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A Cationic Guest in a 24⁺ Cationic Host

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Electrostatic interaction is often employed as an important attractive force both in biological and in artificial molecular recognition.¹ While the interaction between oppositely charged molecules is attractive, that between identically charged ones is of course repulsive. Therefore, a cationic (anionic) host shows a very poor ability to bind a cationic (anionic) guest even if their shapes are well compatible with each other. Contrary to such a general understanding, we have found an unprecedented host–guest interaction where a cationic host accommodates a cationic guest despite the 24^+ charge of the host framework.

The cationic host discussed here is tetrahedral coordination cage 1^{24+} with $M_{12}L_6$ stoichiometry where M and L denote (en)Pd²⁺ coordination block² (Pd) and 1,4-bis(3,5-pyrimidyl)benzene (2), respectively (eq 1).³ This cage complex was designed by extending hypothetical metallacalix[3]arene structure **3** (eq 2) into a three-dimensional linkage. Molecular modeling predicted that the angles between the C_2 axes of two pyrimidine rings are roughly 60°.⁴ We therefore expected that this unit would occupy every corner of a tetrahedron by bridging two pyrimidyl rings with a rigid phenylene spacer. Here, we report the self-assembly of $M_{12}L_6$ tetrahedron 1^{24+} as well as its binding of cationic guests. We show that the unusual cation–cation host–guest chemistry is described by a unique onionlike shell structure of the host–guest complex where two cationic spheres are mediated by an anionic sphere of a counteranion assembly.^{1e,f}



Ligand **2**, obtained in a good yield using Suzuki–Miyaura coupling of 1,4-dibromobenzene and the corresponding pyrimidylborolane,⁵ was suspended in an acetone solution of $(en)Pd(OTf)_2$ (2 equiv), and the mixture was stirred for 5 h at room temperature. The resulting clear solution was analyzed by NMR which clearly evidenced the predominant formation (>90%) of a well-defined



Figure 1. Monitoring of the inclusion of 4^+ into tetrahedral cage 1^{24+} by ¹H NMR (500 MHz, acetone- d_6 , 25 °C): (a) Empty tetrahedral cage 1^{24+} . (b) Complex $1\cdot 4^{25+}$ after 5 h at 25 °C (∇ , encapsulated 4^+ ; \bigcirc , free 4^+). This spectrum was obtained by adding 2 equiv of $4\cdot$ OTf and 8 equiv of NaBF₄ because BF₄⁻ is found to be important for the complexation as is discussed later in the text. (c) Pure inclusion complex $1\cdot 4^{25+}$ after purification by precipitation with hexane (∇ , encapsulated 4^+). Note that minor peaks at δ 7.6 and 10.7 involved in the spectrum of empty 1^{24+} .

assembly. The ¹H NMR spectrum displayed a set of three signals in the aromatic region (Figure 1a), indicating that the product is placed in a highly symmetrical environment. CSI-MS (cold-spray ionization mass spectroscopy)^{6,7} of the solution revealed the formation of an $M_{12}L_6$ assembly. Considering the symmetry and the stoichiometry, we assigned the product as tetrahedral cage complex 1·24(OTf). Addition of hexane to the acetone solution resulted in the formation of a white precipitate, which was recovered by centrifugation, washed with hexane, and dried under vacuum to give 1·24(OTf) in 85% yield.

During host—guest experiments using a variety of small organic guests, we unexpectedly found that a cationic guest, NBu₄⁺ (**4**⁺), is efficiently accommodated by host 1^{24+} despite its 24+ charge.⁷ Thus, the addition of 8 equiv of NBu₄BF₄ to an acetone solution of 1^{24+} resulted in the quantitative inclusion of 4^+ inside the cavity of 1^{24+} . The inclusion complex $1 \cdot 4^{25+}$ was clearly observed by ¹H NMR spectroscopy, which displayed a new highly upfield-shifted set of signals for 4^+ with a 1:1 host—guest ratio (Figure 1b).⁸ Addition of hexane precipitated $1 \cdot 4^{25+}$ complex in a pure form (Figure 1c). 2D-NMR spectroscopy of the inclusion complex showed a clear NOESY correlation between the C(3) H_2 and C(4) H_3 of the butyl group and the phenylene protons of **2**, indicating that the ammonium nitrogen is localized in the center of the tetrahedron 1^{24+} with alkyl chains pointing out through the four triangular windows of the cage.

The X-ray crystallographic analysis⁹ of inclusion complex 1.4^{25+} provided not only structural evidence for the complex but also an excellent interpretation for the unusual cation—cation complex-

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Figure 2. (a) The X-ray crystal structure of assembly $1.4.4BF_4^{21+}$. The external counteranions as well as the solvent molecules and hydrogen have been removed for clarity. (b) 2D schematic representation of the onionlike structure of the $1 \cdot 4 \cdot 4BF_4^{21+}$ complex.



Figure 3. Monitoring of the competitive inclusion of NEt_4^+ (5⁺) and NBu_4^+ (4⁺) in cage 1^{24+} by ¹H NMR (500 MHz, acetone- d_6 , 25 °C): (a) Kinetic formation of the 1.5^{25+} complex after 1 min at 25 °C (\bigtriangledown , encapsulated 5⁺; O, free 5^+ and 4^+). (b) Thermodynamic formation of $1 \cdot 4^{25+}$ after 1 week at 25 °C (\bigtriangledown , encapsulated 5⁺; \bigcirc , free 5⁺ and 4⁺).

ation. Single crystals were obtained by slow diffusion of hexane from an acetone solution containing 4 equiv of BF_4^- per cage 1^{24+} . The host-guest complex was revealed, in fact, as a triple-layered onionlike structure in which an anionic sphere of BF₄⁻ ions is mediated between cationic host 1^{24+} and guest 4^+ (Figure 2). Four BF_4^- ions are also accommodated in the cavity of 1^{24+} defining a small sphere of inversed polarity. Within this anionic sphere, NBu₄⁺ is perfectly recognized. In the crystal structure, we could locate all four BF₄⁻ ions inside of the cage, while some of the OTf⁻ ions located outside suffer from heavy disorder.

The presence of the BF4⁻ middle layer was strongly suggested even in solution by ¹⁹F NMR, which displayed two different BF₄⁻ signals.⁷ With 8 equiv of BF₄⁻, four anions were found inside (being upfield shifted), while four were outside (being normal). No encapsulation of the ammonium ion could be observed in the absence of BF₄⁻, indicating a clear role of the anion in the encapsulation process. Very interestingly, the inclusion of BF₄⁻ ions was not observed in the absence of 4^+ . These observations show that the triple-layered onionlike structure is essential for accommodating not only NBu₄⁺ but also BF₄⁻ ions in the cavity. While NMe₄⁺ was also encapsulated, its neutral analogue, tetramethylsilane, was not effective for the formation of the complex.

It is noteworthy that the alkyl side chains also take an important role in stabilizing the whole. Cationic guests such as NH4⁺ and alkali metal ions (Na⁺, K⁺), whose dimensions nicely match those in the anionic sphere of BF_4^- ions, were not encapsulated. Competition experiments with NEt_4^+ (5⁺) and 4⁺ showed an interesting kinetic aspect: when 4^+ and 5^+ are simultaneously mixed with cage 1^{24+} , we first observed the encapsulation of 5^+ arising from a kinetic selection of the smaller guest. However, this small guest is slowly exchanged by 4^+ to exclusively give the thermodynamic product after 1 week (Figure 3).

In summary, we presented the inclusion of a cationic guest inside the highly positively charged host through the formation of an anionic sphere of counterions in the middle. This exceptional hostguest behavior would lead to a new type of pairwise selective sensing where a host recognizes two different species only if they coexist.

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Supporting Information Available: Preparation and physical properties of 1^{24+} , 2, $1\cdot 4^{25+}$, crystallographic data of $1\cdot 4^{25+}$, calculated structure of **3** (PDF and CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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 (9) Crystal data of 1·4·4BF₄·210^Tf·16Me₂C=O: monoclinic, space group $C^{2/c}$, λ (Mo K α) = 0.71073 Å, T = 113(2) K, a = 39.300(6) Å, b = 1000(6)37.740(6) Å, c = 25.965(4) Å, $\beta = 104.308(3)^\circ$, V = 37316(10) Å³, Z =4, $d_{calcd} = 1.545 \text{ Mg/m}^3$. Least-squares refinement (1738 parameters) on 42 630 independent merged reflections ($R_{int} = 0.1130$) converged at $wR_2(F^2) = 0.3994$ for all data; $R_1(F) = 0.1087$ for 17 214 observed data $(I \ge 2\sigma(I))$, GOF = 1.145. The final difference Fourier electron density map and thermal temperature factors indicate that several CF₃SO₃ anions, acetone, a central phenyl ring of a dipyrimidine ligand, and ethylenediamines are severely disordered. Therefore, some restraints and constraints were applied to the disordered groups. Further modeling for residual electrons did not considerably improve the R factor. See also the Supporting Information.

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