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Host–Guest Systems

Quantitative Dynamic Interconversion between Ag^I-Mediated Capsule and Cage Complexes Accompanying Guest Encapsulation/Release**

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Multicomponent self-assembly leading to discrete molecular architectures through reversible hydrogen bonding[1] or metal-coordination bonding[2] has attracted a great deal of attention. So far, many excellent examples of well-defined 3D structures, such as capsules,[3] cages,[4] boxes,[5] and tubes,[6] have been reported, and their inner spaces have been efficiently used as recognition[7] and reaction centers[8] for neutral molecules and ionic species. External stimuli-responsive supermolecules are considered as molecular devices in which conformational or configurational transitions of the molecules allow on–off switching of their functions such as motion, molecular recognition, and reaction control. However, to date, only a few examples have been reported on quantitative dynamic interconversions between differentiated self-assembled molecules formed from identical chemical components. To realize such a dynamic system, metal-mediated self-assembly has a great advantage in that the coordination number and geometry of transition-metal ions can be reversibly changed by their oxidation states[9] and concentration ratios of metal to ligand.[10,11] Such metal-centered changes should allow dynamic interconversion through metal–ligand exchanges between different kinds of metal-assembled structures.

Recently, we established an Ag^I-mediated interconvertible system with a disk-shaped trismonodentate ligand (L) in which three 2-benzimidazolyl rings and three methyl groups are alternately attached to the central benzene ring.[10] In this system, a structural interconversion between a capsule-shaped and a sandwich-shaped complex accompanies encapsulation/release of anionic molecules and was established by varying the metal-to-ligand ratio. In the study described herein, a disk-shaped trismonodentate ligand **1**, which has

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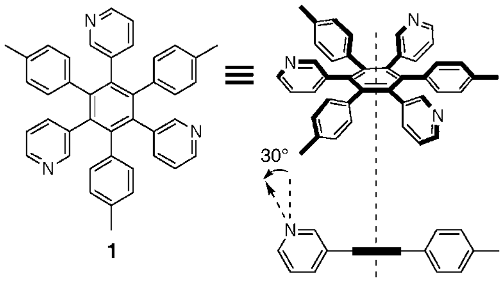

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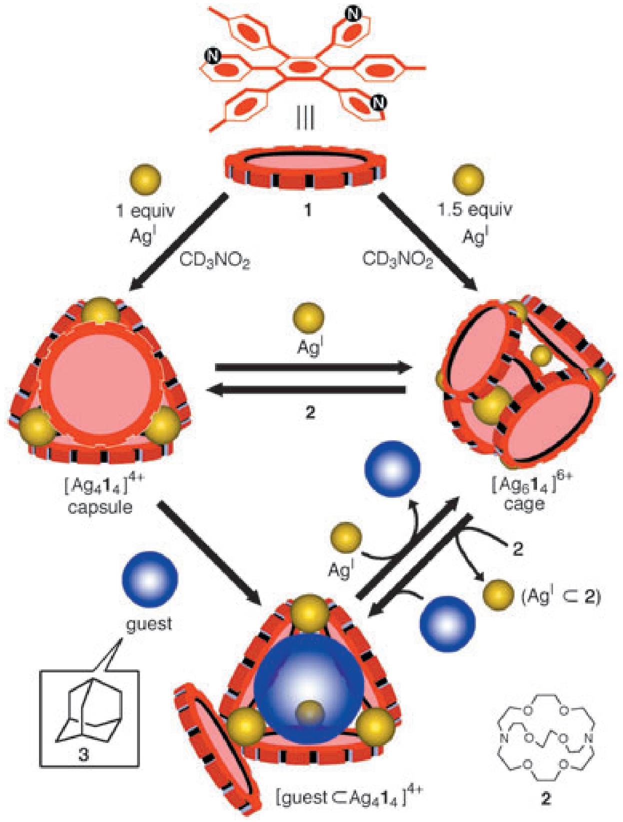

Figure 1. Schematic representation of the interconversion between [Ag$_4$**1**$_4$]$^{4+}$ capsule and [Ag$_6$**1**$_4$]$^{6+}$ cage complexes by changing the [Ag^I]/[**1**] ratio from 1:1 to 1.5:1. The [Ag$_4$**1**$_4$]$^{4+}$ capsule complex can entrap a neutral organic molecule such as adamantane in the inner space, while the [Ag$_6$**1**$_4$]$^{6+}$ cage complex cannot practically encapsulate the guest molecule. The encapsulation/release of the guest molecule is coupled with the reversible Ag^I-dependent capsule↔cage interconversion. A front disk is opened to show clearly a guest molecule encapsulated in the inner space of [guest⊂Ag$_4$**1**$_4$]$^{4+}$.

three 3-pyridyl and *p*-tolyl groups attached alternately to the central benzene ring, was designed with the aim of constructing larger capsule molecules that allow encapsulation/release of organic guest molecules. Each pyridyl ring is almost perpendicular to the central ring plane as a result of the steric hindrance between the neighboring pyridyl and *p*-tolyl groups. The coordination direction of each nitrogen donor atom of the 3-pyridyl groups is thereby somewhat distorted away from the central ring by 30°. From a molecular-modeling study, we expected that the combination of the ligand **1** with Ag^I, which can assume both a three-coordinate trigonal-planar and a two-coordinate linear geometry with monodentate ligands, should generate two different 3D structures with inner spaces when the metal-to-ligand ratios are 4:4 and 6:4.[12] Moreover, the quantitative, reversible structural interconversion between these two structures would provide an excellent molecular encapsulation/release system if only one of them binds preferentially to some given guest molecules.

Herein we present a quantitative interconversion between two Ag^I-containing molecular architectures, a capsule-shaped [Ag$_4$**1**$_4$]$^{4+}$ and a cage-shaped [Ag$_6$**1**$_4$]$^{6+}$ complex (Figure 1). These two complexes were self-assembled from trismonodentate disk-shaped ligands **1** and Ag^I by changing the **1**/Ag^I concentration ratios in the presence or absence of guest molecules. Indeed, the [Ag$_4$**1**$_4$]$^{4+}$ capsule complex could accommodate a neutral organic molecule such as adamantane in the inner space with a high affinity. On the other hand, as soon as the capsule complex was converted into the cage-shaped counterpart, [Ag$_6$**1**$_4$]$^{6+}$, the included guest molecule was immediately released. X-ray single-crystal analysis revealed a [Ag$_4$**1**$_4$]$^{4+}$ capsule structure in which an adamantane molecule is trapped inside. Furthermore, the encapsulation and release of the guest molecule could be dynamically controlled by the quantitative Ag^I-dependent capsule↔cage interconversion.

^{1}H NMR titration experiments with ligand **1** and AgPF$_6$ in CD$_3$NO$_2$ revealed the quantitative formation of two different Ag^I complexes depending on the [Ag^I]/[**1**] ratios. Upon addition of an equimolar amount of AgPF$_6$ to a solution of **1** in CD$_3$NO$_2$ ([Ag^I]:[**1**] = 1:1), the signals for metal-free ligand **1** completely disappeared and one set of new signals simultaneously appeared in a highly symmetrical pattern (Figure 2a). The signals for the *p*-tolyl ring moieties, H$_e$ and H$_f$, are divided into two sets, which indicate that the Ag^I ions are placed only on one side of the disk-shaped ligand **1**. Notably, the signals for one of the *p*-tolyl protons (H$_f$) and for the methyl protons (H$_g$) are shifted upfield ($\Delta\delta = -2.0$ and -0.4 ppm for H$_f$ and H$_g$, respectively). This is probably due to the shielding effects of the Ag^I-bound aromatic ligands that form a self-assembled capsulelike structure.

On the other hand, when 1.5 equivalents of AgPF$_6$ were added ([Ag^I]/[**1**] = 1.5:1), the ^{1}H NMR spectrum showed another set of highly symmetrical signals (Figure 2b), which indicate the quantitative formation of another Ag^I complex. In this case, the signals for the *p*-tolyl proton H$_f$ do not shift upfield, which suggests that the ligand array should be different from that of a complex formed from a 1:1 mixture of Ag^I and **1**. These results demonstrated that two highly symmetrical structures were quantitatively formed from Ag^I and **1** in 1:1 and 1.5:1 ratios. The interconversion between these two thermodynamically stable complexes was fast and reached equilibrium within a few minutes after changing the Ag^I/**1** ratios.

ESI-TOF mass spectra confirmed the formation of [Ag$_4$**1**$_4$]$^{4+}$ and [Ag$_6$**1**$_4$]$^{6+}$ complexes with [Ag^I]/[**1**] ratios of 1:1 and 1.5:1, respectively (see Supporting Information). The ESI-TOF mass spectrum of a mixture of AgPF$_6$ and **1** in a 1:1 ratio showed a signal at $m/z = 965.2$, which was assigned to [Ag$_4$**1**$_4$·PF$_6$]$^{3+}$. In contrast, the spectrum of a mixture of AgPF$_6$ and **1** in a 1.5:1 ratio showed signals at $m/z = 814.1$ and 1133.9,

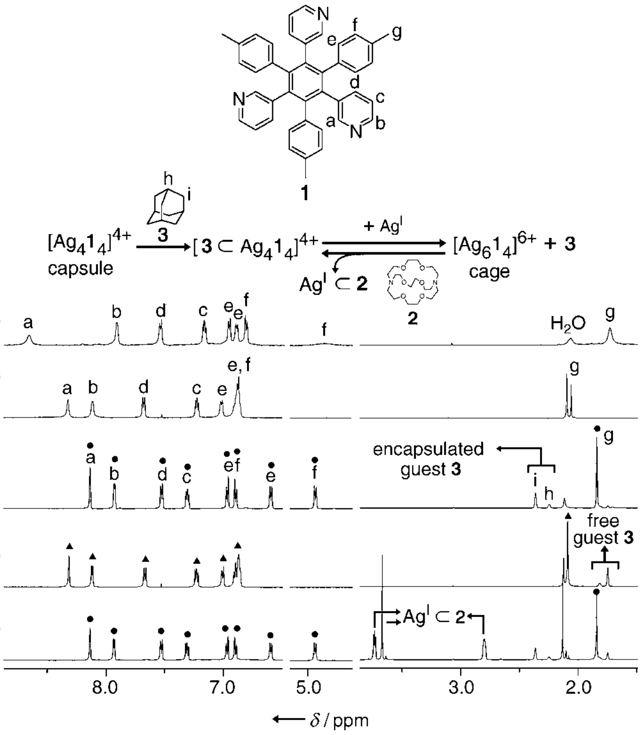

Figure 2. a)–b) ^{1}H NMR spectra (500 MHz) of $[Ag_4\mathbf{1}_4]^{4+}$ capsule and $[Ag_6\mathbf{1}_4]^{6+}$ cage complexes (CD_3NO_2, 293 K, $[\mathbf{1}] = 5.9$ mM); a) $Ag_4\mathbf{1}_4{\cdot}(PF_6)_4$ and b) $Ag_6\mathbf{1}_4{\cdot}(PF_6)_6$. c)–e) Encapsulation of a guest molecule **3** in the $[Ag_4\mathbf{1}_4]^{4+}$ capsule complex and encapsulation/release of the guest molecule triggered by the capsule↔cage interconversion (^{1}H NMR (CD_3NO_2, 273 K, $[\mathbf{1}] = 10.8$ mM)); c) $[\mathbf{3}{\subset}Ag_4\mathbf{1}_4]^{4+}$, $[Ag_4\mathbf{1}_4{\cdot}(PF_6)_4] = [\mathbf{3}] = 2.7$ mM. d) Upon addition of $AgPF_6$ (2.0 equiv) to the sample for (c), encapsulated **3** was released from inside as a result of the interconversion from the capsule into the cage. e) Upon addition of [2,2,2]cryptand **2** (2.0 equiv) to the sample for d), an $Ag_4\mathbf{1}_4$ capsule complex was formed and **3** was immediately encapsulated again in the capsule. Filled circles and triangles denote the inclusion complex $[\mathbf{3}{\subset}Ag_4\mathbf{1}_4]^{4+}$ and the $[Ag_6\mathbf{1}_4]^{6+}$ cage complex, respectively.

which are ascribable to $[Ag_6\mathbf{1}_4{\cdot}(PF_6)_2]^{4+}$ and $[Ag_6\mathbf{1}_4{\cdot}(PF_6)_3]^{3+}$, respectively. These mass spectral data and the symmetrical patterns of the ^{1}H NMR spectra overall suggest that the $[Ag_4\mathbf{1}_4]^{4+}$ complex should assume a trigonal-pyramidal, capsule-shaped structure in which four Ag^I ions are arranged in a tetrahedral fashion and three pyridyl nitrogen donor atoms coordinate to each Ag^I. Similarly, an octahedral structure was proposed for the $[Ag_6\mathbf{1}_4]^{6+}$ complex in which six two-coordinate Ag^I ions are arranged in an octahedral fashion so that half of the faces of octahedron are occupied by ligands **1** and the other half is opened to form an Ag^I-linked cage-shaped complex.[12]

From a molecular-modeling study in light of the ^{1}H NMR and ESI-TOF spectra, the Ag^I complexes should have the inner spaces for small molecules, and, in particular, the $[Ag_4\mathbf{1}_4]^{4+}$ complex was expected to have an enclosed space with an encapsulation function. Indeed, the investigation of the ability of $[Ag_4\mathbf{1}_4]^{4+}$ for molecular inclusion revealed that adamantane (**3**) is a suitable guest. The ^{1}H NMR spectrum of an equimolar mixture of **3** and the $[Ag_4\mathbf{1}_4]^{4+}$ capsule in CD_3NO_2 at 273 K gave rise to signals for **3** at $\delta = 2.4$ ppm and $\delta = 2.3$ ppm with downfield shifts of $\Delta\delta = +0.60$ and $+0.41$ ppm, respectively, as a result of the deshielding effect from the pyridyl and *p*-tolyl rings of the ligand part of the inclusion complex (Figure 2c). Under these conditions, approximately 91% of the guest molecules are included in the $[Ag_4\mathbf{1}_4]^{4+}$ complex and the guest **3** moves in and out of the interior slowly on the NMR timescale. The significant upfield shift of H_a ($\Delta\delta = -0.59$ ppm) upon inclusion suggests that the N–Ag^I distances are somewhat lengthened as the four ligands move slightly apart from each other as a result of the encapsulation of **3** accompanying an increase in the inner volume.[13] Evidence for the formation of the 1:1 inclusion complex, $[\mathbf{3}{\subset}Ag_4\mathbf{1}_4]^{4+}$, was provided by the ESI-TOF mass spectrum, which showed a signal that was assigned to $[\mathbf{3}{\subset}Ag_4\mathbf{1}_4]^{4+}$ at $m/z = 721.7$ (see Supporting Information). Thermodynamic parameters were determined for the encapsulation of **3** into the inner space of the $[Ag_4\mathbf{1}_4]^{4+}$ by variable-temperature ^{1}H NMR measurements.[14] The negative values of $\Delta H = -63.3\ \text{kJ mol}^{-1}$ and $\Delta S = -144\ \text{J mol}^{-1}\text{K}^{-1}$ in the encapsulation process indicate the great contribution of enthalpy-driven association to the stability through van der Waals contacts between the $[Ag_4\mathbf{1}_4]^{4+}$ capsule and the guest **3** as well as by the solvophobic effects on the process. The binding constant ($K = [\mathbf{3}{\subset}Ag_4\mathbf{1}_4]/([\mathbf{3}]{\cdot}[Ag_4\mathbf{1}_4])$; M^{-1}) was thus determined to be $3.8 \times 10^4\ \text{M}^{-1}$ at 273 K. A structurally similar 1-adamantanol was also encapsulated in the $[Ag_4\mathbf{1}_4]^{4+}$ capsule but the binding constant was decreased to $1.3 \times 10^3\ \text{M}^{-1}$, which indicated that only 59% of 1-adamantanol was included under the same conditions. As for 1-chloroadamantane with a larger Cl group, only a slight binding affinity ($K < 1\ \text{M}^{-1}$) was observed. These results indicate that the $[Ag_4\mathbf{1}_4]^{4+}$ capsule has a high selectivity for unsubstituted adamantane in the recognition of adamantane derivatives.[15,16] On the other hand, the $[Ag_6\mathbf{1}_4]^{6+}$ cage complex did not include any guest molecules tested, probably owing to its larger inner space, the absence of preferable interaction between the host and guest, and the presence of the openings in the cagelike structure.

The interconversion between the two Ag^I complexes was fast, as expected from the labile nature of the Ag^I-centered ligand exchange reactions. Furthermore, under the condition employed, the ratios of the two complexes were highly dependent on the $[Ag^I]/[\mathbf{1}]$ ratios (Figure 3a). This tendency was also observed when an adamantane was added to the solution, as shown in Figure 3b.

Similar results were obtained when silver trifluoromethanesulfonate (AgOTf) was used instead of $AgPF_6$ which indicated that counteranions have no significant influence on the interconversion process and on the encapsulation property of the cationic part, $[Ag_4\mathbf{1}_4]^{4+}$. Finally, X-ray analysis of the neutral inclusion complex $\mathbf{3}{\subset}Ag_4\mathbf{1}_4{\cdot}(TfO)_4$ revealed a capsule-shaped coordination structure in which one adamantane molecule is accommodated in the inner space (Figure 4). The capsule complex is composed of four pyridyl ligands **1** and four Ag^I ions, which are arranged 10.0 Å apart from each other in a tetrahedral fashion. Three pyridyl nitrogen atoms from three disk-shaped ligands (Ag–N: 2.29 Å (average)) and an oxygen atom of TfO^- coordinate to each Ag^I center (Ag–O: 2.50 Å (average)) in a distorted tetrahedral geometry. The mean deviation of the Ag^I from the N_3 plane is 0.391 Å. One

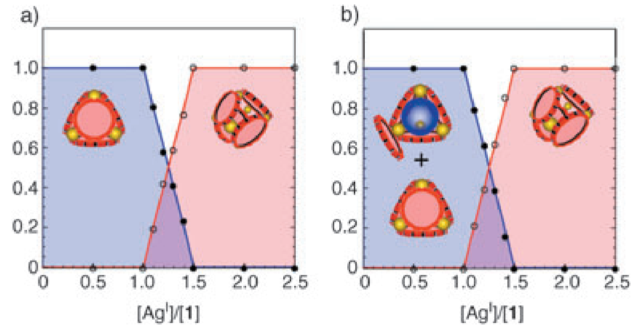

Figure 3. Effects of the presence of adamantane (**3**) on the interconversion between $[Ag_4\mathbf{1}_4]^{4+}$ and $[Ag_6\mathbf{1}_4]^{6+}$. a) Plot of $[Ag_4\mathbf{1}_4]/([Ag_4\mathbf{1}_4]+[Ag_6\mathbf{1}_4])$ (filled circles) and $[Ag_6\mathbf{1}_4]/([Ag_4\mathbf{1}_4]+[Ag_6\mathbf{1}_4])$ (open circles) against $[Ag^I]/[\mathbf{1}]$ determined from the ^1H NMR integral ratios. Solid lines are theoretically drawn for $[Ag_4\mathbf{1}_4]/([Ag_4\mathbf{1}_4]+[Ag_6\mathbf{1}_4])$ (blue) and $[Ag_6\mathbf{1}_4]/([Ag_4\mathbf{1}_4]+[Ag_6\mathbf{1}_4])$ (red) as a function of $[Ag^I]/[\mathbf{1}]$. b) Plot of $([\mathbf{3}\subset Ag_4\mathbf{1}_4]+[Ag_4\mathbf{1}_4])/([\mathbf{3}\subset Ag_4\mathbf{1}_4]+[Ag_4\mathbf{1}_4]+[Ag_6\mathbf{1}_4])$ (filled circles) and $[Ag_6\mathbf{1}_4]/([\mathbf{3}\subset Ag_4\mathbf{1}_4]+[Ag_4\mathbf{1}_4]+[Ag_6\mathbf{1}_4])$ (open circles) against $[Ag^I]/[\mathbf{1}]$ determined from the ^1H NMR integral ratios. Solid lines are theoretically drawn as a function of $[Ag^I]/[\mathbf{1}]$. A front disk is opened to clearly show a guest molecule in the inner space for the $[\mathbf{3}\subset Ag_4\mathbf{1}_4]^{4+}$ complex.

adamantane molecule is closely packed in the inner space and surrounded by the four ligands. The hydrogen atoms of **3** are close to *p*-tolyl H_e or pyridyl H_a within approximately 2.2–3.1 Å, as suggested by the ^1H NMR data for $\mathbf{3}\subset Ag_4\mathbf{1}_4\cdot(PF_6)_4$. The distance between H_h of **3** and the central benzene ring of **1** is 2.85 Å, thus indicating that there are no CH–π interactions between them.

As described above, the $[Ag_4\mathbf{1}_4]^{4+}$ capsule and the $[Ag_6\mathbf{1}_4]^{6+}$ cage complexes are totally different from each other in shape, volume, and internal structures, thus resulting in the large difference in their affinity for guest molecules. That is, an adamantane (**3**) is encapsulated in the $[Ag_4\mathbf{1}_4]^{4+}$ capsule with high affinity, whereas the $[Ag_6\mathbf{1}_4]^{6+}$ cage has practically no interaction with **3**. We exploited this switching system for the encapsulation/release of the guest molecule through the interconversion between the capsule- and cage-shaped structures. First, the $[Ag_4\mathbf{1}_4]^{4+}$ complex entrapped **3** into its inner space to form a 1:1 complex (Figure 2c). Upon addition of 2.0 equivalents of $AgPF_6$, the encapsulated **3** was immediately released to the bulk solvent as a result of the structural conversion from the $[Ag_4\mathbf{1}_4]^{4+}$ capsule into the $[Ag_6\mathbf{1}_4]^{6+}$ cage (Figure 2d). When 2.0 equivalents of [2,2,2]-cryptand **2** were added to the solution, two Ag^I ions of the $[Ag_6\mathbf{1}_4]^{6+}$ complex were trapped by **2**, and then the $[Ag_4\mathbf{1}_4]^{4+}$ capsule was reconstructed with simultaneous inclusion of **3** in the capsule (Figure 2e). This encapsulation/release cycle could be repeated at least three times without any loss of efficiency within a few minutes for each encapsulation/release cycle.[17]

In summary, we have developed an Ag^I-mediated structural on–off switching system in which the Ag^I-linked capsule ($[Ag_4\mathbf{1}_4]^{4+}$) and cage ($[Ag_6\mathbf{1}_4]^{6+}$) complexes are quantitatively interconverted, depending on the ratios of Ag^I to **1**. The capsule complex only has a large affinity for small neutral organic molecules such as adamantane, and its crystallographic analysis revealed the structure of the 1:1 inclusion complex with an adamantane molecule. Finally, we have established an excellent dynamic system for the encapsulation/release of guest molecules by the use of metal-mediated interconversion between the capsule and cage complexes constructed from trismonodentate ligands and Ag^I in a self-assembled manner. These results would open up prospects for exploiting nanocapsules for molecular transport systems. The construction of larger metallocapsules with dynamic properties is currently ongoing.

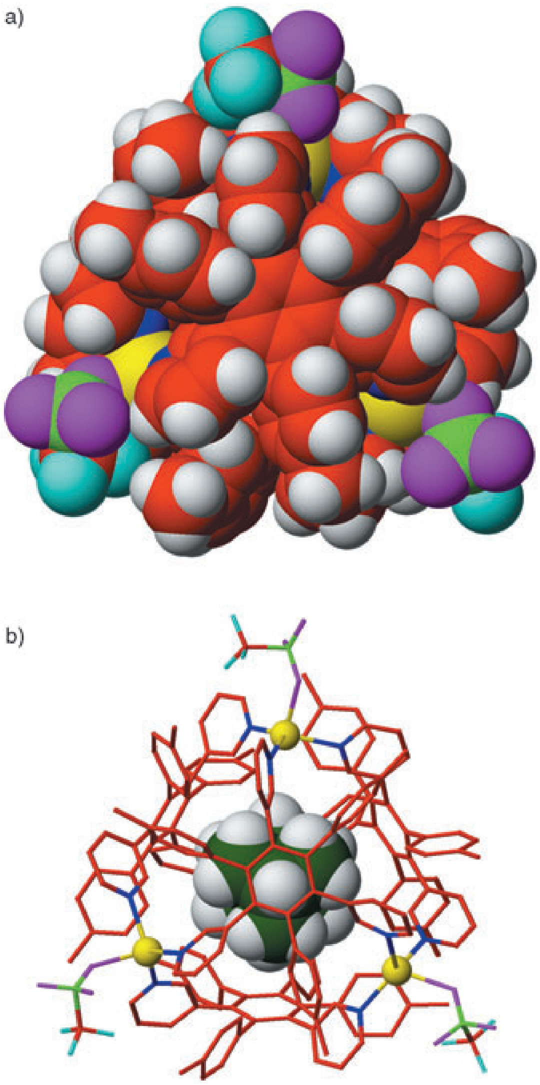

Figure 4. The crystal structure of $\mathbf{3}\subset Ag_4\mathbf{1}_4\cdot(TfO)_4$. Color labels: red (carbon), turquoise (carbon of **3**), blue (nitrogen), yellow (silver), purple (oxygen), light green (sulfur), cyan (fluorine), and white (hydrogen). a) A space-filling model; b) the capsule structure is depicted as a cylinder model. Hydrogen atoms of the $[Ag_4\mathbf{1}_4]^{4+}$ moiety are omitted for clarity.

Experimental Section

$\mathbf{3}\subset Ag_4\mathbf{1}_4\cdot(TfO)_4$: A single crystal suitable for X-ray crystallographic analysis was obtained from a saturated solution of $Ag_4\mathbf{1}_4\cdot(TfO)_4$ and **3** (1:1 mixture) in CD_3NO_2 at 253 K. Crystallographic data ($C_{185}H_{173}Ag_4F_{12}N_{15}O_{26}S_4$): $M = 3810.18$, colorless, $0.20\times0.12\times$

0.07 mm^3, orthorhombic, space group $Pccn$, $a = 16.414(11)$, $b = 32.34(2)$, $c = 37.30(2)$ Å, $V = 19\,800(21)$ Å^3, $Z = 4$, $R_1(I > 2\sigma(I)) = 0.1532$, $wR(F_o^2) = 0.4282$, GOF = 1.091; intensity data were measured at 93.1 K on a Rigaku RAXIS-RAPID Imaging Plate diffractometer with graphite monochromated $\mathrm{Mo}_{K\alpha}$ ($\lambda_\alpha = 0.71075$ Å) radiation; structure solution was carried out with the program PATTY (P. Beurskens, T. Admiraal, G. Beurskens, G. Bosman, W. P. de Gelder, R. Israel, J. M. M. Smits, PATTY: The DIRDIF-94 Program System, Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands, **1994**). Considerably large R_1 and wR values might be due to the missing of one of four anions and a poor quality of the crystal used. CCDC-248 984 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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[12] The possibility of a sandwich-shaped $[\mathrm{Ag}_3\mathbf{1}_2]^{3+}$ structure is ruled out because the coordination direction of pyridyl nitrogen atoms of **1** does not meet the requirements for the formation of $[\mathrm{Ag}_3\mathbf{1}_2]^{3+}$, as suggested by its molecular-modeling study.

[13] The changes in the chemical shift of $\mathrm{H_a}$ signal of the $[\mathrm{Ag}_4\mathbf{1}_4]^{4+}$ capsule complex should be affected by both the bonding nature of the Ag–N bonds and the deshielding effects of the *p*-tolyl rings in the neighboring ligands. Upon encapsulation of **3** in the $[\mathrm{Ag}_4\mathbf{1}_4]^{4+}$ complex, the Ag–N bonds are lengthened so as to maximize van der Waals interaction between the $[\mathrm{Ag}_4\mathbf{1}_4]^{4+}$ capsule and **3**. The movement of the four ligands away from each other with increasing Ag–N bond lengths of the $[\mathbf{3}\subset\mathrm{Ag}_4\mathbf{1}_4]^{4+}$ should decrease the deshielding effects of the *p*-tolyl rings.

[14] The binding constant was determined by the ^{1}H NMR integral ratios of the $[\mathbf{3}\subset\mathrm{Ag}_4\mathbf{1}_4]^{4+}$ and $[\mathrm{Ag}_4\mathbf{1}_4]^{4+}$, and the thermodynamic parameters (ΔH and ΔS) were calculated from the ΔG values obtained at temperatures ranging from 273 to 333 K by the least-square method. Experimental data are shown in the Supporting Information.

[15] Several halogenated methanes were also encapsulated in the $\mathrm{Ag}_4\mathbf{1}_4$ complex. Their binding constants K (M^{-1}) at 273 K are 7.5×10^2 ($\mathrm{CBr_4}$), 1.0×10^2 ($\mathrm{CBr_2Cl_2}$), 14 ($\mathrm{CFBr_3}$), 18 ($\mathrm{CBrCl_3}$), and 1.4 ($\mathrm{CCl_4}$).

[16] ^{19}F NMR spectra of the $\mathrm{Ag}_4\mathbf{1}_4$ capsule and $\mathrm{Ag}_6\mathbf{1}_4$ cage complexes showed one set of signals similar to that of $\mathrm{AgPF_6}$ or AgOTf which suggests that the counteranions should exist outside their inner space.

[17] An excellent example is reported in reference [7c] for the release of guest molecules in the hydrogen-bonded cage triggered by the change of their components. However, the reversible encapsulation/release process was not established by this system.