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noncovalent interactions including anion $-\pi$ ,

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Designed self-assemblies based on cooperative

lone-pair electron- $\pi$  and hydrogen bonding<sup>+</sup>

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A dual functional tetraoxacalix[2]arene[2]triazine derivative as a building block was synthesized. Designed self-assemblies were obtained under the guidance of multiple noncovalent interactions including anion $-\pi$ , lone-pair electron $-\pi$  and hydrogen bonding.

Inspired by the pioneering theoretical reports by Alkorta, Besnard and Dougherty, in which the favorable interactions between electron-deficient aromatic rings and electron donating small molecules were suggested,<sup>1</sup> Mascal, Devà and Alkorta published independently their theoretical studies on the noncovalent interaction between anions and electron-deficient aromatics such as triazine, hexafluorobenzene and perfluoroaromatic compounds.<sup>2</sup> Since then an ion- $\pi$  interactions have attracted increasing interest.3 According to the theoretical calculations, four types an ion- $\pi$  interactions, namely typical noncovalent, weak  $\sigma$ , strong  $\sigma$  and C-H···X<sup>-</sup> hydrogen bonding were proposed. The nature, from the theoretical view, of anion- $\pi$  interaction was ascribed mainly to electrostatic attraction, anion induced polarization, charge-transfer (CT) and dispersion.<sup>2b,3c,4,5a</sup> In contrast with the largely developed theoretical results, experimental evidences for an ion- $\pi$  interactions based on charge-neutral electron-deficient aromatics are still rare.5 For example, several groups including ourselves demonstrated the crystal structures of both typical noncovalent and weak  $\sigma$ anion- $\pi$  interactions.<sup>5a,c-g,n,o</sup> Recent remarkable reports from Dunbar,<sup>5g</sup> Saha<sup>5k-m</sup> and Ballester<sup>5p</sup> et al. revealed experimentally the charge-transfer nature of an ion- $\pi$  interactions. In spite of the increasing experimental evidences of an ion- $\pi$  interaction,

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<sup>†</sup> Electronic supplementary information (ESI) available: Experimental details, crystal structures, <sup>1</sup>H and <sup>13</sup>C NMR spectra of products, spectroscopic titration data. CCDC 968607–968610 for  $Et_4N^+(4\mathbf{a}\cdot Cl)^-$ ,  $Et_4N^+(4\mathbf{a}\cdot Br)^-$ ,  $Et_4N^+(4\mathbf{a}\cdot NO_3)^-$  and **4a**. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c3ra47748g

however, study of molecular self-assembly with an ion- $\pi$  interaction as a guiding force is very rare.<sup>5b,d,e,g,6</sup>

As a typical representative of heteracalixaromatics, tetraoxacalix[2]arene[2]triazines have been shown to be unique anion receptors based on anion- $\pi$  interactions.<sup>5d-f,6,7</sup> We have previously demonstrated that tetraoxacalix[2]arene[2]triazine interacted with halides and water in solid state, forming a ternary complex based on an ion- $\pi$  and lone pair electron- $\pi$  interactions.54,6 The included halide anion and water molecule interacted to each other through hydrogen bonding. Moreover, two ternary complexes self assembled into cage structures through a hydrogen bond network between two halides and two water molecules. Noteworthy, such cage self-assemblies are discrete due to the binding saturation of water molecule. Our interests on anion- $\pi$  interaction and anion- $\pi$  guided supramolecular self-assembly led us to carry out the current study. We envisioned then to introduce hydroxyl groups on the larger rim of benzene rings of tetraoxacalix[2]arene[2]triazine. Such host molecule is dual functional with electron-deficient triazines as  $\pi$  receptors and hydroxyl groups as lone pair electrons and hydrogen bond donors. In the presence of anions, the hydroxyl groups are expected to form ternary complex with anion and the V-shaped cavity of the host molecule instead of water molecule, which would led to the formation of infinite self-assemblies. Reported herein is the synthesis of dihydroxylsubstituted tetraoxacalix[2]arene[2]triazine and the sequential anion guided self-assemblies in solid state.

We initiated our synthesis taking benzyl protected phloroglucin **1** and cynuric chloride **2** as the starting materials. In the presence of diisopropylamine (DIPEA), the reaction of **1** and **2** in THF at 0 °C afforded the trimer **3**. The macrocyclization reaction of trimer **3** with monomer **1** proceeded smoothly at ambient temperature in acetone to give **4b** in 48% yield. The AlCl<sub>3</sub>mediated debenzylation of **4b** was then performed with CHCl<sub>3</sub> as the solvent, affording the larger-rim dihydroxylated tetraoxacalix[2]arene[2]triazine **4a** in 21% yield (Scheme 1).

The structures of the synthesized compounds were established on the basis of spectroscopic data and microanalyses



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(see Fig. S14–19†). From the X-ray molecular structures of 4a, which was shown in Fig. 1, the larger-rim dihydroxylated macrocyclic molecule adopts a 1,3-alternate conformation, similar with other tetraoxacalix[2]arene[2]triazine derivatives.<sup>8</sup> Two triazine rings form an electron-deficient V-shaped cavity with the larger-rim distance of the cavity being 9.218 Å (d<sub>C1···C11</sub>). The two benzene rings, meanwhile, construct an electron-rich cavity with the larger-rim distance of the cavity being 5.373 Å (d<sub>C6···C15</sub>). The introduced hydroxyl groups act as hydrogen bond donor and form hydrogen bonds with oxygen of water molecule or nitrogen of triazine rings, leading to linear self-assembly (Fig. S1†).

To investigate the anion- $\pi$  interactions between **4a** and anions at molecular level and anion guided self-assemblies, single crystals of the complexes were cultivated through diffusion of ethyl ether into the acetone solution of the host-guest mixtures at room temperature. The crystallography data of the complexes between host **4a** and Et<sub>4</sub>NX (X = Cl<sup>-</sup>, Br<sup>-</sup> and NO<sub>3</sub><sup>-</sup>) are listed in Table S1.<sup>†</sup>

As depicted in Fig. 2 and Fig. S2–S4,† the host molecule **4a** forms 1 : 1 complexes with Cl<sup>-</sup>, Br<sup>-</sup> and NO<sub>3</sub><sup>-</sup>. The anions are included in the V-shaped electron-deficient cavity forming typical anion– $\pi$  interactions with one of the triazine rings. This was evidenced by the observation of shorter distances between anions and plane of the triazine ring being 3.418 (d<sub>Cl-plane</sub>), 3.486 (d<sub>Br-plane</sub>) and 2.880 Å (d<sub>O7-plane</sub>), respectively, than the sums of their van der Waals radius.<sup>10</sup> Different interaction



Fig. 1 Crystal structure of 4a (A) top view and (B) side view. The ellipsoid probability is 25 percentage. Hydrogens are omitted for clarity.



**Fig. 2** Crystal structure of complex  $Et_4N^+(4a \cdot Cl^-)$  (A) side view, (B) top view, (C) ion pair complex and (D) infinite self-assembly. Selected distances (Å): 3.418 [Cl(3)…triazine(1) plane], 3.033 Cl(3)…O(5), 3.308 [O(5)…triazine(2) plane], 8.909 C(1)…C(11), 4.136 C(9)…C(18), 7.433 C(6)…C(15). The ellipsoid probability is 25 percentage. Hydrogens are ommitted for clarity.

modes between anions and 4a in comparison with that between anions and the parent host molecule tetraoxacalix[2]arene[2]triazine were noticeable. In the case of 4a-halide complexes, for instance, one hydroxyl group of another host molecule is included in the cavity, with oxygen atom locating above the other triazine ring and forming short contacts with the plane of triazine ring. Consequently, the deliberately introduced hydroxyl group serves as lone pair electrons and hydrogen bond donor instead of water molecule and form 4a-halide-hydroxyl ternary complexes, which is in contrast to the host-halidewater ternary complex of the parent host molecule.<sup>5d</sup> In case of  $Et_4N^+(4a \cdot NO_3^-)$  complex, which is shown in Fig. S4,<sup>†</sup> nitrate straights up in the cavity with the plane of nitrate orthogonal with one of the triazine rings. Such direction of nitrate in the cavity prevents it from forming typical and weak  $\sigma$  anion- $\pi$ interactions with both triazine rings, the interaction mode in the complex of nitrate and the parent molecule,<sup>5f</sup> but renders the formation  $4a-NO_3^{-}$ -hydroxyl ternary complex. The location of tetraethylammonium ion in the aforementioned host-guest complexes is interesting. In sharp contrast with the parent host-anion complexes, in which tetraethylammonium ion showed no contact with the macrocyclic receptor, the cation in 4a-anion complexes occupies the electron-rich cavity constructed with the larger rims of benzene rings. The distances of alkyl C-H and planes of benzene rings for the three complexes are in the range of 2.871 to 3.298 Å, suggesting possible cation- $\pi$  interactions. Noteworthy, in order to accommodate the tetraethylammonium ion, 4a self tuned the cavity formed with larger rims of the benzene rings from 5.373 Å in host 4a to 7.024 in  $(4a \cdot NO_3)^-$ , 7.428 in  $(4a \cdot Br)^-$  and 7.433 Å in

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 $(4\mathbf{a}\cdot \mathrm{Cl})^-$  complexes, respectively. Hence the functionalized tetraoxacalix[2]arene[2]triazine **4a** serves as a ditopic receptor to simultaneously complex anion with its V-shaped electron-deficient cavity and cation with its V-shaped electron-rich cavity, respectively, leading to ion-pair interaction based on anion- $\pi$  and cation- $\pi$  interactions. The aforementioned ion-pair interactions are probably due to the electronic donating effect of the attached hydroxyl groups, which increased the electronic density of the benzene rings and facilitated the cation- $\pi$  interaction.

Last but not the least, the anion directed self-assemblies were worth addressing. In the presence of anions, as shown in Fig. 2D and Fig. S2–S4,† the hydrogen bonding linked selfassembly of the host molecule **4a** was disrupted (Fig. S1†). Alternatively, under the guiding of cooperative anion– $\pi$ interaction, lone-pair electron– $\pi$  and intermolecular hydrogen bonding interactions, an infinite linear self-assembly or supramolecular wire was formed (Fig. 2D and Fig. S3E and S4E†). In addition, cavity-included anions also interact with a second hydroxyl group of another host molecule from outside the cavity (Fig. S2A, S3D and S4D†), which links the wires together and leads to a mesh assembly (Fig. S2B, S3F and S4F†).

By means of <sup>1</sup>H NMR titrations, the interactions of **4a** and anions in solution were investigated. Job's plot experiments demonstrated that the anions formed 1 : 1 complex with **4a** in d<sub>6</sub>-acetone solution (Fig. S5–S7†). The addition of anions to the solution of **4a** led to a downfield shift of the hydroxy-H (H<sup>3</sup>), indicating the formation of O–H…anion hydrogen bonding. The formation of hydrogen bonding between the hydroxyl group and anions also caused the slight downfield movement of aryl-H (H<sup>2</sup>). The NMR titration data were fitted with a HyperNMR program giving the association constants for anions being 127 ± 10 M<sup>-1</sup> (**4a**·Cl)<sup>-</sup>, 43 ± 0.3 M<sup>-1</sup> (**4a**·Br)<sup>-</sup> and  $42 \pm 0.2 M^{-1} ($ **4a** $\cdot NO_3)^-$ , respectively. Moreover, ESI-MS experiments also gave 1 : 1 complexes between **4a** with anions in gaseous state, which is in agreement with the results in solution (Fig. S11–S13†).

In addition to the host-guest binding affinity determination, diffusion-ordered NMR spectroscopy (DOSY) experiments were applied to find the possible self-assemblies in solution, taking the interaction between 4a and chloride as a representative example. As depicted in Fig. S8A and B,† in d<sub>6</sub>acetone and at 213 K, the host 4a and guest Bu<sub>4</sub>NCl in the free states give diffusion coefficients of 6.47  $\times$   $10^{-10}\mbox{ cm}^2\mbox{ s}^{-1}$  $(D_{\rm host})$  and 10.34  $\times$  10<sup>-10</sup> cm<sup>2</sup> s<sup>-1</sup> ( $D_{\rm guest}$ ), respectively. The larger diffusion coefficient of guest than that of host is reasonable due to its smaller molecular weight. However, in the mixture of 4a and  $Bu_4NCl$  (1 : 2), only one diffusion band in addition to the band of solvent was observed. The apparent diffusion coefficients decreased from 6.47  $\times$   $10^{-10}$ cm<sup>2</sup> s<sup>-1</sup> ( $D_{\rm free}$ ) to 5.12  $\times$  10<sup>-10</sup> cm<sup>2</sup> s<sup>-1</sup> ( $D_{\rm bound}$ ) for the host and from 10.34  $\times$  10<sup>-10</sup> cm<sup>2</sup> s<sup>-1</sup> ( $D_{\rm free}$ ) to 5.12  $\times$  10<sup>-10</sup> cm<sup>2</sup>  $s^{-1}$  ( $D_{bound}$ ) for the guest, respectively. The almost identical apparent diffusion coefficients of the bound guest  $(5.82 \times 10^{-10})$ cm<sup>2</sup> s<sup>-1</sup>) and the bound host (5.12  $\times$  10<sup>-10</sup> cm<sup>2</sup> s<sup>-1</sup>) in the mixture indicate the formation of strong complex in solution.9

In the premise of assuming fast exchange on the NMR timescale, the apparent diffusion coefficient  $(D_{app})$  of the host should be a weighted average of the free and bound diffusion coefficients (D<sub>free</sub> and D<sub>bound</sub>, respectively).9 According to the bound fraction of the host 4a, which was calculated from the association constant ( $K_a = 127 \text{ M}^{-1}$ ) between 4a and Cl<sup>-</sup>, the calculated bonded diffusion coefficient of 4a was 4.39  $\times$  $10^{-10}$  cm<sup>2</sup> s<sup>-1</sup>. On the assumption that the molecules are spherical, the molecular weight of the complex calculated from the equation  $M_{\text{complex}}/M_{\text{free}} = (D_{\text{free}}/D_{\text{bound}})^3$  is 1506, which is double of the sum of host ( $M_w = 475.2$ ) and guest ( $M_w = 278.0$ ), suggesting the complex has an approximate structure of  $[Bu_4N^+(4\mathbf{a}\cdot Cl)^-]_2$ . Noticeably, such outcomes also support the apparent 1:1 stoichiometry obtained by Job's plot. The NMR titration results indicate that hydrogen bonding is one of the guiding forces of the host-guest interaction in solution. In addition, DOSY experiments showed the formation of low-level preorganzied self-assemblies in dilute solution, suggesting the probable existence of cooperative interactions. We further applied 1-D Selective NOESY experiments (performed at 213 K in order to inhibit the exchange of active hydroxyl-H) to get more information of the interactions in solution. In the absence of chloride (Fig. S9A<sup>†</sup>), selective excitation of proton H<sup>3</sup> on the hydroxyl group does not produce inverted signals of H<sup>1</sup>, excluding the intermolecular short contact between the two protons. In the presence of chloride, however, an inverted signal of H<sup>1</sup> was observed (Fig. S9B<sup>+</sup>). This result, in combination of the slightly upfield shift of H<sup>1</sup> during the titration of 4a with chloride, and the aforementioned formation of O-H… chloride hydrogen bonding, indicate probably the existence of cooperative anion- $\pi$  interaction and intermolecular hydrogen bonding in solution. In addition, <sup>1</sup>H NMR spectra showed a upfield shift of the protons of TBA cation in the presence of host (Fig. S10<sup>†</sup>), and selective excitation of the protons of the butyl groups of TBA caused an inverted signal of  $H^2$  and a relatively weak inverted signal of H<sup>3</sup> (Fig. S9C<sup>†</sup>), suggesting the probable inclusion of TBA cation in between the Vshaped benzene rings in solution.

In summary, we have synthesized a hydroxyl functionalized tetraoxacalix[2]arene[2]triazine host molecule through a fragment coupling followed by AlCl<sub>3</sub> mediated deprotection protocol. The introduction of hydroxyl groups on the larger rim rendered the macrocyclic molecule as an unique donor-acceptor functional building block. Infinite selfassemblies were then obtained under the directing of cooperative anion- $\pi$ , lone-pair electron- $\pi$  interactions and intermolecular hydrogen bonding. Our study indicated that anion- $\pi$  interaction directed self-assembly could be designed through the rational fabrication of building blocks.

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