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Anion-directed assembly of a rectangular supramolecular cage in the solid state with electron-deficient phenoxylated oxacalix[2]arene[2]triazine[†]

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Chloride– π interaction along with lone-pair electrons– π interaction, hydrogen bonding and π – π stacking induced the hexameric assembly of the parent macrocycle into a rectangular supramolecular cage in the solid state.

Anion receptors bearing π electron-deficient arenes have attracted increasing interest during the past decade.¹ The anion- π interaction between charge neutral electron-deficient aromatic rings, as predicted by theoreticians,² has been evidenced experimentally both by solid state and solution investigations.^{3–5} For example, in the solid state, while weak σ -interaction in which anions interact with π electron-deficient arenes such as, tetracyanobenzene,^{3c} tetracyanopyrazine^{3a,b} and 1,4,5,8,9,12-hexaazatriphenylenehexacarbonitrile,^{3e} from the periphery of the aromatic rings has been shown, typical anion $-\pi$ interaction in which an anion (halide) is located just over the triazine centroid of a macrocyclic oxacalix[2]arene[2]triazine host molecule has been observed.3d Despite the increasing number of examples of anion- π interactions being reported in the literature, it is worth addressing that as an emerging catalog of non-covalent bond interaction, the directing ability of an inn- π interaction to induce the molecular assembly based on charge neutral electron deficient arenes has rarely been studied.^{3a,b,d,e,4d}

As one of the typical macrocyclic molecules of heteracalixaromatics, a new generation of host molecules in supramolecular chemistry,⁶ the 1,3-alternate conformational oxacalix[2]arene[2]triazines have been shown to use their electron-deficient V-shaped cleft to interact with anions through anion– π interactions.^{3d,4d,7} Our previous study has demonstrated that the binding ability of tetraoxacalix[2]arene[2]triazines towards anions was affected remarkably by the electronic nature of the substituents on triazine rings.^{3d} In other words, the anion– π interaction of triazine toward anions was regulated by the substituents. We have also demonstrated that anion– π interaction along with hydrogen bonds led to interesting self-assembled structures in the solid state.^{3d,4d} Our interest in directing the effect of anion– π interactions on molecular self-assembly has led us to the current study. To fine-tune the anion– π binding ability of triazine rings, and also to append potential π – π stacking moieties, phenoxy and perfluorophenoxy substituents are introduced into triazine rings of oxacalix[2]arene[2]triazine. We were delighted to find out that chloride– π interaction along with lone-pair electron– π interaction, hydrogen bonding and π – π stacking induced the hexameric assembly of the parent macrocycle into a rectangular supramolecular cage in the solid state.

To synthesize the target macrocyclic molecules, we first carried out aromatic nucleophilic substitution reaction starting from parent dichloro-substituted oxacalix[2]arene[2]triazine 1^{3d} with pentafluorophenol **2** and phenol. The reaction between **1** and **2** proceeded efficiently in the presence of K₂CO₃ in acetonitrile at room temperature, giving **5b** almost quantitatively. However, similar reaction using phenol as a nucleophilic agent yielded unfortunately a trace amount of desired product **5a**. A one-pot protocol with resorcinol **3** and 2,4-dichloro-6-phenoxy-1,3,5-triazine **4** (see ESI† for synthesis of **4**) as the starting materials was then employed, which gave successfully **5a** in 39% yield (Scheme 1).

The structures of all the synthesized compounds were established on the basis of their spectroscopic data and microanalysis



Scheme 1 Synthesis of oxacalix[2]arene[2]triazine derivatives 5a and 5b.

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[†] Electronic supplementary information (ESI) available: Experimental details, crystal structures, ¹H and ¹³C NMR spectra of products, spectroscopic titration data. CCDC 897876 (**5a**), 897874 (**5b**), 897875 (**5a** (**Et**₄NCI) \cdot H₂O). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2cc36465d



Fig. 1 X-ray structures of (A) **5a** (side view), (B) and (C) a cyclic hexamer of **5a** through intermolecular lone pair electrons– π interaction and hydrogen bonding (benzene rings attached on triazines and hydrogens are omitted for clarity) and (D) anion induced rectangular cage structure through multiple weak noncovalent interactions. The probability is 25%.

(see Fig. S34-S39, ESI[†]). To get the structural information at the molecular level, single crystals of compounds 5a and 5b were cultivated through slow evaporation of mixtures of dichloromethane and hexane, acetone and hexane, respectively.[‡] Both oxacalix[2]arene[2]triazine derivatives 5a and 5b adopt the 1,3-alternate conformation with the introduced benzene and perfluorobenzene rings on the triazine rings being trans-aligned (Fig. 1 and Fig. S3, ESI⁺). The introduction of benzene and perfluorobenzene rings modified the intermolecular interaction, which led to interesting molecular self-assemblies in the solid state. In the case of 5a, one nitrogen of the triazine of one molecule interacted with the triazine of another molecule forming lone pair electrons- π (lpe- π) interaction with the distance ($d_{\text{N-plane}}$) being 3.092 Å (Fig. 1B). In addition, weak intermolecular hydrogen bonds between hydrogen bond acceptors such as triazine nitrogen, bridging oxygen and hydrogens of

the benzene rings were also observed. Directed by the multiple weak noncovalent interactions, 5a formed a unique cyclic hexamer structure in the solid state (Fig. 1B and C and Fig. S2, ESI[†]). Due to the electronic nature of the introduced perfluorobenzenes, multiple intermolecular lone pair electrons– π interactions were formed in the case of 5b. leading to a noncovalently bonded dimer structure. For example, one of the perfluorobenzene rings of one molecule located in the V-shaped cavity formed by the two triazine rings of another molecule forms multiple lone pair electrons- π interactions (F:-triazine) with the distances ($d_{\text{F-plane}}$) being 3.077 and 3.394 Å, respectively. Meanwhile, the perfluorobenzene ring served as a π -electron deficient acceptor and formed intermolecular σ -type lone pair electrons– π interactions with the nitrogen of triazine and the bridging oxygen atom, giving distances of 3.127 and 2.917 Å, respectively (Fig. S4, top, ESI⁺).

To investigate the host-guest chemistry between macrocycles and anions, the single crystals of the complexes were cultivated by slow evaporation of a mixture of dichloromethane and methanol and the complex of 5a and tetraethylammonium chloride was obtained. Interestingly, the cyclic hexamer self-assembly of the host molecule 5a was disrupted in the complex, instead, two [5a-Cl⁻·H₂O] ternary complexes self-assembled into a rectangular cage structure (Fig. 1D and Fig. S5, ESI†) through a hydrogen bond network between two chloride and two water molecules, and also the π - π stacking between the benzene rings on triazines. Some details of the structure are worth addressing. As shown in Fig. 1D, chloride was located almost above the center of one of the triazine rings of 5a, the distance of chloride to the plane and centroid of triazine was 3.238 ($d_{\text{chloride-plane}}$) and 3.258 Å ($d_{\text{chloride-centroid}}$), respectively, forming typical noncovalent chloride– π interaction. On the other hand, a water molecule formed lone pair electrons– π interaction with the other triazine ring of 5a, giving distances of 2.773 (d_{oxygen-plane}) and 2.830 Å (d_{oxygen-centroid}), respectively. The included chloride and water in the cavity of 5a interacted with each other through hydrogen bonding judged from the distance of 3.123 Å between chloride and water oxygen $(d_{\Omega-Cl})$. The two introduced benzene rings on the triazine rings, on the other hand, changed their alignment from a trans-form (Fig. 1A) to cis-form in the complex, in order to form π - π stacking between the two face-to-face ternary complexes (Fig. 1D). In addition, the host molecules interacted with each other through CH– π interactions between the benzene rings, which led to an infinite two dimensional cagelike selfassembly (Fig. S5, ESI[†]). The formation of a supramolecular cage is mainly attributable to multiple non-covalent interactions of anion- π , lpe- π , hydrogen bond and π - π stacking effects among the neutral and charged components, though the crystal packing forces could not be excluded completely.

The interaction of the synthesized macrocyclic host molecules **5a** and **5b** with anions including Cl⁻, Br⁻, N₃⁻, NO₃⁻, HSO₄⁻ and H₂PO₄⁻ in tetrabutylammonium salts in acetonitrile was also studied by means of fluorescence titration. As shown in Fig. S6–S13 (ESI[†]), the interaction of **5a** with anions caused quenching of the fluorescence emission of the host at 354 nm except for Cl⁻, which caused the quenching of the fluorescence intensity at 354 nm with a concomitant bathochromic-shift to 362 nm (Fig. S7, ESI[†]). The association constants for 1 : 1 host–guest complexes ($K_{a(1:1)}$) were calculated using a Hyperquad program based on the fluorescence titration data,⁸ giving $7.33 \times 10^2 \text{ M}^{-1}$ for (**5a**·Cl⁻), $1.67 \times 10^2 \text{ M}^{-1}$ for (**5a**·Br⁻), $1.68 \times 10^3 \text{ M}^{-1}$ for (**5a**·N₃⁻), $6.84 \times 10^2 \text{ M}^{-1}$ for (**5a**·NO₃⁻), $2.93 \times 10^2 \text{ M}^{-1}$ for (**5a**·HSO₄⁻) and $6.04 \times 10^3 \text{ M}^{-1}$ for (**5a**·H₂PO₄⁻), respectively. Surprisingly, the response of **5b** towards anions based on the fluorescence titration was very different from that of **5a**. For example, the addition of anions such as, Cl⁻, Br⁻, NO₃⁻, HSO₄⁻ and H₂PO₄⁻ did not change the fluorescence of **5b** at all, whereas the addition of N₃⁻ led to quenching of the fluorescence intensity at 360 nm, indicating a selective interaction constant ($K_{a(1:1)}$) for the complex of **5b** with N₃⁻ was up to $1.95 \times 10^4 \text{ M}^{-1}$.

We further examined the interaction between host molecules 5a, 5b and the anions by means of NMR spectroscopy. No variation at all in the ¹H NMR spectra of **5a** occurred with the addition of anions (Fig. S14-S19, ESI[†]). The result is consistent with our previous observation, reflecting that an ion- π interactions are responsible for the change of fluorescence spectrum of the host molecule.^{3d,4d,7} In the case of **5b** (Fig. S20–S25, ESI⁺), whereas the proton signals remained intact with the addition of other anions, the addition of 0.25 to 1 equivalent of azide, however, resulted in the observation of many signals, which most probably indicated the conformational changes after complexation (Fig. S22, ESI[†]). The formation of a complex between host 5b and azide was further evidenced by the observation of an upfield shift of ¹⁹F signals (Fig. S26, ESI⁺). The outcomes of both spectroscopic titration and NMR experiments indicated that the interaction between azide and **5b** is most probably different from that of **5a**. Last but not least, the interaction of host molecules 5a and 5b with anions was also evidenced by the observation of ion peaks of the complexes in ESI mass spectra (see Fig. S27-S33, ESI⁺).

In summary, we have synthesized phenoxy- and perfluorophenoxy-substituted oxacalix[2]arene[2]triazine derivatives **5a** and **5b**. In the solid state, **5a** and **5b** formed a unique cyclic hexamer and non-covalently bonded dimer structure, respectively. In the presence of chloride, the cyclic hexamer of **5a** was turned into a rectangular supramolecular cage structure due to the formation of chloride– π , H₂O:– π , hydrogen bonding (Cl···H–O) and π – π stacking interactions. On the basis of fluorescence titration, the host molecule **5a** was found to be able to interact with the examined anions in solution, giving association constants ($K_{a(1 : 1)}$) in the range of 1.67×10^2 M⁻¹ to 6.04×10^3 M⁻¹. Whereas **5b** selectively recognized azide with an association constant of up to 1.95×10^4 M⁻¹. The present study indicated that anion– π interaction would find applications in anion-directed molecular self-assembly.

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Notes and references

[‡] Crystallographic data for **5a** (C₃₀H₁₈N₆O₆): $M_r = 558.50$, trigonal, space group R_3^3 , a = 35.328 (5), b = 35.328 (5), c = 12.311 (3) Å, $\alpha = 90.00^\circ$, $\beta = 90.00^\circ$, $\gamma = 120.00^\circ$, V = 13307 (4) Å³, T = 173 (2) K, full-matrix least-squares refinement on F^2 converged to $R_F = 0.0704$ [$I > 2\sigma(I)$], 0.0900 (all data) and $Rw(F^2) = 0.1557$ [$I > 2\sigma(I)$], 0.1609 (all data), goodness of fit 1.178. CCDC 897876. Crystallographic data for **5b**. (C₃₀H₈F₁₀N₆O₆): $M_r = 738.42$, monoclinic, space group P2(1)/n, a = 12.587 (3), b = 18.349 (4), c = 13.403 (3) Å, $\alpha = 90.00^\circ$,

 $β = 106.57^\circ$, $γ = 90.00^\circ$, V = 2967 (10) Å³, T = 173(2) K, full-matrix least-squares refinement on F^2 converged to $R_F = 0.1296$ [$I > 2\sigma(I)$], 0.1540 (all data) and $Rw(F^2) = 0.2943$ [$I > 2\sigma(I)$], 0.3110 (all data), goodness of fit 1.386. CCDC 897874. Crystallographic data for complex **5a**·(**Et_4NCI**)-**H_2O** ($C_{38}H_{40}$ CIN₇O₇): $M_F = 742.22$, triclinic, space group $P\bar{1}$, a = 12.102 (2), b = 12.290 (3), c = 13.841 (3) Å, $\alpha = 66.29^\circ$, $\beta = 76.08(3)^\circ$, $\gamma = 86.19^\circ$, V = 1828.6 (6) Å³, T = 173(2) K, full-matrix least-squares refinement on F^2 converged to $R_F = 0.0508$ [$I > 2\sigma(I)$], 0.0610 (all data) and $Rw(F^2) = 0.1127$ [$I > 2\sigma(I)$], 0.1183(all data), goodness of fit 1.10. CCDC 897875.

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