Template Synthesis of Cages

Multicomponent Assembly of a Pyrazine-Pillared Coordination Cage That Selectively Binds Planar Guests by Intercalation**

*Kazuhisa Kumazawa, Kumar Biradha, Takahiro Kusukawa, Takashi Okano, and Makoto Fujita**

Aromatic intercalation is an important phenomenon both in chemistry and biology. When large aromatic molecules are intercalated, their chemical and physical properties are expected to change significantly.[1] To exploit such unique properties, several molecular tweezers and boxes based on large π systems (for example, anthracene or porphyrin) have

[*] Prof. M. Fujita, K. Kumazawa, Dr. K. Biradha, Dr. T. Kusukawa
Department of Applied Chemistry
School of Engineering, The University of Tokyo
Bunkyoku, Tokyo 113-8656 (Japan)
Fax: (+81) 3-5841-7257
E-mail: mfujita@appchem.t.u-tokyo.ac.jp
Dr. T. Okano
Department of Applied Chemistry
Graduate School of Engineering, Nagoya University
Chikusaku, Nagoya 464-8603 (Japan)

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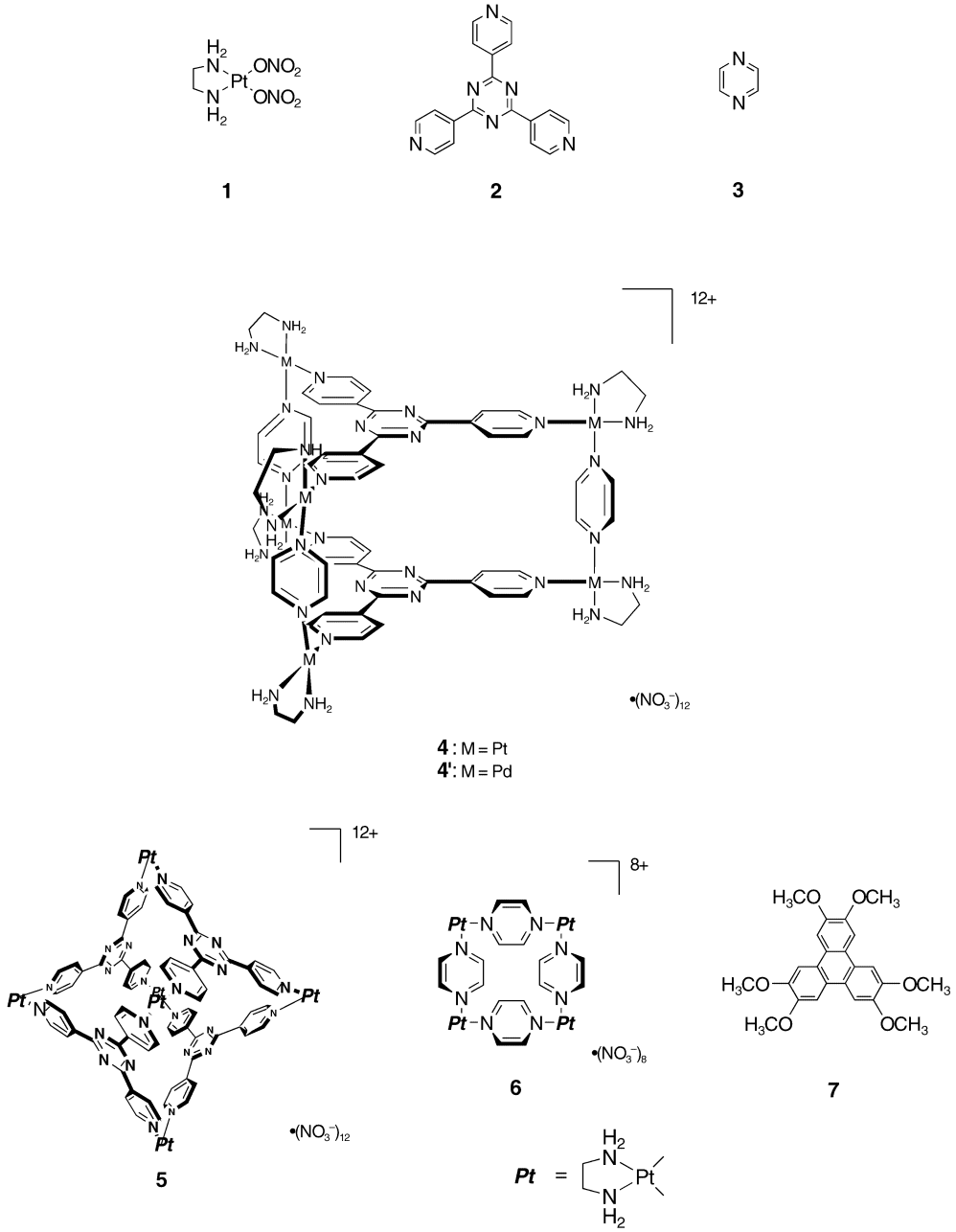
been developed,[2] yet the precise construction of rigid, three-dimensional cages for efficient aromatic intercalation still remains tedious. We now discuss the self-assembly of large prismlike cage **4** in which end-capped Pt^{II} ions **1** link two panel-like ligands **2** with three pyrazine pillars **3** (Scheme 1). This cage is expected to bind aromatic guests since the predicted interplane separation is ideal for aromatic intercalation (about 3.5 Å). To selectively obtain the desired cage **4** from multicomponents (**1**–**3**), however, the assembly of homotopic discrete compounds **5** and **6** need to be avoided. In this regard, we have found a remarkable template effect of large aromatic molecules:[3] for example, triphenylene derivative **7** efficiently templates the selective multicomponent assembly of cage **4**. This cage is stable even when the template is removed and the empty cage strongly binds other large aromatic molecules. The multicomponent assembly of metal-linked cages has been previously reported by Lehn and co-workers,[4] Stang and co-workers,[5] and others,[6] but the binding of such large aromatic compounds has been not documented.

The guest-templated assembly of cage **4** from multicomponents **1**–**3** was clearly observed by NMR spectroscopic analysis. When components **1**–**3** were combined in a 6:2:3 ratio in D_2O, a complicated mixture was obtained which gave an NMR spectrum that was very difficult to interpret (Figure 1 a). However, the addition of hexamethoxytriphenylene **7** (an excess amount) as a suspension and on heating the mixture at 100 °C resulted in the appearance of prominent peaks and the spectrum became simpler within hours. After 48 h, we finally obtained a quite simple NMR spectrum that



Scheme 1. Building blocks and products.

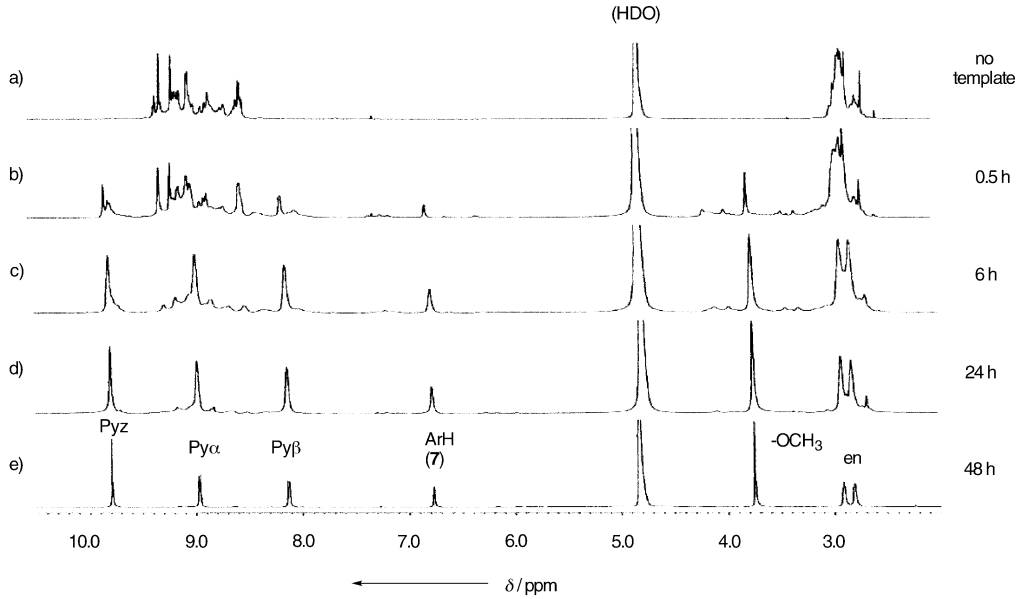


Figure 1. ^{1}H NMR spectra showing the guest-templated assembly of **7**⊂**4** complex (500 MHz, D_2O, 25 °C). a) A mixture of **1**, **2**, and **3**. Template **7** was added to this solution and the mixture was heated at 100 °C for b) 0.5 h, c) 6 h, d) 24 h, and e) 48 h. Pyz = pyrazine.

contained only four signals in the aromatic region: two doublets at $\delta = 8.96$ and 8.13 ppm for component **2**, a singlet at $\delta = 9.78$ ppm for component **3**, and another singlet at $\delta = 6.77$ ppm for guest **7** (Figure 1e). This spectrum was in accordance with the quantitative formation of complex **7**⊂**4**, where cage **4** accommodated guest **7** in the cavity. The signals of component **2** and guest **7** are shifted upfield as a result of face-to-face contact with each other, while that of component **3** is shifted downfield as a consequence of edge-to-face contact with the guest. The integral ratio indicated a 1:1 host–guest complexation. NOE correlation between the host and the guest in a NOESY spectrum is further support for the efficient complexation (see Supporting Information).

The template effect in the assembly of cage **4** is clearly apparent since, in the absence of the template, we could not observe the selective formation of **4** even after heating the solution for a few days; instead a mixture of **5**, **6** (ca. 1:0.7 ratio), and some uncharacterized components was obtained. We also examined the assembly of Pd^{II}-linked analogue **4′**. The formation of **4′** was dominant but not quantitative, presumably because of the weaker ligand field of Pd^{II} ions relative to the Pt^{II} ions.

It is noteworthy that homotopic cages **5** and **6**, which were not formed in the reaction of **1**–**3**, are thermodynamically stable. The quantitative formation of **5** from **1** and **2** has been well-documented;[7] square-shaped complex **6** was also found to efficiently assemble from **1** and **3** as confirmed by NMR spectroscopic and X-ray analysis (Figure 2).[8,9] Therefore, the exclusive formation of **4**, despite the sufficient stability of **5** and **6**, strongly shows the remarkable stabilization of **4** by the host–guest interaction.

The efficient intercalation of **7** in the cavity of **4** was evidenced by X-ray crystallographic analysis of single crystals obtained by slow evaporation of an aqueous solution of **7**⊂**4** (Figure 3).[10] The pyrazine pillars stand perpendicularly on a plane defined by three Pt^{II} ions which are connected to an

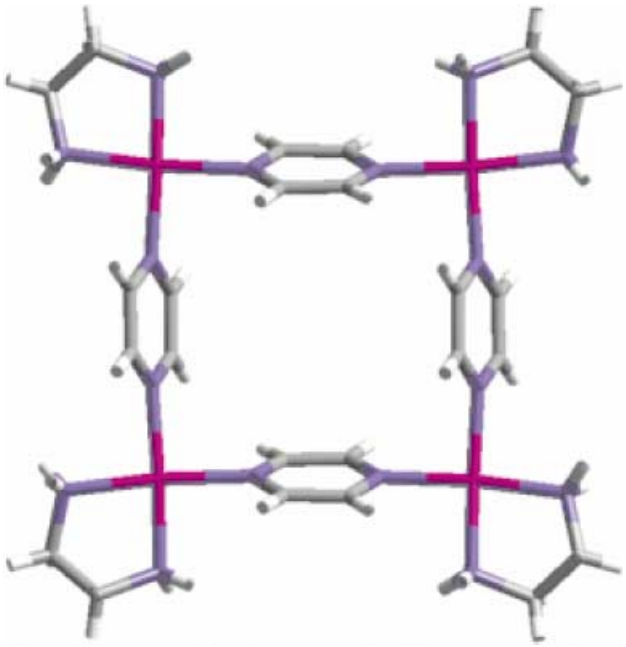


Figure 2. Crystal structure of **6**. Counterions and water molecules are omitted for clarity.

identical triazine ligand. The template molecule is intercalated in such a way that aromatic contact is maximized. As a result, the host–guest complex has D_{3h} symmetry. The face-to-face distance between the host and the guest is 3.3 Å, which is slightly shorter than the sum of the van der Waals distances, which suggests there are strong π-π interactions. A new absorption band appearing at 472 nm in the UV/Vis spectrum is attributed to charge transfer between **4** and **7**.

Cage **4** has kinetic stability and thus remained stable at room temperature even after the guest was removed by extraction with $CHCl_3$ (Figure 4a).[11] The empty cage of

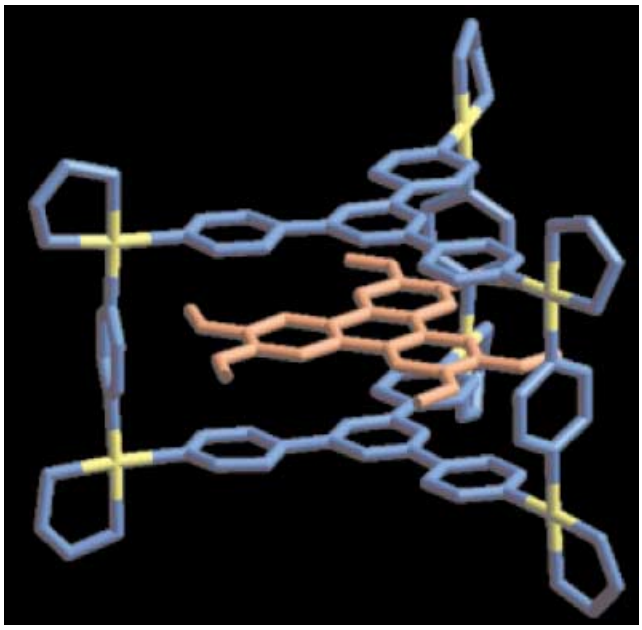


Figure 3. Crystal structure of **7**⊂**4**. Hydrogen atoms, other solvents, and counterions are omitted for clarity.

course was able to bind other neutral aromatic molecules well. For example, pyrene (**8**) was efficiently included inside the cage by suspending it in a D_2O solution of the empty cage **4** (Figure 4b). Though the host symmetry (D_{3h}) does not match the guest symmetry (D_{2h}), minimal numbers of signals were observed in the NMR spectrum, which suggests there is an unrestricted orientation of **8** in the cavity.

The efficient intercalation of planar guest molecules within the cage of **4** was applied to the control of the equilibration between planer and nonplaner molecules. Keto and enol tautomers of β-diketone **9**, which exist in a 15:85 ratio in CD_3CN, can never be separated because of rapid tautomerization. When complexed with cage **4**, however, this molecule was found to exist only in the enol form.[12] The exclusive enolization of **9** is interpreted by the selective intercalation of a planer enol form over a nonplaner keto form. H/D exchange of the CH proton of complexed **9** in D_2O was very slow ($t_{1/2} = 40$ h) relative to the rapid exchange in free **9**. This result clearly shows the inhibition of the keto–enol tautomerization of **9** in the cavity of cage **4**.[13]

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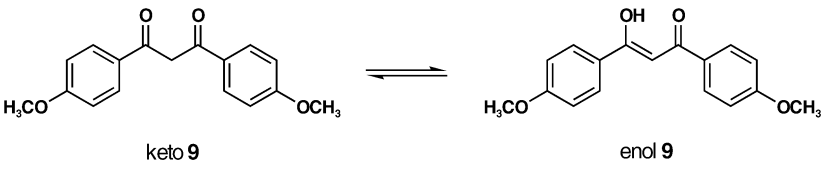

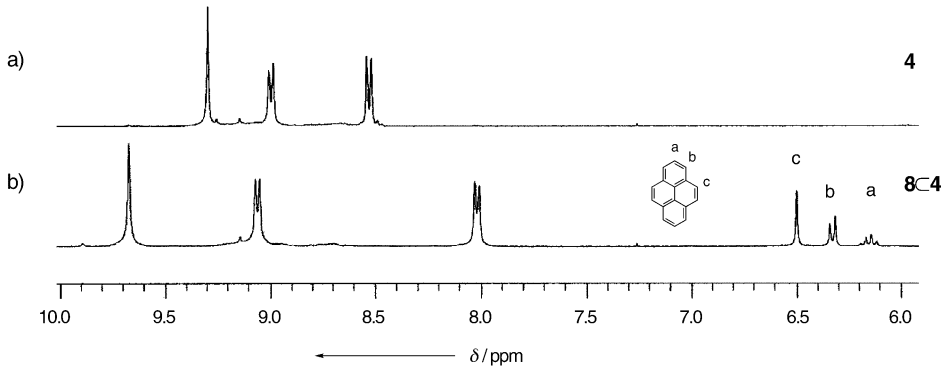

Figure 4. ^{1}H NMR spectra (300 MHz, D_2O, 25 °C) of aromatic regions of a) free **4** after extraction of template and b) **8**⊂**4** after the subsequent reinclusion of **8**.

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[8] Crystal data for **6**: $C_{24}H_{48}N_{24}O_{24}Pt_4 \cdot 4H_2O$, $M_r = 1909.29$, crystal dimensions $0.15 \times 0.15 \times 0.15$ mm^3, triclinic, space group $P\bar{1}$, $a = 8.0932(13)$, $b = 12.085(2)$, $c = 14.318(2)$ Å, $V = 1302.8(3)$ Å^3, $Z = 1$, $\rho_{calcd} = 2.434$ g cm^{-3}, $F(000) = 904$, $\lambda(Mo_{K\alpha}) = 0.71073$ Å, $T = -100$ °C, 6958 reflections collected, 4530 independent reflections observed; 361 number of parameters; $R_1 = 0.0568$; $wR_2 = 0.1587$.

[9] For related pyrazine bridged complexes, see the following: a) Re^{I}–pyrazine square complex: T. Rajendran, B. Manimaran, F.-Y. Lee, P.-J. Chen, S.-C. Lin, G.-H. Lee, S.-M. Peng, Y.-J. Chen, K.-L. Lu, *J. Chem. Soc. Dalton Trans.* **2001**, 3346; b) Ru^{II}/Ru^{III}–pyrazine square complex: C. Victor, C. C. Lau, L. A. Berben, J. R. Long, *J. Am. Chem. Soc.* **2002**, *124*, 9042 – 9043; c) Pt^{II}–pyrazine trianglar complex: M. Schweigner, S. R. Seidel, A. M. Arif, P. J. Stang, *Angew. Chem.* **2001**, *113*, 3575 – 3577; *Angew. Chem. Int. Ed.* **2001**, *40*, 3467 – 3469.

[10] a) Crystal data for **7**⊂**4**: $C_{84}H_{108}N_{42}O_{42}Pt_6 \cdot 9H_2O$, $M_r = 3723.91$, crystal dimensions $0.10 \times 0.10 \times 0.60$ mm^3, trigonal, $P\bar{3}$, $a = b = 19.8516$ (12), $c = 19.515(2)$ Å, $V = 6660.3(10)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.857$ g cm^{-3}, $F(000) = 3626$, $\lambda(Mo_{K\alpha}) = 0.71073$ Å, $T = -100$ °C, 20206 reflections measured, 4033 independent reflections observed; 509 number of parameters; $R_1 = 0.0672$; $wR_2 = 0.1836$. Further refinement was unsuccessful because of the high degree of disorder of the counterions and water molecules.

[11] We have previously reported that Pt^{II}–pyridine bonds have dual nature: labile at elevated temperature but inert at ambient temperature. By exploiting the dual nature, thermodynamic structure assembled at elevated temperature can be kinetically "locked" at ambient temperature (referred to as molecular lock concept). a) M. Fujita, F. Ibukuro, K. Yamaguchi, K. Ogura, *J. Am. Chem. Soc.* **1995**, *117*, 4175 – 4176; b) F. Ibukuro, T. Kusukawa, M. Fujita, *J. Am. Chem. Soc.* **1998**, *120*, 8561 – 8562.

[12] Confirmed by ^{1}H, ^{13}C, and COSY NMR spectra. See Supporting Information.

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[14] CCDC-205061 (**6**) and CCDC-205062 (**7**⊂**4**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

