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Triangular Assembly Through Charged Hydrogen Bonds in Polar Solvent

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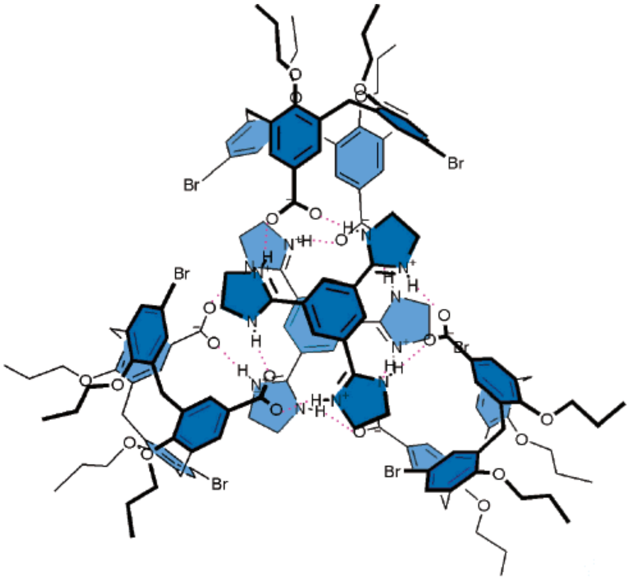

We have demonstrated a triangular assembly driven by 12 charged hydrogen bonds and $\pi-\pi$ interactions. This assembly is stable even in polar solvents because of its charged hydrogen-bond nature. Helical arrangement of the complex is confirmed by its crystal structure. A solution structure is assigned to the D_3 isomer corresponding to the solid-state structure by temperature-dependent ^{1}H NMR experiments.

Self-assembly has been employed as a powerful tool for constructing various types of supramolecular structures based on the simultaneous assembly of preorganized building blocks. Consequently, there is continuous interest in designing preorganized building blocks. Calixarenes have been widely used as building blocks because of their unique structure,[1] easy functionalization of the lower and upper rims, and bowl-shaped structure. These structural features encouraged many supramolecular chemists to construct various three-dimensional assembly structures. In the early days, various types of box- or capsule-like structures were constructed using neutral hydrogen bonds.[2] However, most of these systems work in nonpolar solvents because of the relatively weak nature of hydrogen bonds in polar solvent systems. Recently, different approaches involving multiple ionic interactions have been widely studied to develop capsule-like structures that are operative in polar solvents.[3] Another type of an interesting supramolecular structure using calixarene building blocks is the double rosette assembly reported by Reinhoudt and co-workers.[4] They found that calix[4]arenes substituted with two melamine units at the upper rim form box-like assemblies together with barbituric acid and cyanuric acid derivatives. These assemblies show unique properties in terms of asymmetric induction,[5] noncovalent synthesis,[6] and guest encapsulation.[7] Here, we report on the double rosette-type assembly driven by charged hydrogen bonding and $\pi-\pi$ interactions between tris(imidazoline) **1** and calix[4]arene dicarboxylic acid (**2**) in polar solvent.

Modeling predicted that 2:3 self-assembly of tris(imidazoline) (**1**) and bidentate carboxylic acid (**2**) would give a triangular assembly. We used cone-shaped calix[4]arene (**2**) substituted with two alternating carboxylic acids oriented in the same direction on the upper rim as a bidentate carboxylic acid

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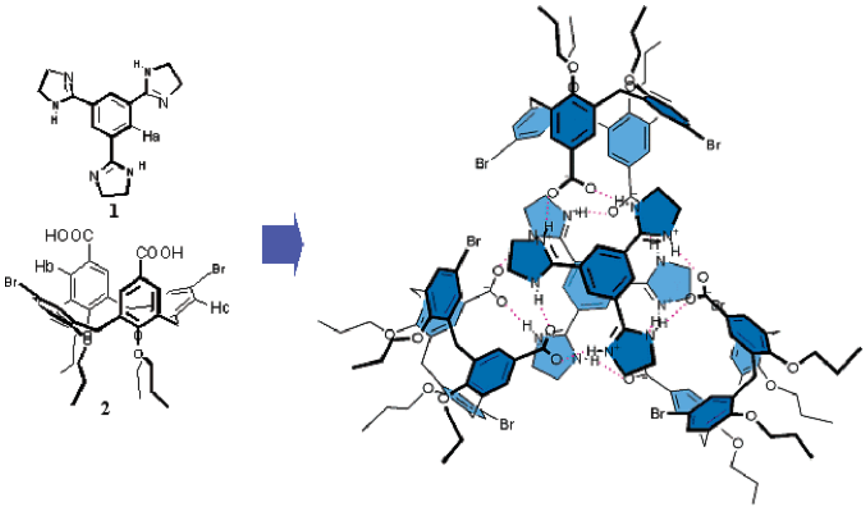
SCHEME 1



(Scheme 1).[8] NBS bromination of tetrapropoxycalix[4]arene followed by treatment of the resulting 5,11,17,23-tetrabromotetrapropoxycalix[4]arene with excess *n*-BuLi in THF at −78 °C and quenching with CO_2 led to the selective conversion to 5,17-dibromo-11,23-dicarboxy-25,26,27,28-tetrapropoxycalix[4]arene (**2**) in the cone conformation.

The ^{1}H NMR spectrum of a 2:3 mixture of **1** and **2** in $CDCl_3$/CD_3OD (v/v = 1:1) shows a highly symmetric one-set signal, suggesting the formation of a symmetric structure (Figure 1). The aromatic proton (H_a) of **1** is strongly shifted downfield ($\Delta\delta_{Ha} = 1.46$ ppm), coupled with an upfield shift of the aromatic proton (H_b) of **2** substituted with carboxylic acid ($\Delta\delta_{Hb} = -0.39$ ppm). The shifts are the result of proton transfer from the carboxylic acid to the tris(imidazoline) base. Methylene protons of **1** at ∼4 ppm become broadened. This signal change comes from protonation and hindrance of free rotation of **1** upon complexation.

^{1}H NMR spectrum changes were monitored adding **1** to **2** in $CDCl_3$/CD_3OD (v/v = 1:1) (Figure 1). As **1** was added to **2**, a new set of peaks assigned to the 2:3 assembly appeared. Signals corresponding to the assembled structure became major ones at a 2:3 ratio of **1** and **2** as the signals of free **2** mostly disappeared. At a 1:3 ratio of **1** and **2**, we cannot observe peaks of free **1**, which was mostly used for constructing the assembly. When an excess of **1** was added, signals of free **1** remained at the same position. At a 4:3 ratio of **1** and **2**, there are only two sets of signals assigned to the complex and free **1**. This indicates that exchange between the complex and free ligands is slow on the NMR time scale. Also, there are no intermediate structures such as partial assemblies (1:1, 2:2, 1:3, etc.) or oligomeric species. The assembly works in a wide range of polarities from neat $CHCl_3$ to $CHCl_3$/MeOH = 1:2 (v/v). However, a more polar solvent system cannot be used because of solubility issues.

The assembly $\mathbf{1}_2\cdot\mathbf{2}_3$ was also characterized by MALDI-TOF mass spectrometry. The spectrum shows a peak at *m/z* 2983 of the assembly $[\mathbf{1}_2\cdot\mathbf{2}_3 - 2CO_2]^+$. The major peak at *m/z* 2083 is assigned to $[\mathbf{1}_2\cdot\mathbf{2}_2\cdot Na - 4\ CO_2]^+$ and another peak at *m/z* 2001 to $[\mathbf{1}\cdot\mathbf{2}_2\cdot Na]^+$.

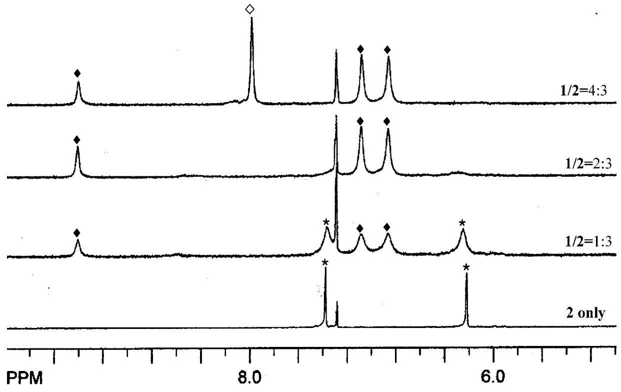


FIGURE 2. Partial ^{1}H NMR spectra upon adding **1** to **2** ([**1**] = 5 mM and [**2**] = 30 mM) in $CDCl_3$/CD_3OD (v/v = 1:1) at room temperature. ◆: Complex of **1** and **2**, ◇: free **1**, and *: free **2**.

Two-dimensional NOESY experiments were performed to locate the spatial proximity of various protons of complex $\mathbf{1}_2\cdot\mathbf{2}_3$. NOE connectivities were observed for the methylene protons of **1** with aromatic protons (H_b and H_c) of **2**. The presence of these NOE connectivities provides strong evidence for the fact that **1** and **2** form a close contact structure in solution.

Crystals suitable for X-ray diffraction analysis were obtained by slow evaporation of a 2:3 mixture of **1** and **2** in a 1:1 (v/v) mixture of $CHCl_3$ and MeOH. The crystal structure reveals that

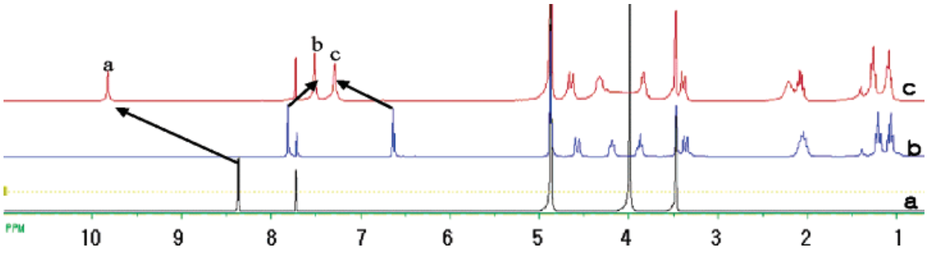


FIGURE 1. ^{1}H NMR spectral changes upon complexation in $CDCl_3$/CD_3OD (v/v = 1:1) at room temperature. (a) **1**, (b) **2**, and (c) $\mathbf{1}_2\cdot\mathbf{2}_3$.

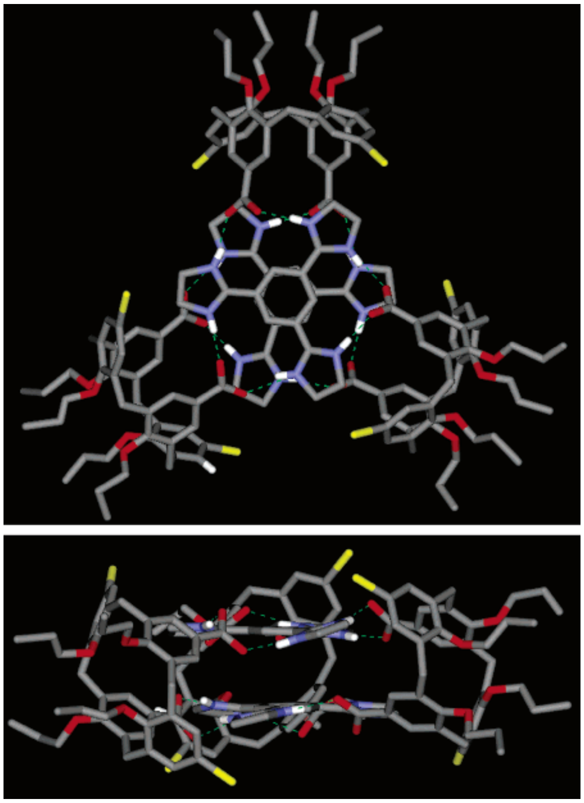


FIGURE 3. Crystal structures of $\mathbf{1}_2\cdot\mathbf{2}_3$. C (gray), O (red), N (blue), Br (yellow), and H (white). Hydrogen bonds are indicated in green dotted lines. All hydrogen atoms except for two hydrogen atoms in the imidazolinium group are omitted for clarity.

1 and **2** are held together by 12 Coulombic H-bonds forming a triangular assembly (Figure 3). Sides of an overall triangular assembly (distances between terminal methyl carbon atoms of the propyl group at the corners of $\mathbf{1}_2\cdot\mathbf{2}_3$) are approximately 2.5 nm long. Two central tris(imidazolinium)s are stacked by $\pi-\pi$ interactions. The two central benzene rings of **1** lie nearly parallel to each other with an interplane distance of 3.45 Å, which leaves little space for guest encapsulation in the solid-state structure like Reinhoudt's double rosette. One central benzene ring of **1** is twisted by about 50° with respect to the adjacent benzene ring. Charge−charge repulsion between positively charged imidazoliniums causes them to stack with a staggered mode. As a result, the overall structure of the assembly displays chirality (*P* or *M*), even though there is no chiral center. The calix[4]arene units are organized into a pinched cone conformation suitable for a 2:3 assembly. The phenyl rings substituted with carboxylic acid in calix[4]arene are parallel to each other with an interplane distance of 5.47 Å. The O−N distance forming Coulombic hydrogen bonds lies between 2.65 and 2.80 Å. Presumably, $\pi-\pi$ stacking of the central phenyl rings of **1** and the charged hydrogen bonds between carboxylate and imidazolinium are the major driving forces for spontaneous assembly of the 2:3 mixture of **1** and **2** into a helical structure.

2:3 assembly of **1** and **2** can be present as two conformational isomers in solution: the D_3 isomer (staggered and chiral as shown in the solid-state structure) and the D_{3h} isomer (eclipsed and achiral).[9] Since one set of signals of the aromatic protons of calix[4]arene was obtained at room temperature, we examined low-temperature NMR of 1:3 mixture of **1** and **2** to find a major isomer in solution (Figure 4). As the temperature drops, aromatic protons of free **2** become sharp, while aromatic protons of **2** corresponding to the complex $\mathbf{1}_2\cdot\mathbf{2}_3$ split into two sets without showing D_{3h} isomer signals, which indicates that the D_3 isomer is dominant in solution. Temperature-dependent NMR of a ∼2:3 mixture of **1** and **2** shows a similar pattern to the 1:3 mixture.

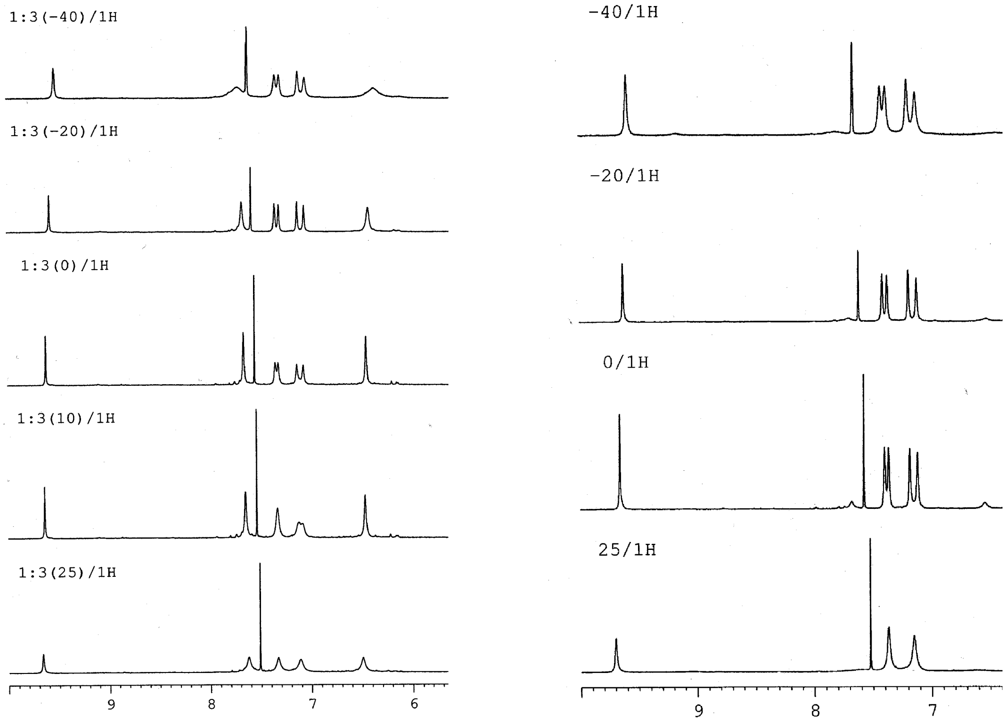


FIGURE 4. Partial views of temperature-dependent ^{1}H NMR spectra. 1:3 mixture of **1** and **2** (left, 25, 10, 0, −20, and −40 °C) and 2:3 mixture of **1** and **2** (right, 25, 0, −20, and −40 °C).

We can only observe the D_3 isomer and residual signals of free **2**.

In conclusion, we have demonstrated a triangular assembly driven by 12 charged hydrogen bonding and $\pi-\pi$ interactions. This assembly is stable even in polar solvents because of its charged hydrogen-bond nature. Helical arrangement of the complex is confirmed by its crystal structure. A solution structure is assigned to the D_3 isomer corresponding to the solid-state structure by temperature-dependent ^{1}H NMR experiments.

Experimental Section

5,17-Dibromo-11,23-dicarboxy-25,26,27,28-tetrapropoxycalix-[4]arene (2). To a stirred of solution of 5,11,17,23-tetrabromo-25,26,27,28-tetrapropoxycalix[4]arene (1 g, 1.1 mmol) in dry THF (100 mL) at −78 °C was added *n*-BuLi in hexane (2.76 mL, 4 equiv, 1.6 M). The yellow solution was stirred at −78 °C for 5 min, quenched with dry CO_2 (g) (large excess), and stirred for 30 min. The reaction mixture was poured into ice-cold 1 M hydrochloric acid and extracted with $CHCl_3$ three times. The organic layer was washed with water and brine, $MgSO_4$-dried, and evaporated in vacuo. Recrystallization from THF/MeOH (v/v = 1:1) gave **2** as white crystals (460 mg, 50% yield).

^{1}H NMR (300 MHz, DMSO-d_6) : δ 12.56 (s, 2H), 7.68 (s, 4H), 6.42 (s, 4H), 4.33 (d, 4H, J = 13.2), 4.01 (t, 4H, J = 7.9), 3.72 (t, 4H, J = 6.6), 3.38 (d, 4H, J = 13.5), 1.89−1.84 (m, 8H), 1.07 (t, 6H, J = 7.2), 0.92 (t, 6H, J = 7.2).

^{13}C NMR (75 MHz, $CDCl_3$): δ 171.60, 158.97, 156. 81, 138.42, 133.21, 131.80, 129.87, 123.71, 115.04, 77.46, 76.90, 31.23, 23.80, 23.11, 11.16, 9.94.

HRMS (FAB): Calcd for $C_{42}H_{46}Br_2O_8$ (M^+): 836.1559, found: 836.1553.

Preparation of Complex ($\mathbf{1_2{\cdot}2_3}$). The assembly ($\mathbf{1}_2{\cdot}\mathbf{2}_3$) can be obtained by two ways. For ^{1}H NMR analysis, **1** and **2** were mixed in 2:3 ratio in $CDCl_3$ and CD_3OD (v/v = 1:1). **1** and **2** were mixed in a 2:3 ratio in EtOH and heated until the mixture became clear and cooled down to room temperature, which gave a colorless crystalline solid. A solid obtained by two methods shows the same property (^{1}H NMR, ^{13}C NMR, Mass).

^{1}H NMR (300 MHz, $CDCl_3$ + MeOD-d_3 (v/v = 1:1)): 9.37 (s, 6H, aromatic protons in **1**), 7.05 (s, 12H, aromatic protons of **2** substituted by carboxylic acid), 6.83 (s, 12H, aromatic protons of **2** substituted by bromine), 4.21 (d, 12H, J = 13.08, $ArCH_2Ar$ of **2**), 3.87 (broad t, 12H, $OCH_2CH_2CH_3$ of **2**), 3.68 (broad s, 24H, NCH_2CH_2N of **1**), 3.39 (broad t, 12H, $OCH_2CH_2CH_3$ of **2**), 2.95 (d, 12H, J = 13.24, $ArCH_2Ar$ of **2**), 1.73 (broad m, 12H, 12H, $OCH_2CH_2CH_3$ of **2**), 1.68−1.58 (m, 12H, $OCH_2CH_2CH_3$ of **2**), 0.81 (broad t, 18H, $OCH_2CH_2CH_3$ of **2**), 0.69 (broad t, 18H, $OCH_2CH_2CH_3$ of **2**).

^{13}C NMR (125 MHz, $CDCl_3$ + MeOD-d_3 (v/v = 1:1)): 174.48, 161.65, 158.73, 157.72, 139.98, 134.53, 132.58, 131.98, 130.76, 130.06, 125.37, 115.17, 77.67, 77.34, 49.65, 49.48, 49.31, 49.14, 48.97, 48.80, 48.63, 46.27, 46.00, 31.69, 24.14, 23.55, 11.13, 10.21.

Mass (MALDI-TOF): m/z 2983 $[\mathbf{1}_2{\cdot}\mathbf{2}_3 - 2CO_2]^+$; m/z 2083 $[\mathbf{1}_2{\cdot}\mathbf{2}_2{\cdot}Na - 4CO_2]^+$; m/z 2001 $[\mathbf{1}_2{\cdot}\mathbf{2}{\cdot}Na]^+$.

Crystal Data of $\mathbf{1_2{\cdot}2_3}$. Crystal structure of $\mathbf{1}_2{\cdot}\mathbf{2}_3$: $C_{156}H_{174}Br_6N_{12}O_{24}$, MW = 3080.53, colorless crystal 1.00 mm × 0.25 mm × 0.20 mm, trigonal $P3_221$, $a = b$ = 34.775 (1), c = 31.201(1); V = 32676(2) Å^3, Z = 6, ρ_{calcd} = 0.939 Mg/m^3, $\mu(\lambda$ = 0.82657 Å) = 1.155 mm^{-1}, $2\theta_{max}$ = 48.9°; 131 468 measured reflections, 22 709 unique of which 13 296 were observable [$I > 2\sigma(I)$]. The refinement converged to a final R1 = 0.1255 and wR2 = 0.3215 for observed reflections of $I > 2\sigma(I)$. Structure refinement following modification of the data with the SQUEEZE routine in PLATON:[10] R1 = 0.0778 ($I > 2\sigma(I)$), wR2 = 0.2136, GOF = 1.002, max/min residual electron density 0.852/0.867 e Å.[3] Crystallographic details are in the Supporting Information.

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Supporting Information Available: Spectral data of new compounds and [$\mathbf{1}_2{\cdot}\mathbf{2}_3$] and crystallographic data of [$\mathbf{1}_2{\cdot}\mathbf{2}_3$]. This material is available free of charge via the Internet at http://pubs.acs.org.

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