flections with $I > 2\sigma(I)$], $S = 1.041$ for 136 parameters. A final difference Fourier map showed no residual density below -0.30 or above 0.28 e Å^{-3}. Crystal data for $\mathbf{3}\cdot C_9H_{16}N_6O$: $M_r = 224.27$, colorless needle-shaped crystal ($0.05 \times 0.10 \times 0.50$ mm^3), triclinic, space group $P\bar{1}$ (no. 2), $a = 4.703(2)$, $b = 7.924(6)$, $c = 15.833(18)$ Å, $\alpha = 78.69(9)$, $\beta = 86.18(6)$, $\gamma = 74.43(6)°$, $V = 557.3(8)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.3365(19)$ g cm^{-3}, $F(000) = 240$, $\mu(Mo_{K\alpha}) = 0.9$ cm^{-1}. Data collection and reduction as well as solution and refinement were conducted as described for **1**. Of 4350 measured reflections, 2567 were independent; $R_{int} = 0.059$, ($1.3 < \tau < 27.5$). The refinement converged at $wR_2 = 0.1323$, $w = 1/[\sigma^2(F^2) + (0.0465P)^2 + 0.07P]$, $R_1 = 0.0553$ [for 1474 reflections with $I > 2\sigma(I)$], $S = 1.021$ for 193 parameters. A final difference Fourier map showed no residual density below -0.22 or above 0.27 e Å^{-3}. Crystal structure data for $\mathbf{5}\cdot C_{16}H_{26}N_4O_2$: $M_r = 306.41$, colorless block-shaped crystals ($0.2 \times 0.3 \times 0.5$ mm^3), triclinic, space group $P\bar{1}$ (no. 2), $a = 4.9675(11)$, $b = 8.1236(7)$, $c = 20.911(3)$ Å, $\alpha = 100.663(9)$, $\beta = 93.080(15)$, $\gamma = 91.680(12)°$, $V = 827.4(2)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.2299(3)$ g cm^{-3}, $F(000) = 332$, $\mu(Mo_{K\alpha}) = 0.8$ cm^{-1}. Data collection and reduction as well as solution and refinement were conducted as described for **1**. Of 4552 measured reflections, 3814 were independent, $R_{int} = 0.055$, ($1.0 < \tau < 27.5$). The refinement converged at $wR_2 = 0.1567$, $w = 1/[\sigma^2(F^2) + (0.0880P)^2 + 0.31P]$, $R_1 = 0.0553$ [for 2963 reflections with $I > 2\sigma(I)$], $S = 1.015$ for 277 parameters. A final difference Fourier map showed no residual density below -0.27 or above 0.34 e Å^{-3}. Crystal structure data for $\mathbf{6}\cdot C_{11}H_{17}N_5O_2$: $M_r = 251.29$, colorless needle-shaped crystals ($0.1 \times 0.1 \times 0.7$ mm^3), monoclinic, space group $C2/c$ (no. 15), $a = 20.119(18)$, $b = 5.194(2)$, $c = 25.186(16)$ Å, $\beta = 94.55(4)°$, $V = 2624(3)$ Å^3, $Z = 8$, $\rho_{calcd} = 1.2722(15)$ g cm^{-3}, $F(000) = 1072$, $\mu(MoK_\alpha) = 0.9$ cm^{-1}. Of 8860 measured reflections, 3007 were independent; $R_{int} = 0.075$, ($1.0 < \tau < 27.3$, $T = 293$ K) using an Enraf–Nonius FAST area detector on a rotating anode. Data collection and reduction as well as solution and refinement were conducted as described for **1**. The refinement converged at $wR_2 = 0.1332$, $w = 1/[\sigma^2(F^2) + (0.0300P)^2 + 4.33P]$, $R_1 = 0.0644$ [for 2305 reflections with $I > 2\sigma(I)$], $S = 1.160$ for 214 parameters. A final difference Fourier map showed no residual density below -0.25 or above 0.25 e Å^{-3}. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-100480. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: int. code + (44) 1223-336033; e-mail: deposit@ccdc.cam.ac.uk).

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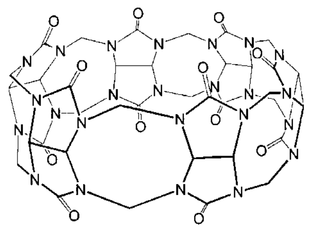
A Molecular Bowl with Metal Ion as Bottom: Reversible Inclusion of Organic Molecules in Cesium Ion Complexed Cucurbituril**

Dongmok Whang, Jungseok Heo, Joo Hyun Park, and Kimoon Kim*

Molecular containers,[1] rigid molecules with large cavities in which small molecules can be encapsulated, are of much interest because of their potential applications in separations, catalysis, sensors, and drug delivery. Although a number of molecular container systems have been studied only a few of them have demonstrated reversible encapsulation and release of their guests at ambient temperatures.[2, 3] We recently reported[4] a novel molecular container assembly based on cucurbituril (**1**),[5, 6] a macrocyclic cavitand with a hollow core of ≈5.5 Å diameter, which is accessible through two portals laced with carbonyl groups. In aqueous solution containing sodium ions, two Na$^+$ ions and their coordinated water molecules cover each portal of cucurbituril like a lid on a barrel.[4, 7] The "Na$^+$-lidded" cucurbituril can encapsulate small organic molecules such as THF and benzene. Moreover, the encapsulation and release of the guest molecules can be controlled by complexation and decomplexation of the sodium ions at the portals. Extending this work to cucurbiturils complexed to other alkali metal ions, we thought cesium-complexed cucurbituril would be particularly interesting because Cs$^+$, whose ionic radius is 1.81–2.02 Å seems to fit the portal better. Indeed, Cs$^+$-complexed cucurbiturils are drastically different from the Na$^+$-complexed cucurbiturils.[4] Here we report the cesium-complexed cucurbiturils, which uniquely behave like a "metal-ion-bottomed" molecular bowl.



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Although cucurbituril is sparingly soluble in water it dissolves appreciably in cesium chloride solution (≈5.9×10^{-2} mol in 1.0 L of 0.2 M CsCl solution at room temperature) as it does in aqueous solutions of other alkaline metal salts. Slow diffusion of ethanol into cucurbituril dissolved in 0.2 M CsCl solution results in the formation of crystals of **2**. The X-ray crystal structure of **2** (Figure 1)[8] reveals that a cesium ion is coordinated to each portal of cucurbituril, but the structure is in sharp contrast to the sodium-complexed cucurbituril in which two sodium ions are coordinated to each portal of cucurbituril.[4] The cesium ion leans toward one side of the portal, being coordinated to only four carbonyl oxygen atoms

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[*] Prof. K. Kim, Dr. D. Whang, J. Heo, J. H. Park
Department of Chemistry, Center for Biofunctional Molecules and School of Environmental Engineering
Pohang University of Science and Technology
San 31 Hyojadong, Pohang 790–784 (South Korea)
Fax: Int. code + (82) 562-279 3399
e-mail: kkim@vision.postech.ac.kr

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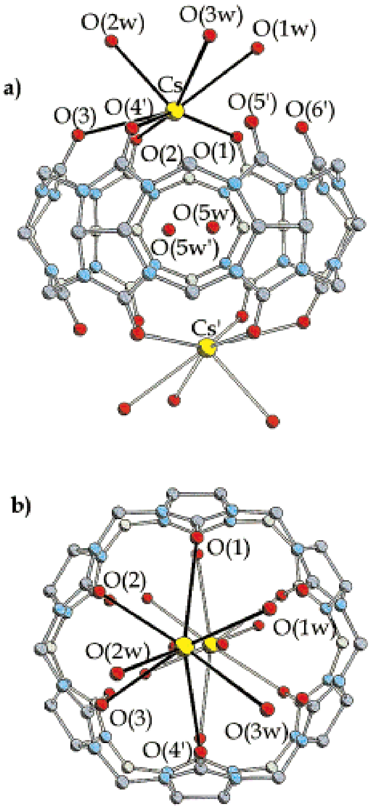


Figure 1. X-ray crystal structure of **2**: a) side view; b) top view. Color codes: Cs yellow, O red, N blue, C gray. Selected bond lengths [Å]: Cs–O(1) 3.378(6), Cs–O(2) 3.110(6), Cs–O(3) 3.100(6), Cs–O(4) 3.321(5), Cs–O(1w) 3.214(7), Cs–O(2w) 3.027(7), Cs–O(3w) 3.487(7).

at the portal with Cs–O distances of 3.100(6)–3.378(6) Å. Three water molecules O(1w)–O(3w) are also bound to the metal ion from outside with distances of 3.027(7)–3.487(7) Å. The cesium ion is 0.684(2) Å above the mean plane of the six carbonyl oxygen atoms of the portal. This value is much smaller than the average displacement of the sodium ions (1.577(4) Å) from the six-oxygen plane of the portal in the sodium-complexed cucurbituril. The smaller displacement from the portal and larger ionic radius of the cesium ion make the size of the cavity in **2** considerably smaller than that in the sodium-complexed cucurbituril. This is illustrated by the fact that only one disordered water molecule resides in the cavity of **2** whereas three water molecules exist in the Na^+-lidded cucurbituril. We therefore expected that the cavity of the Cs^+-complexed cucurbituril is not large enough to accommodate a tetrahydrofuran (THF) molecule which can be encapsulated in the Na^+-complexed cucurbituril.

To our surprise, however, when THF was added to the cucurbituril in 0.4 M CsCl solution two sets of signals for THF were observed in the ^1H NMR spectrum, the second of which is shifted upfield from that assigned to the free THF molecules. This NMR spectrum supports inclusion of a THF molecule inside the cucurbituril dissolved in CsCl solution. The formation constant of this inclusion complex **3** is estimated to be $(1.1 \pm 0.1) \times 10^3\,\text{M}^{-1}$ at room temperature,[9] which is even larger than that in the sodium-complexed cucurbituril ($(5.1 \pm 0.5) \times 10^2\,\text{M}^{-1}$).[4] Thermodynamic parameters[10] associated with the inclusion phenomenon are quite different from those for the Na^+ case: $\Delta H^\circ = -9.8 \pm 1.0\,\text{kcal mol}^{-1}$ and $\Delta S^\circ = -19 \pm 2\,\text{cal mol}^{-1}\text{K}^{-1}$ (Cs^+) and $\Delta H^\circ = -5.8 \pm 0.6\,\text{kcal mol}^{-1}$ and $\Delta S^\circ = -7.4 \pm 0.7\,\text{cal mol}^{-1}\text{K}^{-1}$ (Na^+).[4] The apparent conflict of this observation with our earlier expectation prompted us to study the X-ray structure of the crystal of **3**.[8] As we suspected, the X-ray structure reveals a THF molecule encapsulated in the cucurbituril cavity. The structure of **3** is, however, quite different from that of **2**; in particular, only one cesium ion is bound to cucurbituril in **3** (Figure 2). This is in contrast to the Na^+-lidded cucurbituril, in which the host structure of the complex that includes THF is nearly identical to that of the one free of the organic guest. In **3**, which is on a mirror plane in the crystal, the cesium ion is located at the center of the portal, which shows a severe ellipsoidal distortion. This distortion is manifested in the uneven distances between cesium and carbonyl oxygens at the portal: two of the six carbonyl oxygen atoms (O(1) and O(4)) are much closer to the metal center (Cs–O(1) = 3.250(7) Å, Cs(O(4) = 3.144(6) Å) than the four other carbonyl oxygens (Cs–O(2) = Cs–O(2′) = 3.584(8) Å; Cs–O(3) = Cs(O(3′) = 3.574(6) Å). The included THF molecule is coordinated to the metal ion (Cs–O(21) = 2.934(10) Å), and the molecular plane lies along the long axis of the ellipsoidal host molecule. Two water molecules and a disordered chloride ion are coordinated to the cesium ion from outside.[8]

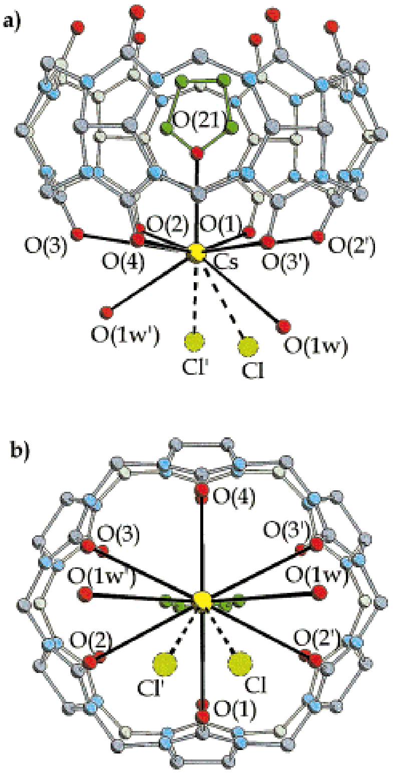
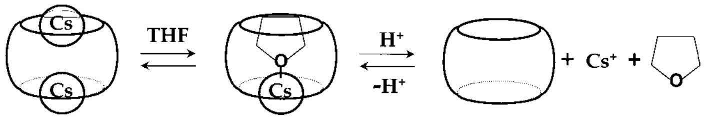


Figure 2. X-ray crystal structure of **3**: a) side view; b) top view. Color codes: Cs yellow, Cl greenish yellow, O red, N blue, C gray. The coordinated THF is highlighted in green. The coordinated Cl^- is disordered over two sites with half occupancy. Selected bond lengths [Å]: Cs–O(1) 3.250(7), Cs–O(2) 3.584(8), Cs–O(3) 3.574(6), Cs–O(4) 3.144(6), Cs–O(21) 2.934(10), Cs–O(1w) 3.591(10), Cs–Cl 3.365(3).

The coordination of the guest THF to the cesium ion bottom of the molecular bowl may be responsible for the larger formation constant in the Cs^+-complexed cucurbituril than for the Na^+ analogue in which the encapsulated THF is not coordinated to the sodium ion lids. The larger enthalpy and entropy changes for the inclusion in the former than in the latter are also consistent with the coordination of the substrate. The fact that the inclusion complex formation constant for noncoordinating benzene in this Cs system is $2.1\,\text{M}^{-1}$, which is only 1/10 of that for the Na^+ case, also supports this explanation.

Reversible inclusion and release of the guest molecule in the cesium-complexed cucurbituril upon change in pH of the medium is observed as in the sodium-lidded cucurbituril.[4] Specifically, when trifluoroacetic acid is added to the solution containing the cesium-complexed cucurbituril and THF, the ^1H NMR signals for THF included in the cavity decrease, whereas those for free THF increase. Upon addition of about 300 equivalents of trifluoroacetic acid the signals for the bound THF essentially disappear. When the solution is neutralized again by adding Cs_2CO_3 the signals for the encapsulated THF are almost fully restored. A series of these observations suggests that the cesium ion coordinated to the portal is removed in strongly acidic solution due to the protonation of the carbonyl groups at the cucurbituril portals; consequently, the encapsulated THF molecule can escape from the cavity readily (Scheme 1). Neutralization of the solution restores the cesium ion bottom of the cucurbituril bowl and therefore also the ability to encapsulate THF.



2 3

Scheme 1. Encapsulation and release of the THF guest molecule from the Cs-complexed cucrbituril host molecule.

In summary, we present a novel metal-ion-bottomed molecular bowl in which inclusion of a guest molecule can be reversibly controlled by the acidity of the medium. This work demonstrates the advantages of using metal ions as key control elements for reversible inclusion: 1) easy blocking and unblocking of portals and 2) coordination of encapsulated substrates. The latter provides additional guest selectivity of the inclusion process. Furthermore, the metal ion bottom may serve as a Lewis acid site for substrate activation and chemical catalysis. Work along this line is currently in progress.

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[8] Crystal data of **2**: $[(C_{36}H_{36}N_{24}O_{12})Cs_2(H_2O)_6\cdot(H_2O)](Cl)_2\cdot 2H_2O$, $M_r = 1495.75$, monoclinic, $P2_1/n$, $a = 14.277(2)$, $b = 11.887(1)$, $c = 15.901(3)$ Å, $\beta = 94.085(8)^\circ$, $V = 2691.8(7)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.845\,\text{g cm}^{-3}$, $T = 296$ K, Enraf-Nonius CAD4 diffractometer, $Mo_{K\alpha}$ ($\lambda = 0.71073$ Å), $\mu = 15.54\,\text{cm}^{-1}$. Structure was solved by Patterson method (SHELXS-86). All non-hydrogen atoms were refined anisotropically (SHELXL-93). Final full-matrix least-squares refinement on F^2 with all 3288 reflections and 388 variables converged to $R1$ ($I > 2\sigma(I)$) = 0.058, $wR2$ (all data) = 0.160 and GOF = 1.10. Crystal data of **3**: $[(C_{36}H_{36}N_{24}O_{12})CsCl(H_2O)_2\cdot C_4H_8O]\cdot 5H_2O$, $M_r = 1363.46$, orthorhombic, $Cmc2_1$, $a = 19.457(3)$, $b = 16.137(3)$, $c = 15.917(1)$ Å , $V = 4997(1)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.812\,\text{g cm}^{-3}$, $T = 193$ K, Enraf-Nonius CAD4 diffractometer, $Mo_{K\alpha}$ ($\lambda = 0.71073$), $\mu = 9.02\,\text{cm}^{-1}$. Structure was solved by Patterson methods, and all non-hydrogen atoms were refined anisotropically. Final refinement on F^2 with all 2340 reflections and 431 variables converged to $R1$ ($I > 2\sigma(I)$) = 0.035, $wR2$ (all data) = 0.096 and $GOF = 1.16$. Crystallographic Data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications no. CCDC-100615. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: int. code + (44) 1223-336033; e-mail: deposit@ccdc.cam.ac.uk).

[9] The formation constant of the inclusion complex was estimated by the integration of the signals for the free and bound THF in ^1H NMR spectra of 0.4 M CsCl solutions (in D_2O) containing cucurbituril (2.6×10^{-2} M) and THF ($1.7-2.8 \times 10^{-2}$ M).

[10] The thermodynamic parameters were estimated from the temperature dependence of the formation constants between 20 and 60°C.