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Molecular Binding Behaviors of Sulfonated Calixarenes with Phenanthroline-diium in Aqueous Solution and Solid State: Cavity Size Governing Capsule Formation

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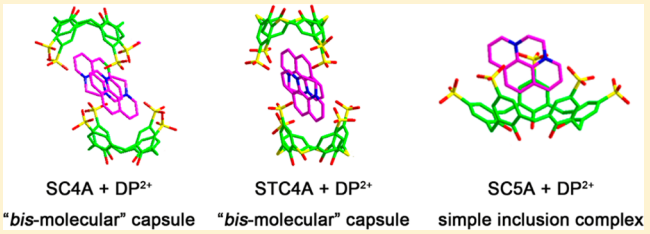
Supporting Information

ABSTRACT: The molecular binding behaviors of *p*-sulfonatocalix[4]arene (SC4A), *p*-sulfonatocalix[5]arene (SC5A), and *p*-sulfonatothiacalix[4]arene (STC4A) with 5,6-dihydropyrazion[1,2,3,4-*lmn*][1,10]phenanthroline-4,7-diium (DP^{2+}) were systematically investigated by crystallography, NMR spectroscopy, and microcalorimetry at pH 1−2. The obtained results showed that, in both aqueous solution and the solid state, DP^{2+} was immersed into the cavity of the sulfonated calixarene host in a slantwise degree with the aromatic moiety being included first. The different slantwise degree of the guest in the host cavity determined whether the host−guest capsule could be formed in the solid state. Furthermore, all three sulfonated calixarene hosts showed high affinities with DP^{2+} in the magnitude of 10^5−10^6 M^{-1} in aqueous solution, and the binding modes for host−guest complexation were explained from a thermodynamic viewpoint.



INTRODUCTION

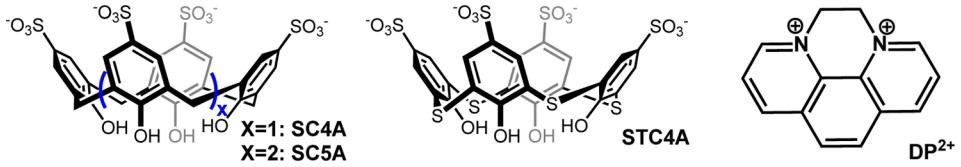
Construction of molecular capsules is a significant topic of research for their various applications in binding, separation, and sensing of small molecules and ions; stabilization of reactive intermediates; and catalysis.[1] Calixarenes are one class of important building blocks to construct molecular capsules as a result of their intrinsic bowl shape.[2] Hydrogen bonds[3] and metal-coordination bonds[4] are two more widely employed tools in the construction of molecular capsules. Furthermore, the preparation of molecular capsules in aqueous solution based on ionic interaction is also very important for their biochemical applications.[5]

Sulfonated calixarenes, possessing three-dimensional, flexible, π-electron-rich cavities, have gained increasing attention in the past three decades due to their inclusion properties with numerous guests.[6] Benefiting from the high affinity and selectivity for the complexation of sulfonated calixarene hosts with different kinds of guests in water,[7] and also benefiting from their nontoxic character,[8] sulfonated calixarenes have been popularly applied in many fields,[9] of course including the construction of molecular capsules in biocompatible environments.[10] Raston and co-workers opened the field toward the development of solid-state molecular capsules based on sulfonated calixarenes.[11] Most of the reported solid-state molecular capsules based on sulfonated calixarenes were formed by using suitable guest molecules as templates. In other words, guest size and shape are important factors in the formation of a molecular capsule. In a previous study,[12] we selected 1,10-phenanthrolinium ion (Phen) as a template to prepare molecular capsules with sulfonated calixarenes because the complexation of sulfonated calixarenes with Phen was likely to result in the formation of a π-stacked motif.[13] The obtained results showed that *p*-sulfonatocalix[4]arene (SC4A), *p*-sulfonatocalix[5]arene (SC5A), and *p*-sulfonatothiacalix[4]-arene (STC4A) could all form solid-state molecular capsules with Phen at pH 1−2. However, these capsules could not be formed in a more acidic mother liquor of 1 M HCl. In other words, the acidity of the mother liquor is another important factor in the construction of a molecular capsule.

Herein, we wish to report the solid-state structures of three complexes of 5,6-dihydropyrazion[1,2,3,4-*lmn*][1,10]-phenanthroline-4,7-diium (DP^{2+}) with sulfonated calixarene hosts (DP^{2+}⊂SC4A, DP^{2+}⊂STC4A, and DP^{2+}⊂SC5A) at pH 1−2 (Scheme 1). The obtained results showed that DP^{2+} was immersed into the cavity of the sulfonated calixarene host in a slantwise degree with the aromatic moiety being included first. The cavity size of the sulfonated calixarene determined the slantwise degree of the guest in the host cavity, which also

Received: May 20, 2014
Revised: July 11, 2014
Published: July 16, 2014

Scheme 1. Structural Illustration of Sulfonated Calixarene Hosts (SC4A, SC5A, and STC4A) and DP^{2+} Guest



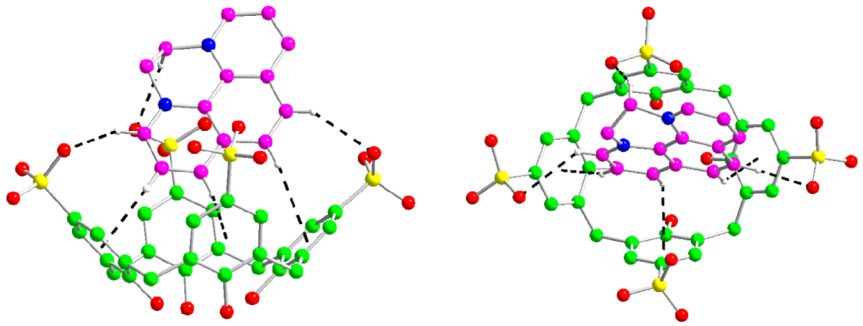


Figure 1. Solid-state inclusion structures of DP^{2+}⊂SC4A. The broken lines represent the intermolecular hydrogen bonds or the C−H···π interactions between host and guest.

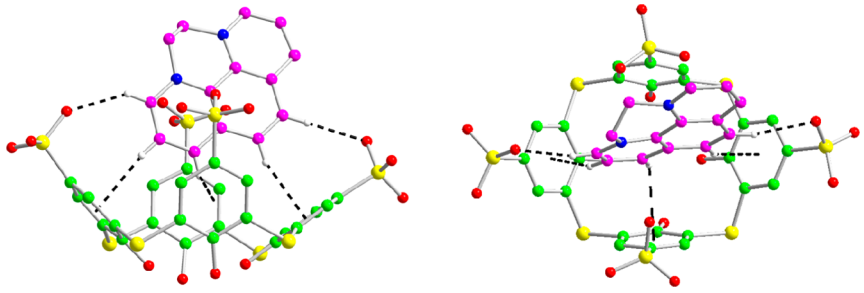


Figure 2. Solid-state inclusion structure of DP^{2+}⊂STC4A. The broken lines represent the intermolecular hydrogen bonds or the C−H···π interactions between host and guest.

governed whether the host−guest capsule could be formed in the solid state: capsule complexes DP^{2+}⊂SC4A and DP^{2+}⊂STC4A were formed at pH 1−2, whereas only the simple inclusion complex DP^{2+}⊂SC5A was formed under the same condition. In other words, in this study, we found that the cavity size of the sulfonated calixarene host was also a governing factor in the construction of a molecular capsule. A host−guest solution study was further performed by using NMR spectroscopy and microcalorimetry at pH 2.0 in order to understand the factor of cavity size for constructing molecular capsules better.

RESULTS AND DISCUSSION

Solid-State Structures of DP^{2+}⊂SC4A, DP^{2+}⊂STC4A, and DP^{2+}⊂SC5A. Single-crystal X-ray diffraction analyses supply quantitative information for the structures of host−guest complexes in the solid state. The three complexes of DP^{2+} with sulfonated calixarene hosts, DP^{2+}⊂SC4A, DP^{2+}⊂STC4A, and DP^{2+}⊂SC5A, were all obtained in their monocrystalline forms at pH 1−2. All three complexes crystallized in the same triclinic space group $P\bar{1}$. Among the three crystals, some sulfonate groups of hosts and several water molecules disordered at two or more positions. In all three crystal structures, only one DP^{2+} guest was immersed into the host cavity in the slantwise orientation with the aromatic moiety being included first, whereas the other DP^{2+} guests located in the crystal lattice as counterions.

In complex DP^{2+}⊂SC4A (Figure 1), the aromatic moiety of DP^{2+} is captured into the cavity of SC4A via three C−H···π interactions (C62−H62···ring of C51−C56, 2.984(1) Å and 141.6(4)°; C64−H64···ring of C30−C35, 2.820(1) Å and 139.8(4)°; C65−H65···ring of C37−C42, 2.515(1) Å and 164.1(4)°) and two unconventional hydrogen bonds (C61···O32, 3.359(8) Å and 147.9(4)°; C66···O22, 3.515(8) Å and 132.8(4)°), whereas the methylene moieties are fixed at the upper rim of SC4A, captured by one sulfonate group via an unconventional hydrogen bond (C69···O26, 3.28(1) Å and 140.5(4)°).

In complex DP^{2+}⊂STC4A (Figure 2), the aromatic moiety of DP^{2+} is immersed into the cavity of STC4A via three C−H···π interactions (C40−H40···ring of C13−C18, 2.591(1) Å and 157.0(1)°; C41−H41···ring of C7−C12, 2.902(1) Å and 119.2(1)°; C43−H43···ring of C1−C6, 2.553(1) Å and 153.2(1)°) and two unconventional hydrogen bonds (C39···O10, 3.083(1) Å and 141.4(1)°; C44···O2, 3.326(1) Å and 167.0(1)°). Compared to the accommodation of DP^{2+} in a lightly slantwise manner in complex DP^{2+}⊂SC4A, the guest molecule is more slantways encapsulated into the cavity of STC4A. This structure difference can be ascribed to the replacement of bridging atoms from methylenes to sulfide linkages, which brings about a 15% enlargement of the cavity size and enables the host to accommodate most of the volume of the guest molecule.[14] To accommodate the guest well, STC4A adopts a more distorted C_{2v} symmetry conformation

dx.doi.org/10.1021/cg500730m | Cryst. Growth Des. 2014, 14, 4631−4639

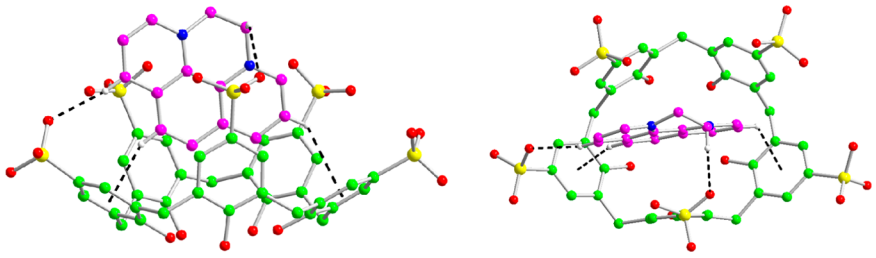


Figure 3. Solid-state inclusion structure of DP^{2+}⊂SC5A. The broken lines represent the intermolecular hydrogen bonds or the C−H···π interactions between host and guest.

with S···S distances of trans sulfonate groups of 7.767(2) and 12.384(3) Å as compared with the S···S distances of 8.605(4) and 11.781(5) Å in DP^{2+}⊂SC4A. Moreover, the actual φ and χ torsion angle values (degrees), which are used to define the solid-state conformation of calixarene according to the Ugozzoli−Andreetti convention,[15] are 113.7(1), −81.3(1); 74.4(1), −99.9(1); 103.6(1), −77.0(1); 69.0(1), −109.3(1) for DP^{2+}⊂STC4A and 96.9(6), −77.6(6); 77.9(7), −102.1(6); 102.0(6), −79.7(6); 75.6(6), −97.7(6) for DP^{2+}⊂SC4A, respectively.

In complex DP^{2+}⊂SC5A (Figure 3), the aromatic moiety of DP^{2+} is captured into the cavity of SC5A via two C−H···π interactions (C40−H40···ring of C15−C20, 2.528(1) Å and 155.8(3)°; C44−H44···ring of C29−C34, 3.191(1) Å and 126.7(4)°) and one unconventional hydrogen bond (C38···O11, 3.332(7) Å and 167.9(4)°), whereas the methylene moieties are fixed at the upper rim of SC5A, captured by one sulfonate group via an unconventional hydrogen bond (C48···O16, 3.200(6) Å and 123.7(3)°). Compared with the structure of DP^{2+}⊂SC4A, we notice that DP^{2+} penetrates into the SC5A cavity to a deeper depth, which can be reflected from the distances between the nitrogen atoms of DP^{2+} and the planes of carbon atoms of methylenes in calixarenes. The distances involved in complex DP^{2+}⊂SC5A are 5.449(4) and 6.654(4) Å, which are shorter than 5.771(5) and 7.696(5) Å involved in complex DP^{2+}⊂SC4A. Owing to the deeper immersion of DP^{2+}, the pinched symmetry can be observed in SC5A, as shown by the actual φ and χ torsion angle values (degrees): 94.6(4), −84.8(5); 45.4(5), −83.3(4); 110.1(4), −75.3(4); 65.6(5), −110.5(4); 89.2(4), −61.6(4). Moreover, compared with the slantwise degree of DP^{2+} in complex DP^{2+}⊂STC4A, the guest molecule is further more slantways encapsulated into the cavity of SC5A, even close to a horizontal orientation. This structural distinction can be ascribed to the fact that the cavity of SC5A is wider: STC4A has a bowl shape, whereas SC5A can be regarded as a shallow-dish shape.

It is worth mentioning that, in the solid-state structures of DP^{2+}⊂SC4A and DP^{2+}⊂STC4A, face-to-face dimers are formed by the π···π stacking interaction of one bound DP^{2+} with another bound DP^{2+} molecule, which results in the formation of 2:2 bis-molecular capsules (Figure 4). However, in complex DP^{2+}⊂SC5A, capsule formation is not possible as a consequence of the nearly horizontal orientation of DP^{2+} encapsulated into the cavity of SC5A. The orientation of a DP^{2+} guest in complex DP^{2+}⊂SC5A cannot lead to the formation of a π···π dimer. Therefore, we can conclude that the π···π stacking interaction of DP^{2+}···DP^{2+}, which is governed by the slantwise degree of the guest in the host cavity, is the key factor in stabilizing these solid-state capsule structures. Essentially, the cavity size of sulfonated calixarene determines

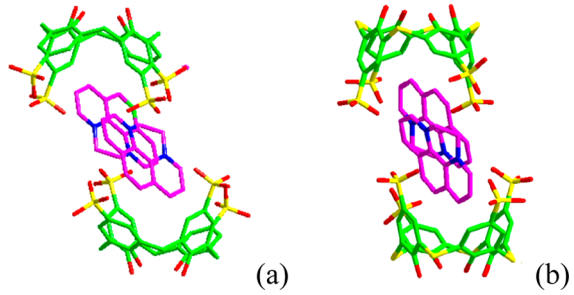


Figure 4. Bis-molecular capsules formed by DP^{2+}⊂SC4A (a) and DP^{2+}⊂STC4A (b).

the slantwise degree of the guest in the host cavity and, as a result, governs the formation of capsules.

As a result of the different binding modes in complexes DP^{2+}⊂SC4A, DP^{2+}⊂STC4A, and DP^{2+}⊂SC5A, the extended structures of these complexes are also different. For example, the packing structures of DP^{2+}⊂SC4A and DP^{2+}⊂STC4A have contorted bilayer arrangements as a result of the dominating forces of π···π interactions, whereas, in the extended structure of DP^{2+}⊂SC5A, SC5A molecules arrange themselves in a typical up−down fashion to form a "zig-zag" bilayer arrangement (Figure 5).

Solution Investigations. A host−guest solution study was further performed by using NMR spectroscopy and microcalorimetry at pH 2.0 in order to understand the factor of cavity size for constructing molecular capsules better. ^{1}H NMR spectroscopy is a powerful tool that can be used to determine the structure of a calixarene complex by analyzing complexation-induced chemical shift changes ($\Delta\delta$) of guest protons.[16] Herein, to obtain the binding modes of DP^{2+} with sulfonated calixarenes at pH 2.0, ^{1}H NMR spectra of DP^{2+} in the absence and presence of these calixarene hosts were measured in pD 2.0 phosphate buffer solutions (Figure 6). The host and guest were mixed in a 1:1 stoichiometry at 10 mM because the Job's plots showed that, in aqueous solution, sulfonated calixarenes also formed 1:1 host−guest complexes with DP^{2+} (see the Supporting Information, Figure S1). As shown in Figure 6, all the protons of DP^{2+} exhibit visible upfield shifts owing to the ring current effect of the aromatic nuclei of calixarenes, indicating that the DP^{2+} guests are encapsulated into the calixarene cavities. Moreover, the DP^{2+} protons are observed as a single resonance because of fast exchange between a free guest and a complexed one on the NMR time scale. The corresponding chemical shift changes ($\Delta\delta$) of DP^{2+} protons in the presence of approximately 1 equiv of hosts are listed in Table 1. The $\Delta\delta$ values differ from each other, which can be used to deduce the binding geometries of host−guest complexes because the proton with the largest $\Delta\delta$ value

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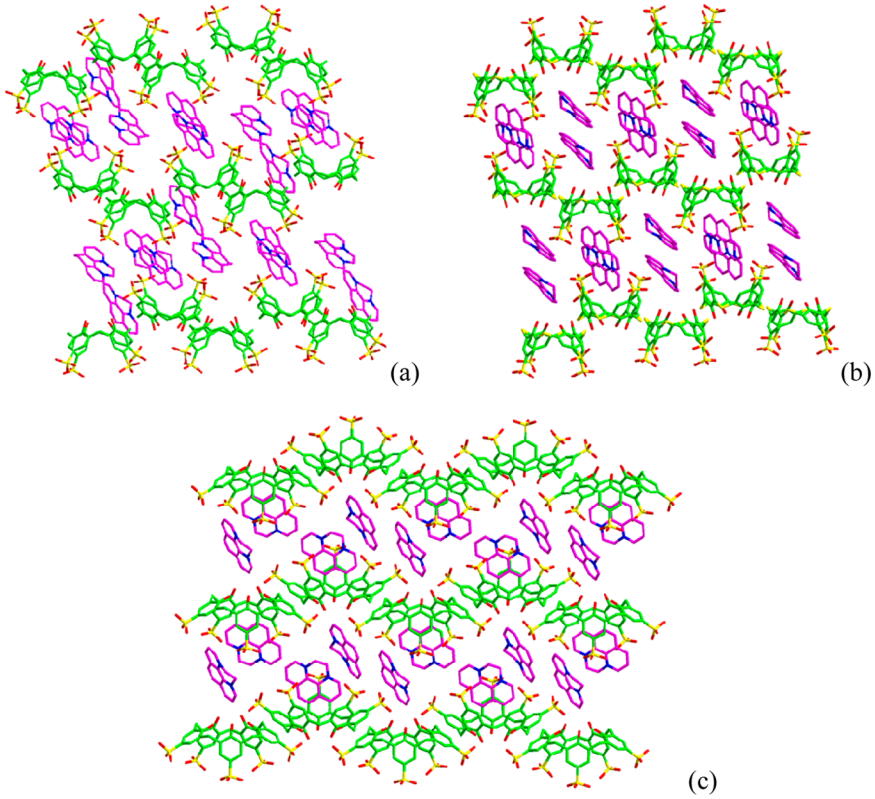

Figure 5. Extended structures of DP^{2+}⊂SC4A (a), DP^{2+}⊂STC4A (b), and DP^{2+}⊂SC5A (c).

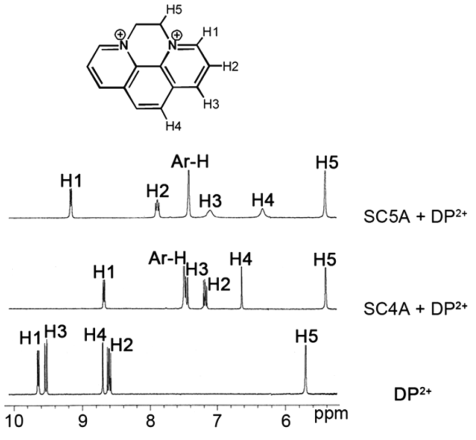

Figure 6. ^{1}H NMR spectra of DP^{2+} in the absence and presence of SC4A and SC5A at pD 2.0. The host and guest were mixed in a 1:1 stoichiometry at 10 mM. Some signals of guest protons were assigned according to 2D NMR spectra.

Table 1. Chemical Shift Changes ($\Delta\delta$, ppm) of DP^{2+} Protons in the Presence of SC4A and SC5A at pD 2.0[a,b]

host	H1	H2	H3	H4	H5
SC4A	−0.96	−1.41	−2.06	−2.05	−0.28
SC5A	−0.50	−0.74	−2.42	−2.38	−0.31

[a] $\Delta\delta = \delta$(presence of 1 equiv of host) − δ(free guest). Negative values indicate upfield shift. [b] The host and guest were mixed in a 1:1 stoichiometry at 10 mM.

would be affected mostly by the ring current effect of the aromatic nuclei of calixarenes. As can be seen from Table 1, upon complexation with SC4A at pD 2.0, the $\Delta\delta$ values of DP^{2+} protons are in the order of H3 ≈ H4 > H2 > H1 > H5, which indicates that DP^{2+} is immersed into the cavity of SC4A in a slantwise degree with the aromatic moiety being included first (Figure 7a). Upon complexation with SC5A at pD 2.0, the

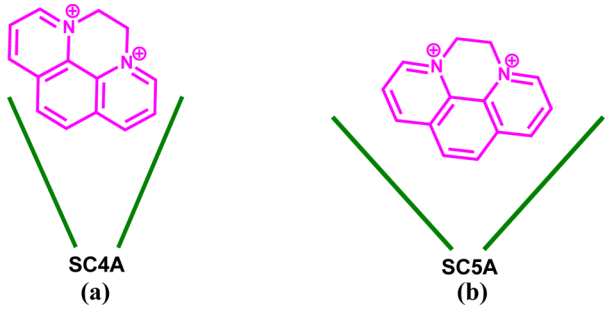

Figure 7. Deduced binding modes of DP^{2+} with SC4A (a) and SC5A (b) at pD 2.0 according to ^{1}H NMR spectra.

$\Delta\delta$ values of H3 and H4 in DP^{2+} are obviously larger than those upon complexation with SC4A, whereas the $\Delta\delta$ values of H1 and H2 in DP^{2+} are obviously smaller than those upon complexation with SC4A, which indicates that H3 and H4 portions of DP^{2+} are close to the aromatic nuclei of SC5A, whereas H1 and H2 portions of DP^{2+} are remote from the cavity of SC5A. Therefore, we rationally deduce that DP^{2+} is nearly horizontally encapsulated into the cavity of SC5A (Figure 7b). The 2D ROESY NMR spectrum of the SC5A +DP^{2+} complex at pD 2.0 was also performed to further identify its binding structure. As shown in Figure 8, the cross-peaks of H3 (C) and H4 (B) of DP^{2+} with the aromatic protons of calixarene are obviously stronger than those of H1 (D) and H5 (A), which strongly supports the deduced binding mode above

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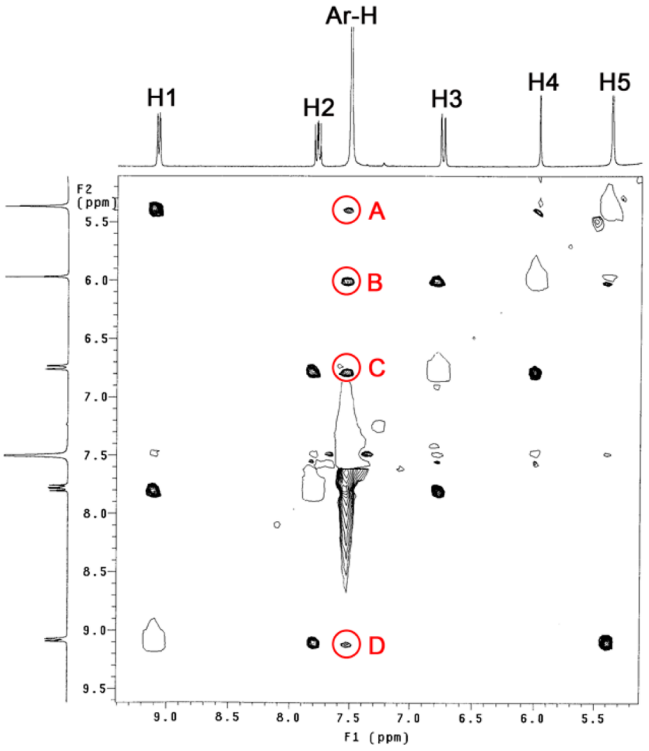

Figure 8. 2D ROESY NMR spectrum of SC5A+DP^{2+} complex at pD 2.0 with a mixing time of 250 ms. The host and guest were mixed in a 1:1 stoichiometry at 10 mM.

by ^{1}H NMR spectra. The deduced binding modes of SC4A +DP^{2+} and SC5A+DP^{2+} complexes in aqueous solution are also in accordance with the binding structures of DP^{2+}⊂SC4A and DP^{2+}⊂SC5A complexes in the solid state. The binding mode of the complex of STC4A with DP^{2+} at pD 2.0 could not be deduced by NMR spectroscopy owing to its poor water solubility.

To understand in depth why the slantwise degree of the DP^{2+} guest in the cavity of the sulfonated calixarene host increases with the increasing size of the host cavity, the microcalorimetric experiments for the intermolecular complexation of SC4A, SC5A, and STC4A with DP^{2+} were performed in pH 2.0 phosphate buffer solutions, which could not only give the binding stability values (K_S) between hosts and guests, but also show the accompanied enthalpy ($\Delta H°$) and entropy ($T\Delta S°$) changes. The obtained results are listed in Table 2 together with our previous thermodynamic results for the complexation of Phen with the three sulfonated calixarenes under the same conditions.[17] All the stoichiometric ratios (*N* values) that we observed from curve-fitting results of the binding isotherm fell within the range of 0.90−1.10:1, which also clearly indicated that all the inclusion complexes had a 1:1 stoichiometry in aqueous solution. As can be seen from Table 2, all three sulfonated calixarene hosts show high affinities with DP^{2+} in the magnitude of 10^5−10^6 M^{-1}. The K_S values for the complexation of DP^{2+} with SC4A, SC5A, and STC4A are much higher than those for the complexation of Phen with the three sulfonated calixarene hosts. After careful analysis of the data in Table 2, we can see that all the entropy changes for the complexation of DP^{2+} with SC4A, SC5A, and STC4A are relatively much more favorable than those for the complexation of Phen with the three sulfonated calixarene hosts, while there are no significant differences for the enthalpy changes for the complexation of DP^{2+} and Phen with the three sulfonated calixarene hosts. It means that the higher K_S values for the complexation of DP^{2+} with SC4A, SC5A, and STC4A are all driven by the entropy term. A reasonable explanation for these thermodynamic data is that all the sulfonate groups of calixarene hosts are ionized at pH 2.0, and the electrostatic interactions between negatively charged SO_3^- in hosts and positively charged N^+ in guests play a crucial role in controlling the binding stability values and selectivity of host−guest complexation. In a Phen guest, there is only one protonated NH^+ at pH 2.0. Therefore, Phen guests are encapsulated into all three sulfonate calixarene hosts from a vertical orientation with the positively charged portion being included first, which is more favorable for the electrostatic interactions between negatively charged SO_3^- in hosts and positively charged NH^+ in a Phen guest. The electrostatic interactions lead to the partial dehydration of NH^+ and SO_3^-, which is favorable for the entropy changes.[18] Even so, all the entropy changes for the complexation of Phen with SC4A, SC5A, and STC4A are quite unfavorable due to the loss of conformational degrees of freedom upon complexation. The vertical orientations of Phen guests in SC4A, SC5A, and STC4A cavities determine that Phen guests can form molecular capsules with all three sulfonated calixarenes at pH 1−2.[12] In a DP^{2+} guest, there are two positively charged N^+ at pH 2.0. Therefore, the electrostatic interactions between sulfonated calixarene hosts and DP^{2+} should be more favorable, and the horizontal orientations of DP^{2+} guests at the upper rim of sulfonate calixarene hosts should be most favorable for the electrostatic interactions between negatively charged SO_3^- in hosts and the two positively charged N^+ in DP^{2+}.[17,19] However, limited by the cavity size of the host, DP^{2+} guests are encapsulated into all three sulfonate calixarene hosts with the orientation changing gradually from vertical to horizontal. The slantwise degree of the guest in the host cavity increases with the increasing size of

Table 2. Complex Stability Values (K_S/M^{-1}), Enthalpy ($\Delta H°$/(kJ·mol^{-1})), and Entropy ($T\Delta S°$/(kJ·mol^{-1})) Changes for 1:1 Intermolecular Complexation of SC4A, SC5A, and STC4A with Phen and DP^{2+} in pH 2.0 Phosphate Buffer Solutions at 298.15 K

hosts	guests	K_S	$\Delta H°$	$T\Delta S°$
SC4A[a]	Phen	2.67×10^4	−44.8	−19.5
SC5A[a]		2.28×10^3	−38.8	−19.7
STC4A[a]		4.98×10^3	−36.6	−15.5
SC4A	DP^{2+}	$(1.35 \pm 0.01) \times 10^6$	−40.5 ± 0.4	−5.54 ± 0.38
SC5A		$(3.11 \pm 0.02) \times 10^5$	−35.8 ± 0.1	−4.44 ± 0.01
STC4A		$(1.34 \pm 0.01) \times 10^5$	−34.8 ± 0.1	−5.57 ± 0.10

[a]Ref 17.

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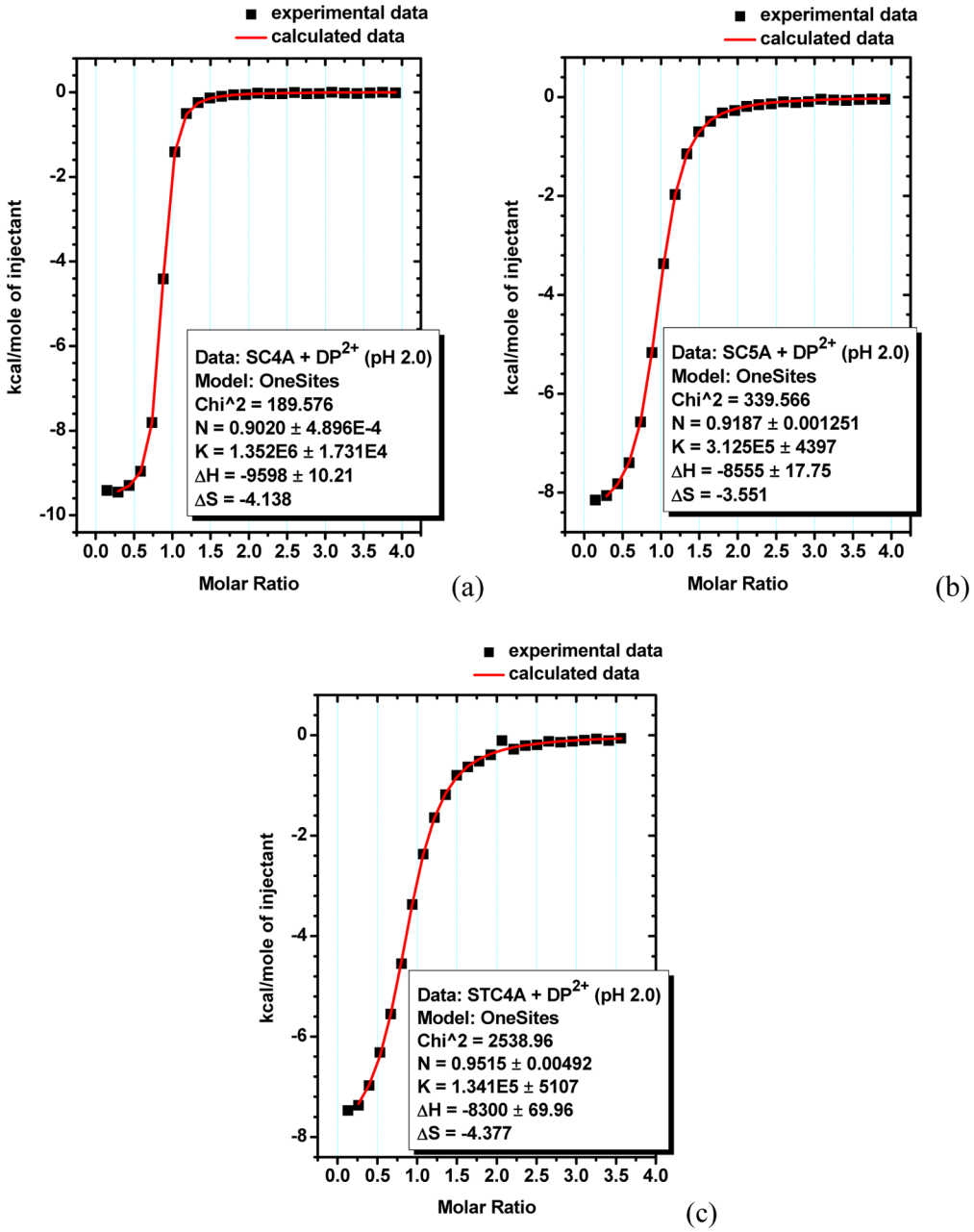

Figure 9. "Net" heat effects of complexation of DP^{2+} with SC4A (a), SC5A (b), and STC4A (c) for each injection, obtained by subtracting the dilution heat from the reaction heat, which was fitted by computer simulation using the "one set of binding sites" model.

the host cavity (SC5A > STC4A > SC4A). The more favorable electrostatic interactions between the three sulfonated calixarenes and DP^{2+} lead to a more favorable dehydration of N^+ and SO_3^-, which is more favorable for the entropy changes. As a result, the entropy changes for the complexation of DP^{2+} with SC4A, SC5A, and STC4A are relatively much more favorable than those for the complexation of Phen with the three sulfonated calixarenes. The cavity size of the sulfonated calixarene determines the slantwise degree of DP^{2+} in the host cavity, which also governs whether the host−guest capsule can be formed in the solid state: capsule complexes DP^{2+}⊂SC4A and DP^{2+}⊂STC4A are formed at pH 1−2, whereas only the simple inclusion complex DP^{2+}⊂SC5A is formed under the same condition.

CONCLUSION

In summary, the molecular binding behaviors of SC4A, SC5A, and STC4A with DP^{2+} were systemically investigated at pH 1−2. In both aqueous solution and the solid state, DP^{2+} is immersed into the cavity of the sulfonated calixarene host in a slantwise degree with the aromatic moiety being included first. The cavity size of sulfonated calixarene determines the slantwise degree of the guest in the host cavity (SC5A > STC4A > SC4A), which also governs whether the host−guest capsule can be formed in the solid state: capsule complexes DP^{2+}⊂SC4A and DP^{2+}⊂STC4A are formed, whereas only the simple inclusion complex DP^{2+}⊂SC5A is formed. Furthermore, all three sulfonated calixarene hosts show high affinities with DP^{2+} in the magnitude of 10^5−10^6 M^{-1}, which are much higher than those for the complexation of Phen with these hosts. The

dx.doi.org/10.1021/cg500730m | Cryst. Growth Des. 2014, 14, 4631−4639

higher K_S values for the complexation of DP^{2+} with SC4A, SC5A, and STC4A are all driven by the entropy term due to a more favorable dehydration of N^+ and SO_3^- upon their electrostatic interactions. The present results will help us to understand the inclusion phenomena, recognition mechanisms, and thermodynamic origins of water-soluble sulfonated calixarenes more systematically and comprehensively. These observations also demonstrate unambiguously that the cavity size of the sulfonated calixarene is another important factor for the construction of molecular capsules.

EXPERIMENTAL SECTION

Materials. The three host molecules, *p*-sulfonatocalix[4]arene (SC4A),[20] *p*-sulfonatocalix[5]arene (SC5A),[21] and *p*-sulfonatothiacalix[4]arene (STC4A),[22] and the guest, 5,6-dihydropyrazion[1,2,3,4-*lmn*][1,10]phenanthroline-4,7-diium (DP^{2+}),[23] were synthesized and purified according to previously reported procedures. These compounds were identified by ^1H and ^{13}C NMR spectroscopy in D_2O, performed on a Varian 300 spectrometer (see the Supporting Information, Figures S2−S9), and elemental analysis, performed on a PerkinElmer 2400C instrument (see the Supporting Information). All other chemicals were commercially available and used without further purification.

The phosphate buffer solution of pH 2.0 was prepared by dissolving sodium dihydrogen phosphate in distilled, deionized water to make a 0.1 M solution, which was then adjusted to pH 2.0 by phosphoric acid. The phosphate D_2O buffer solution of pD 2.0 was prepared by dissolving sodium dihydrogen phosphate (NaH_2PO_4, 0.2379 g) in 20.00 mL of D_2O to obtain a 0.1 M solution, which was then adjusted to pD 2.0 by DCl. The pH and pD values of buffer solutions were verified on a Sartorius pp-20 pH meter calibrated with two standard buffer solutions. pH readings were converted to pD by adding 0.4 units.[24]

Measurements. *NMR Spectroscopy.* ^1H NMR and 2D ROESY (rotating frame Overhauser effect spectroscopy) spectra were recorded at pD 2.0 with a Varian Mercury VX300 spectrometer by using 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) as an external reference.

Isothermal Titration Calorimetry (ITC). A thermostated and fully computer-operated isothermal calorimetry (VP-ITC) instrument, purchased from Microcal Inc. (Northampton, MA) was used for all microcalorimetric experiments. The VP-ITC instrument was calibrated chemically by the measurement of the complexation reaction of *β*-cyclodextrin with cyclohexanol, and the obtained thermodynamic data were in good agreement (error <2%) with the literature data.[25] All microcalorimetric titrations between hosts and guests were performed in aqueous phosphate buffer solution (pH 2.0) at atmospheric pressure and 298.15 K. Each solution was degassed and thermostated by a ThermoVac accessory before the titration experiment. Twenty-five successive injections were made for each titration experiment. A constant volume (10 μL/injection) of guest (or host) solution (2.0 mM) in a 0.250 mL syringe was injected into the reaction cell (1.4227 mL) charged with host (or guest) in the same aqueous phosphate buffer solution (0.1 mM). Each titration of guest (or host) into the sample cell gave an apparent reaction heat caused by the formation of an inclusion complex between host and guest. The reaction heat decreases after each injection of guest (or host) because less and less host (or guest) molecules are available to form inclusion complexes. A control experiment was carried out in each run to determine the dilution heat by injecting a guest (or host) aqueous phosphate buffer solution into a pure aqueous phosphate buffer solution containing no host (or guest) molecules. The dilution heat determined in these control experiments was subtracted from the apparent reaction heat measured in the titration experiments to give the net reaction heat.

The net reaction heat in each run was analyzed by using "one set of binding sites" model (ORIGIN software, Microcal Inc.) to simultaneously compute the binding stoichiometry (N), complex stability value (K_S), standard molar reaction enthalpy (ΔH°), and standard deviation from the titration curve. Generally, the first point of the titration curve was disregarded, as some liquid mixing near the tip of the injection needle is known to occur at the beginning of each ITC run. Knowledge of the complex stability value (K_S) and molar reaction enthalpy (ΔH°) enabled calculation of the standard free energy (ΔG°) and entropy changes (ΔS°) according to

$$\Delta G^\circ = -RT \ln K_S = \Delta H^\circ - T\Delta S^\circ$$

where R is the gas constant and T is the absolute temperature.

The typical curve-fitting results for the complexation of DP^{2+} with SC4A, SC5A, and STC4A at pH 2.0 are shown in Figure 9. To check the accuracy of the observed thermodynamic parameters, two independent titration experiments were carried out to afford self-consistent thermodynamic parameters, and their average values with associated errors are listed in Table 2.

Crystal Preparation. *Preparation of Crystal of DP^{2+}⊂SC4A.* To an aqueous solution of SC4A (0.025 mmol, 10 mL) was added 2 equiv of DP^{2+}. Precipitates were formed as the solution was stirred and adjusted to pH = 1−2 by adding 1 M HCl dropwise. Consequently, the solution was heated until clear. After that, it was stirred for another 4 h at room temperature and filtered. The filtrate was placed to evaporation for several days. Then, the yellow crystal formed was collected along with its mother liquor for the X-ray crystallographic analysis (yield: 53%).

Preparation of Crystal of DP^{2+}⊂SC5A. To an aqueous solution of SC5A (0.025 mmol, 10 mL) was added 2.5 equiv of DP^{2+}. Under stirring, 1 M HCl was dropped to adjust the pH to 1−2, followed by filtration, and the filtrate was placed to evaporate for several days. Then, the yellow crystal formed was collected along with its mother liquor for the X-ray crystallographic analysis (yield: 51%).

Preparation of Crystal of DP^{2+}⊂STC4A. Crystal of DP^{2+}⊂STC4A was obtained by hydrothermal synthesis. To an aqueous solution of STC4A (0.025 mmol, 10 mL) was added 2 equiv of DP^{2+}. Precipitates were formed as the solution was stirred and adjusted to pH = 1−2 by adding 1 M HCl dropwise. Then, the mixture was suspended in a Teflon-lined stainless steel bomb. After the bomb was sealed, the system was heated at 120 °C under hydrothermal conditions for 2 days and then cooled gradually to room temperature at a rate of 2 °C/h. The yellow crystal formed was collected along with its mother liquor for the X-ray crystallographic analysis (yield: 62%).

Crystal Data. The X-ray intensity data for complexes DP^{2+}⊂SC4A, DP^{2+}⊂SC5A, and DP^{2+}⊂STC4A were collected on a Rigaku MM-007 rotating anode diffractometer, equipped with a Saturn CCD area detector system, using monochromated Mo K*α* radiation at T = 113(2) K. Data collection and reduction were performed by the Crystalclear program. The structures were solved by using a direct method and refined, employing full-matrix least-squares on F^2 (CrystalStructure, SHELXTL-97). X-ray structural data for DP^{2+}⊂SC4A: $C_{56}H_{67.50}N_4O_{27.75}S_4$ ($[SC4A^{4-}][DP^{2+}]_2{\cdot}11.75H_2O$), M = 1368.88, triclinic, a = 14.066(3) Å, b = 17.611(4) Å, c = 24.426(5) Å, α = 98.68(3)°, β = 95.62(3)°, γ = 91.79(3)°, space group $P\bar{1}$, Z = 4, calculated density = 1.529 g/cm^3, crystal dimensions (mm^3): 0.18 × 0.16 × 0.12, μ = 0.255 mm^{-1}, $2\theta_{max}$ = 50.04°, 32 851 measured reflections of which 20 247 were unique ($R_{(int)}$ = 0.0463), final R indices [I/σ (I) > 2]: R_1 = 0.1045, wR_2 = 0.2488, R indices (all data): R_1 = 0.1272, wR_2 = 0.2649, GOF on F^2 1.052. X-ray structural data for DP^{2+}⊂SC5A: $C_{63}H_{71}N_4O_{30.50}S_5$ ($[SC5A^{5-} + H^+][DP^{2+}]_2{\cdot}10.50H_2O$), M = 1532.54, triclinic, a = 11.177(2) Å, b = 14.903(3) Å, c = 19.970(4) Å, α = 95.73(3)°, β = 93.96(3)°, γ = 94.51(3)°, space group $P\bar{1}$, Z = 2, calculated density = 1.547 g/cm^3, crystal dimensions (mm^3): 0.20 × 0.10 × 0.07, μ = 0.274 mm^{-1}, $2\theta_{max}$ = 50.04°, 19 210 measured reflections of which 11 536 were unique ($R_{(int)}$ = 0.0336), final R indices [I/σ (I) > 2]: R_1 = 0.0734, wR_2 = 0.2053, R indices (all data): R_1 = 0.0864, wR_2 = 0.2187, GOF on F^2 1.038. X-ray structural data for DP^{2+}⊂STC4A: $C_{52}H_{44}N_4O_{20}S_8$ ($[STC4A^{4-}][DP^{2+}]_2{\cdot}4H_2O$), M = 1301.39, triclinic, a = 12.354(3) Å, b = 14.404(3) Å, c = 16.103(3) Å, α = 69.19(3)°, β = 88.31(3)°, γ = 82.76(3)°, space group $P\bar{1}$, Z = 2, calculated density = 1.627 g/cm^3, crystal dimensions (mm^3): 0.18 × 0.16 × 0.12, μ = 0.422 mm^{-1}, $2\theta_{max}$ = 50.04°, 15 397 measured reflections of which 9297 were unique ($R_{(int)}$ = 0.0580), final R indices [I/σ (I) > 2]: R_1 = 0.0436, wR_2 = 0.1247, R indices (all data):

dx.doi.org/10.1021/cg500730m | Cryst. Growth Des. 2014, 14, 4631−4639

R_1 = 0.0596, wR_2 = 0.1333, GOF on F^2 1.099. CCDC-968385, 968386, and 968387 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, U.K.; Fax: (+44) 1223−336−033; or deposit@ccdc.cam.uk).

■ ASSOCIATED CONTENT

Supporting Information

Job's plots of SC4A+DP^{2+} and SC5A+DP^{2+} systems by ^1H NMR spectroscopy; ^1H and ^{13}C NMR spectra of SC4A, SC5A, STC4A, and DP^{2+} in D_2O; elemental analysis data of SC4A, SC5A, STC4A, and DP^{2+}; and X-ray crystallographic data of DP^{2+}⊂SC4A, DP^{2+}⊂SC5A, and DP^{2+}⊂STC4A in CIF format. 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

This work was supported by the Foundation of Talent Introduction in Tianjin Normal University (5RL122), the Foundation of STITP in Tianjin Normal University (2013119), the 973 Program (2011CB932502), and NSFC (20932004), which are gratefully acknowledged.

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