated for these attractive interactions is less than 1 kcal/mol for each electron-deficient phenyl group. We have shown that the host molecule 1 exhibits significant halide binding ability in the gas phase, but its anion binding geometry and energies in solution are not quite clear. Wang et al. examined the interaction of 1 with halides in acetonitrile by means of isothermal titration calorimetry.[40] Their thermodynamic results indicate a 1:1 binding with all halides and exothermic enthalpy changes. It has also been pointed out that the recognition of anions in solution requires the use of salts as precursors, which complicates the analysis of the titration data and the corresponding estimate of the binding strength.[16] Due to the weak binding energies, theoretical quantification of anion−π interactions in solution is quite challenging, which requires explicit modeling of the solvent molecules. Here, we explore the influence of solvent on the binding properties of host **1** by using the PCM implicit solvent model, which views the solvent as a continnum media with certain dielectric constant. To study the solvent effect on the anion recognition of **1**, we choose four solvents of different polarities: $CHCl_3$, CH_3COCH_3, CH_3CN, and H_2O. The binding free energies of $\mathbf{1}/X^-$ and $\mathbf{1}/(X^-{\cdot}H_2O)$ (X^- = F^-, Cl^-, and Br^-) are calculated using the thermodynamic cycle shown in Scheme 1, where the superscripts ° and * denote the

Scheme 1

$$\begin{tikzcd}
\mathbf{1}\,(\text{gas}) + X^-{\bullet}(H_2O)_n\,(\text{gas}) \arrow[r, "\Delta G^{\circ}_{\text{gas}}"] \arrow[d, "\Delta G^{*}_{\text{S}}(\mathbf{1})\ \ \Delta G^{*}_{\text{S}}(X^-{\bullet}(H_2O)_n)"'] & \mathbf{1}/X^-{\bullet}(H_2O)_n\,(\text{gas}) \arrow[d, "\Delta G^{*}_{\text{S}}(\mathbf{1}/X^-{\bullet}(H_2O)_n)"] \\
\mathbf{1}\,(\text{sln}) + X^-{\bullet}(H_2O)_n\,(\text{sln}) \arrow[r, "\Delta G^{*}_{\text{sln}}"] & \mathbf{1}/X^-{\bullet}(H_2O)_n\,(\text{sln})
\end{tikzcd}$$

standard state using a concentration of 1 atm in the gas phase and 1 mol/L in solution respectively, and n = 0 or 1. The results obtained with the RI-MP2/cc-pVDZ method and the PCM solvation model are listed in Table 4. It can be seen that the binding free energy reduces drastically in solution compared with in the gas phase, and it decreases as the solvent polarity increases. The counterpoise correction, which is known to often overestimate the finite basis sets error,[62] is not applied because it even leads to positive binding energies of $\mathbf{1}/X^-$ in solution. It has been shown that adding explicit solvent molecules around the anions yields better numbers when calculations are carried out using continuum solvent models.[63] In our case, the binding free energies of $\mathbf{1}/(X^-{\cdot}H_2O)$ reported in Table 4 are more reasonable than those of $\mathbf{1}/X^-$, and a better agreement with the experimental observations is achieved. Since the host molecule **1** studied is large, it is not affordable to add more explicit solvent molecules to the current calculations. The treatment of solvation effect by the implicit and combined implicit-explicit solvent models is far from satisfactory. To fully address this issue, it is better to start with small electron-deficient model systems. The application of more accurate QM/MM method is also desirable. The binding free energies obtained with the ωB97XD/6-31++G** method (see Table S1 in the Supporting Information) are in poor agreement with the experimental results whether or not an explicit water is included. The RI-MP2/cc-pVDZ method seems to outperform the ωB97XD/6-31++G** method in this regard.

The weak binding free energies of bis(tetraoxacalix[2]-arene[2]triazine) and other electron-deficient arene model systems in solution suggest that the anion−π interactions can offer potential applications in catalysis and anion transport using synthetic functional materials. Indeed, the anion−π interactions have been seen at work recently. The naphthalenediimide transporters in bilayer membranes are prepared, and the affinity and selectivity sequences of anions are recorded, which provides the first experimental evidence for the functional relevance of anion−π interactions.[15]

4. CONCLUSIONS

To conclude, we have investigated the halide binding geometries and energies in one of three V-shaped clefts of bis(tetraoxacalix[2]arene[2]triazine). The calculated Gibbs free energies of the halides association display similar trends as the experimental results. The gas-phase quantum chemistry calculations show that different types of noncovalent interactions between halides and the host molecule are concurrent, except for F^-, which undergoes a nucleophilic attack on the aryl carbon and forms a strong-σ complex. The contribution of anion−π interactions to the overall stabilization energy is found to be as significant as that of bifurcated hydrogen bond interactions based on the reference system analysis. The interplay between both kinds of noncovalent interactions leads to a cooperative effect. In addition, the presence of a water molecule leads to a remarkable increase in the stability of complex, because the water molecule not only allows the anion to be optimally positioned to interact with one triazine ring, but also establishes hydrogen bond interactions with the anion as well as lone-pair-π interactions with the other triazine ring. In supramolecular chemistry, concurrent non-covalent interactions and their cooperative effect are major driving forces for the host−guest assembly. Though the halides and bis(tetraoxacalix[2]arene[2]triazine) exhibit significantly attractive interactions in the gas phase, the binding energies have been shown to decrease drastically in solution. As the polarity of solvents increases, the stability of anion-receptor complexes decreases. The substantially reduced binding free energies in solution suggest that bis(tetraoxacalix[2]arene[2]-triazine) is not significant for the selective or enhanced binding of anions, it rather offers potential applications for anion transport.

Finally, theoretical quantification of the anion binding properties of bis(tetraoxacalix[2]arene[2]triazine) has helped us to clarify the ambiguities in identifying the anion-binding modes, and the respective contributions of concurrent noncovalent interactions. Meanwhile, the weak binding free energies in solution pose challenges to the accurate

Table 4. Electronic Binding Energies (ΔE) and Binding Free Energies (ΔG) of $\mathbf{1}/X^-$ and $\mathbf{1}/(X^-{\cdot}H_2O)$ (X^- = F^-, Cl^-, and Br^-) without the BSSE Corrections in Four Solvents of Different Polarities Calculated by the RI-MP2/cc-pVDZ Method and the PCM Solvent Model

solvent	energies (kJ/mol)	ε^b	$\mathbf{1}/F^-$	$\mathbf{1}/Cl^-$	$\mathbf{1}/Br^-$	$\mathbf{1}/(F^-{\cdot}H_2O)$	$\mathbf{1}/(Cl^-{\cdot}H_2O)$	$\mathbf{1}/(Br^-{\cdot}H_2O)$
gas phase	ΔE	1.00	−405.61	−167.96	−156.71	−295.29	−177.37	−166.33
	ΔG		−366.03	−134.87	−123.20	−221.04	−118.82	−107.60
$CHCl_3$	ΔE	4.71	−214.85	−36.89	−39.06	−153.48	−72.45	−71.65
	ΔG		−183.19	−11.70	−13.46	−87.14	−21.81	−20.83
CH_3COCH_3	ΔE	20.49	−176.66	−15.46	−20.54	−123.23	−54.30	−55.56
	ΔG		−144.99	9.72	5.06	−56.89	−3.66	−4.75
CH_3CN	ΔE	35.69	−171.89	−13.25	−18.67	−119.36	−52.35	−53.83
	ΔG		−140.23	11.94	6.93	−53.02	−1.71	−3.01
H_2O	ΔE	78.36	−168.40	−11.76	−17.42	−116.51	−51.03	−52.64
	ΔG		−136.73	13.42	8.18	−50.17	−0.39	−1.82

thermodynamic characterization of these noncovalent interactions.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The binding free energies in solution calculated by the ωB97XD/6-31++G** method, the structures optimized by the RI-MP2/cc-pVDZ method, and the Cartersian coordinates of all optimized structures are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors are indebted to Professor Meixiang Wang for insightful discussions on their experiments. This work is supported by the National Natural Science Foundation of China (No. 20903060), the Innovative Research Group Fund of the National Natural Science Foundation of China (No. 21121004), and the Ministry of Science and Technology of China through 973 program (No. 2011CB932304).

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