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Host–guest assembly of pyridinium-conjugated calix[4]arene via cation–π interaction

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Abstract—25-(4-Pyridiniumbutoxy)-26,27,28-trihydroxycalix[4]arene bromide **1** was designed to have both host and guest units in one molecule, and was assembled to become an oligomer via a cation–π interaction. X-ray diffraction (XRD) crystallographic study of **1** revealed that it oriented in a one-dimensional structure. Titrimetric ^{1}H NMR analysis and electrospray ionization mass spectrometry (ESI-MS) analysis indicated that **1** formed an oligomer in solution, and the restraint of the segmental motion would lead to the stabilization of the cation–π interaction compared with a bi-molecular complex composed of 25,26,27,28-tetrahydroxycalix[4]arene and *N*-butylpyridinium bromide.

Recently, unique non-covalent interactions in host–guest complexes have been used to construct self-organizing systems[1] as well as functional materials with outer-stimuli responsive[2] or reversible[3] functions. A molecule which has both host and guest moieties within itself can be constructed as a self-assembled system in which these moieties are connected to each other by a host–guest interaction.[4] If we call this process 'host–guest assembly', we can state that the degree of assembling is dependent on the association constant of the host–guest complex. Therefore, it can be influenced by concentration or temperature, and the dissociation profile can be controlled by external stimuli such as heating, sonication, and competitive guest molecules. Thus, such assemblies continuously connected by host–guest interaction should be a powerful candidate for the reversible or external stimulus response soft materials.[5]

Calix[4]arene is classified as a rigid cyclic molecule composed of phenol and methylene bridge units. It works as a host molecule for several cations such as alkali metal ions and quaternary ammonium or pyridinium ions.[6] Quaternary ammonium or pyridinium ions are known to be attached to the upper rim of the calix[4]arene in the cone conformation via a cation–π interaction.[7]

A calix[4]arene derivative, 25-(4-pyridiniumbutoxy)-26,27,28-trihydroxycalix[4]arene bromide **1**, which has a pyridinium moiety directly bound to its upper rim via a butylene spacer seems to be one of the simplest structure possessing both calix[4]arene and pyridinium moieties. It combines both a host unit and a guest unit in one molecule. The calix[4]arene moiety of **1** acts as a host for the pyridinium moiety of the neighboring **1** compound; thus, we might expect it to form a linear network. In this letter, we discussed its oriented crystal structure by X-ray diffraction (XRD) crystallographic study as well as its solution-state structure by ^{1}H NMR spectroscopic study and electrospray ionization mass spectrometric (ESI-MS) study (Scheme 1).

25,26,27,28-Tetrahydroxycalix[4]arene was treated with sodium methoxide and an excess amount of dibromobutane to give 25-(4-bromobutoxy)-26,27,28-trihydroxycalix[4]arene as a oily residue. Reaction of the oily residue with pyridine afforded **1** in 53% yield.[8]

XRD crystallographic study: The absolute structure of **1** in solid state was determined by XRD crystallographic study.[9] Compound **1** was successfully recrystallized from a chloroform and methanol 4:1 v/v solution under an ethyl acetate atmosphere. In this way, an acicular

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Keywords: Calixarene; Cation–π interaction; Molecular recognition; Host–guest chemistry; Supramolecular chemistry.

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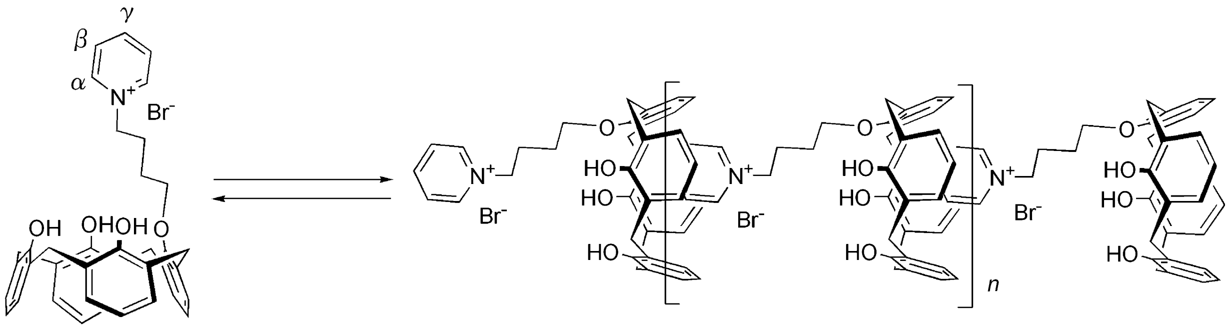


1 **Oligomer 1**

Scheme 1. Host–guest association equilibrium of **1** by cation–π interaction.

single crystal with an approximate size of $1.0 \times 1.0 \times 4.0$ mm was obtained. The crystallographic structure of the unit cell viewed along the normal to the (1 0 0) face is shown in Figure 1(a), and a simplified structure in Figure 1(b). As expected, the calix[4]arene cavity included the neighboring pyridinium moiety attached to its upper rim to form a one-dimensional structure. The conformation of the calix[4]arene moiety was held in the cone conformation by intramolecular hydrogen bonds formed by the three hydroxyl groups and the butoxy ether group; the inclusion of the pyridinium moiety in the calix[4]arene cavity would help to stabilize the cone conformation. The C44–C87 distance was 8.016 Å, whereas the C64–C84 distance was 8.736 Å. Therefore, the structure of the calix[4]arene was assessed to have an asymmetric pinched cone conformation.

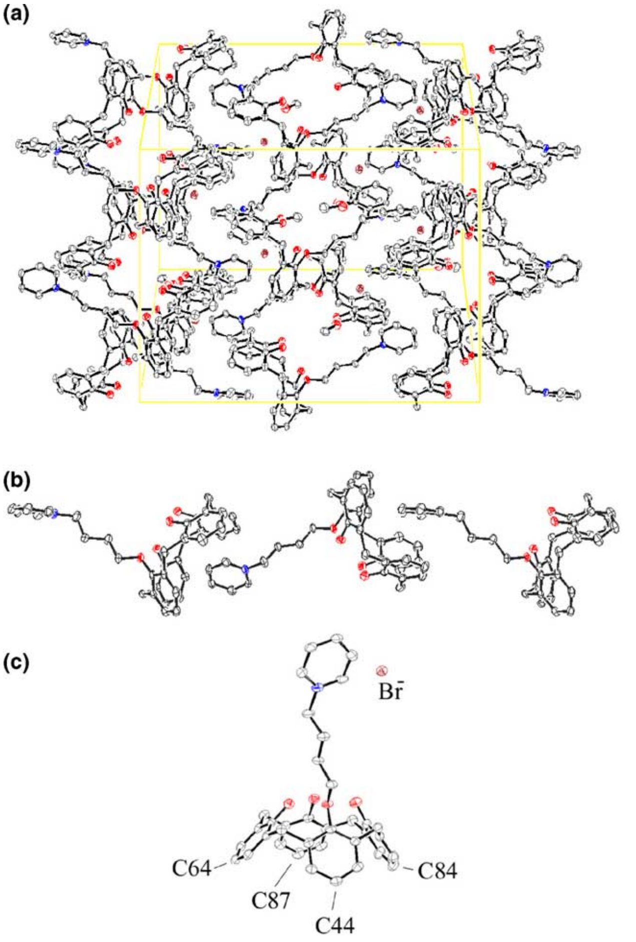
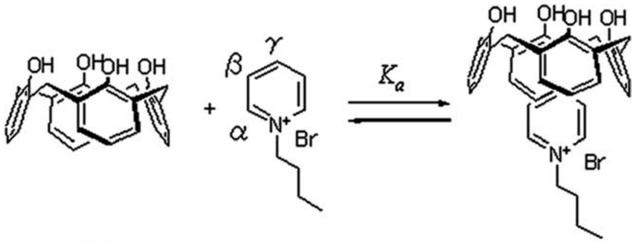


Figure 1. ORTEP drawing of **1**·CH_3OH. Hydrogen atoms were omitted for clarity. Thermal ellipsoids were drawn at 50% probability level. (a) View of unit cell from (1 0 0) axis, (b) simplified view from (1 0 0) axis, and (c) numbering scheme of compound **1**.

^{1}H NMR study: The assembling profile of **1** via cation–π interaction in solution was determined by titrimetric ^{1}H NMR experiments (JEOL JNM-LA 500; 500 MHz). First, the association constant of the complex between 25,26,27,28-tetrahydroxycalix[4]arene and *N*-butylpyridinium bromide (**CA·NBP**), a bi-molecular model complex of **1**, was estimated by a ^{1}H NMR experiment (Scheme 2).

As the concentration of the equivalent molar complex increased, **NBP** revealed the higher magnetic field chemical shift change due to the ring current effect of the **CA** in the complex (from Fig. 2(a) to (b)). The $H_\gamma > H_\beta > H_\alpha$ ordering of the degree of ^{1}H NMR chemical shift change at the positions of the three pyridinium protons indicated that the **NBP** was included into the **CA** at the H_γ position.

^{1}H NMR chemical shift change of H_γ in **CA·NBP** at several concentrations was measured, and the association constant was estimated to be $K_a = 12\ M^{-1}$ by a curve-fitting method[10] (Fig. 3(a) and (b)). If this association constant was applied to calculate the probability molecular weight distribution of oligomer **1** in a solution with a concentration such as 91 mM, we calculated that the unit molar-based percentages of the monomer, dimer, trimer, and tetramer would be 60%, 24%, 10%, and



CA **NBP** **CA•NBP**

Scheme 2. Bi-molecular model complex between **CA** and **NBP**.

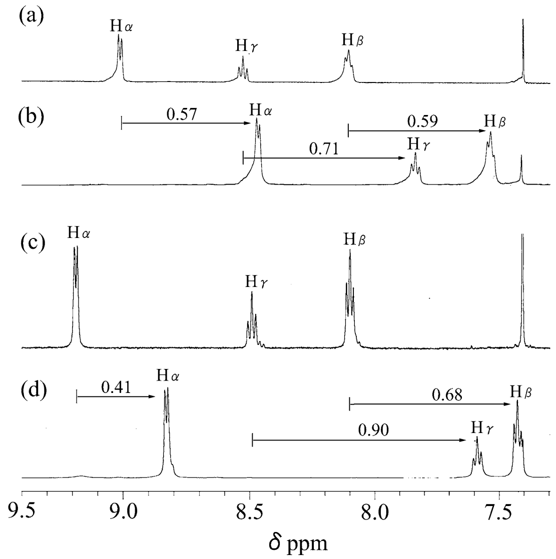


Figure 2. ^{1}H NMR chemical shift change of the pyridinium moiety in $CDCl_3/CD_3OD$ (=4:1) induced by the ring current effect of calix[4]arene. (a) **NBP** at 1 mM, (b) **CA·NBP** at 91 mM, (c) **1** at 1 mM, and (d) **1** at 91 mM.

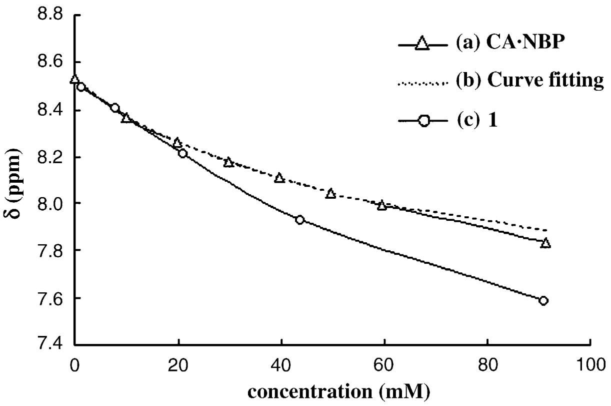


Figure 3. Concentration-dependent ^{1}H NMR chemical shift change of H_γ in the pyridinium moiety in $CDCl_3/CD_3OD$ (=4:1). (a) **CA·NBP**, (b) calculated chemical shift change of **CA·NBP** by curve fitting method for $K_a = 12\ M^{-1}$, and (c) **1**.

4%, respectively. Of course, the molecular weight increases with increasing concentration of **1**; this is one of the typical features of host–guest assembly. Therefore, we view the equilibrium state of **1** in solution as a mixture of oligomers.

Next, the ^{1}H NMR spectra of **1** at low and high concentrations was measured (Fig. 2(c) and (d)), and the degree of the chemical shift change of $H_\gamma$in **1** was compared with that of **CA·NBP** at several concentrations (Fig. 3(a) and (c)). In the low concentration region from 0 to 10 mM, the ^{1}H NMR chemical shift of the H_γ in **1** at 1 mM was almost the same as that of the **CA·NBP**. However, at concentrations higher than 20 mM, **1** showed a much larger change of the chemical shift toward higher field than did **CA·NBP** (Figs. 2(d) and 3(c)). These results suggested that the stability of oligomer **1** relative to that of **CA·NBP** was gradually enhanced as the concentration of **1** increased, and the oligomers **1** should be more stable than the bi-molecular model complex **CA·NBP**. For example, in the 91 mM solution of **CA·NBP**, about 40% of the **NBP** was included in the **CA** cavity. On the other hand, about 57% of the pyridinium moiety of **1** was estimated to be included in the neighboring calix[4]arene cavity. We postulate that oligomer **1** would take a linear or a cyclic state in the highly concentrated solution, and the degree of segmental motion should be restrained in comparison with the motion of a bi-molecular complex such as **CA·NBP**. Therefore, the oligomer **1** was more stable than the complex of **CA·NBP**.

ESI-MS study: ESI-MS is known to have a quite soft ionization process, and the mass spectra obtained by this method are regarded to reflect the state of the molecule in solution.[11] Therefore, we employed the ESI-MS techniques to realize the direct detection of the oligomer **1**. As shown in Figure 4(a), ESI-MS spectra of a 1 mM solution of **1** revealed the strong mass peaks of 558 *m/z* $[\mathbf{1} + Br^-]^+$, 1144 *m/z* $[2{\cdot}\mathbf{1}-2Br^- -1H^+]^+$ and a weak mass peak of 1672 *m/z* $[3{\cdot}\mathbf{1}-3Br^- -2H^+]^+$, that attributed to monomer, dimer, and trimer, respectively.

On the other hand, the ESI-MS spectra of a 1 mM solution of *N*-methylpyridinium iodide (**NMPI**) revealed that the mass peaks at regular interval were attributed to the ion clusters formed by electrostatic interaction (Fig. 4(b)). To confirm that the ESI-MS peaks of oligomer **1** detected in Figure 4(a) were not ion clusters but oligomers formed by cation–π interaction, we applied the competitive EMS-MS techniques by addition of equivalent molar of **NMPI** to **1**[12] (Fig. 4(c)) . The only three strong mass peaks of 558 *m/z* $[\mathbf{1} + Br^-]^+$, 651m/z $[\mathbf{1} + \mathrm{NMPI} - Br^- - I^- - H^+]^+$, and 1144 *m/z* $[2{\cdot}\mathbf{1}-2Br^- -1H^+]^+$ that should be formed by cation–π

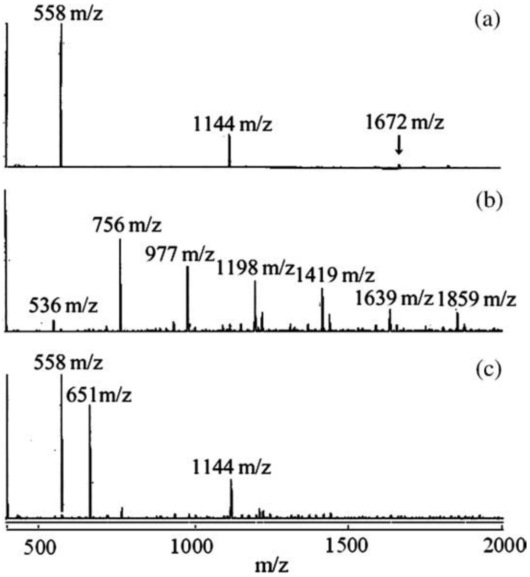


Figure 4. ESI-MS spectra of oligomer **1** and **NMPI** in $CHCl_3/CH_3OH$ (4:1 v/v). Capillary temperature; 180 °C, flow rate; 5 μl min^{-1}, the spray voltage; 4 kV. (a) **1** at 1 mM, (b) **NMPI** at 1 mM, (c) **1** and **NMPI** at 1 mM.

interaction in the 1 mM solution could be detected. The disappearance of the mass peak of the trimer 1672 *m*/*z* was probably due to the dissociation of the trimer **1** by the addition of **NMPI** and appearance of the complex of **1** and **NMPI** in the equilibrium process. Therefore, we could distinguish the mass peaks of oligomer **1** via cation–π interaction from ion clusters by competitive ESI-MS techniques.

In conclusion, a XRD crystallographic study confirmed that calix[4]arene derivative **1** formed a one-dimensional linear structure in the solid state. ^{1}H NMR spectroscopic study and ESI-MS study revealed that an oligomer was formed via cation–π interaction in concentrated solutions. The cation–π interaction was enhanced in the oligomers in comparison with the bi-molecular model complex **CA·NBP** due to the restraint of the segmental motion. This host–guest assembly could be applied to a variety of subjects, such as the design of stimuli-responsive molecular devices or the controlled release systems of polymers or gels. We are now focusing on the more stable host–guest systems to produce high-molecular weight assemblies.

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8. Compound **1**. Yield: 53%; ^{1}H NMR (500 MHz, $CDCl_3$, ppm): 9.02 (d, 2H, Py), 8.52 (t, 1H, Py), 8.03 (d, 2H, Py), 7.52 (m, 8H, Ph), 5.56 (t, 2H, N^+CH_2), 3.79 (t, 8H, OCH_2), 3.66 (m, 8H, Ar-CH_2-Ar), 1.93 (m, 4H, CH_2). ESI-MS(+): *m*/*z* = 558.6 $[M-Br]^+$ (calcd 558.3).
9. CCDC 279268 contains the supplementary crystallographic data for the compound **1**. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).
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12. 1 ml of a solution of **1** (1 mM, $CHCl_3/CH_3OH = 4:1$ (v/v)) was added to a 1 ml quantity of a solution of *N*-methyl pyridinium iodide (1 mM, $CHCl_3/CH_3OH = 4:1$ (v/v)). The mixed solution was heated at 50 °C for 10 min, and sonicated for 1 min. Then, the samples were injected to the ESI-MS instrument (Thermo Quest FINNIGAN LCQ DECA).