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COMMUNICATION

Changing the volume of a giant macrocycle: the swelling of the macrocycle with organic solvents†‡

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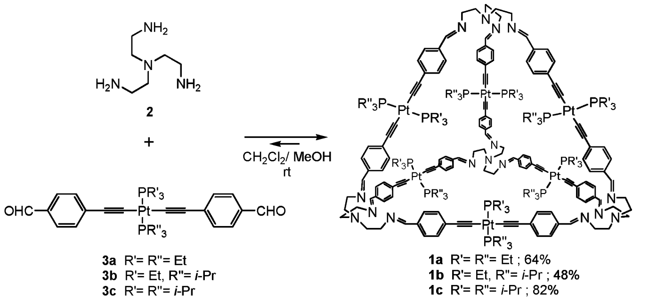
The novel tetrahedral macrocycles 1a–1c have been synthesized. Macrocycles 1a and 1c were revealed to have the property to increase in volume in solution by complexation between the macrocycle and the solvent molecules.

When a molecule contains a large cavity with a void, it can capture guest molecules by a host–guest interaction.[1] With the aid of this attractive force, polymeric materials, for example, allow solvent molecules to penetrate into the polymer networks.[2] The penetration leads to a volume increase of the polymeric materials, *i.e.*, swelling with the guest molecules. The increase in the volume of the materials is observed at macroscopic levels; however, the swelling may be attributed to a local host–guest interaction. Macrocycles **1a** and **1c** can interact with solvent molecules by a host–guest interaction. We wish to report here our finding that macrocycles **1a** and **1c** show a swelling phenomenon with organic solvents by a host–guest interaction.

One of synthetic methods for self-assembled molecules,[3,4] the Schiff base formation between an amine and an aldehyde, is known as a particularly useful one for constructing supramolecular structures and macrocyclic molecules.[4] We became interested in this process with respect to aza-cyclophane chemistry.[5] Therefore, we utilized tris(2-aminoethyl)amine (**2**) as the amine and *trans*-[bis(4-formylphenylethynyl)bis(triethylphosphine)]platinum(II) (**3a**) as the aldehyde for a condensation reaction (Scheme 1). Thus, a reaction of triamine **2** with dialdehyde **3a** in a 2 : 3 ratio in a mixture of CH_2Cl_2 and MeOH smoothly proceeded to give a major product in high yield (*ca.* 90%) as monitored by the ^1H NMR spectrum.[6] The product was isolated in a crystalline form in 64% yield, and was found to be **1a** with a molecular weight of 4506.9 (*m*/*z*), corresponding to the macrocyclic molecule formed from four molecules of amine **2** and six molecules of aldehyde **3a**.



Scheme 1 Synthesis of Schiff base macrocycles **1a–1c**.

Crystals suitable for the X-ray crystallographic analysis were obtained by recrystallization from CH_2Cl_2 and MeOH. The result is shown in Fig. 1a.[6,7] Noteworthy is the fact that the macrocycle **1a** has a giant tetrahedral structure, which consists of the imino groups at the vertices and the acetylide as the edges. The average length of the edges is *ca.* 23 Å. However, the edges of the acetylide are vertically curved toward the inside of the cavity. The average of the Pt–C≡C angle is 174.7°, and the corresponding angle for the calculated structure (HF/LANL2DZ) is 178.7° (Fig. 1b).[8,9] The crystal structure of macrocycle **1a** shows the presence of a void,[7] and a MeOH molecule is included in close vicinity to the PEt_3 moieties (Fig. 1a). Since the cavity was loosely occupied by the

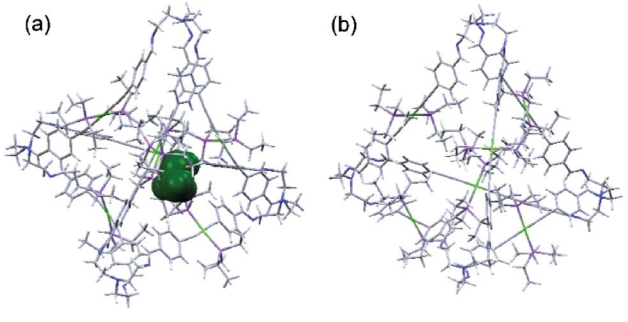


Fig. 1 (a) The X-ray crystal structure of **1a**. The MeOH molecule lying inside the intramolecular void between the PEt_3 moieties is represented by the space-filling model colored a deep green. (b) The optimized structure of **1a** (HF/LANL2DZ). Color coding: C: gray; H: white; N: blue; P: purple; Pt: light green.

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‡ Electronic supplementary information (ESI) available: Further experimental and computational details, ^1H, ^{13}C, and ^{31}P NMR spectra, and the results of time-dependent ^1H NMR spectra, VT NMR spectra, titration study, DLS, and PGSE-NMR spectra. CCDC reference number 795885. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1ob05272a

PEt_3 moieties,[10] we wondered if the macrocycle would be able to incorporate guest molecules.

Thus, we planned to study the complexation between **1a** and solvent molecules in solution. Since **1a** has a single bond at the platinum acetylide moiety, free rotation of the PEt_3 moiety around the acetylide edge should be possible (Fig. 2). This implies that the solvent molecules may go into and out of the cavity of **1a** accompanied by rotation of the PEt_3 moieties.[11] We also prepared compound **1b** with PEt_3 and $P(i\text{-}Pr)_3$ ligands on the platinum atom (Scheme 1). Macrocycle **1b** also has a tetrahedral structure. In the ^{31}P NMR spectrum at ambient temperature, each ^{31}P resonance of PEt_3 and $P(i\text{-}Pr)_3$ ligands in CD_2Cl_2 appeared as a sharp singlet, and did not show any sign of splitting even at −80 °C.[6] In the ^1H NMR spectrum of **1b**, NOE correlation between the methyl groups of the PEt_3 and $P(i\text{-}Pr)_3$ ligands was observed by 1D DPFGSE-NOE experiments (Fig. 3). This indicates the rapid movement of the ligands, like a revolver, going into and out of the cavity.

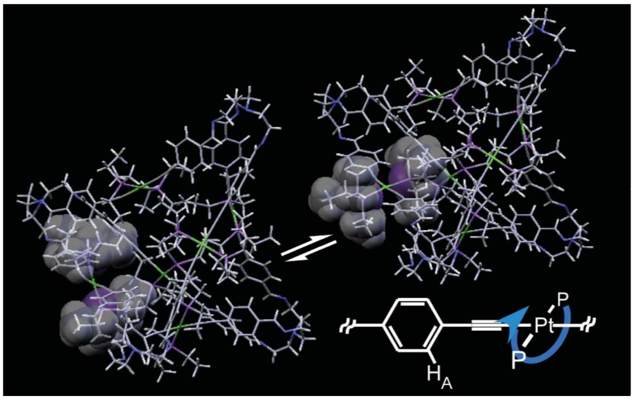


Fig. 2 Schematic representation of the revolving movement of the PEt_3 moiety in **1a**. The PEt_3 moiety under the rotational movement around the acetylide edge is represented by the space-filling model. Color coding: C: gray; H: white; N: blue; P: purple; Pt: light green.

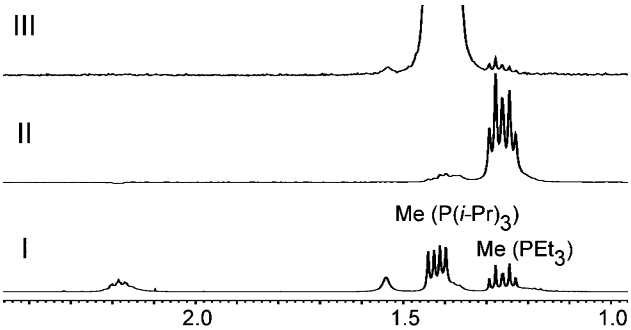


Fig. 3 The results of 1D DPFGSE-NOE experiments of **1b** in CD_2Cl_2. (I) ^1H NMR spectrum of **1b**. (II) Irradiation at Me of PEt_3 gives NOE at Me of $P(i\text{-}Pr)_3$. (III) Irradiation at Me of $P(i\text{-}Pr)_3$ gives NOE at Me of PEt_3.

To examine whether the guest molecules could enter the cavity or not, NMR titration in CD_2Cl_2 solution was performed. However, addition of 50, 100, 200, and 500 molar equivalents of CD_3OD to **1a** only resulted in slight differences in the chemical shift as a result of the averaged signals.[6] The ^1H resonance of the phenyl proton H_A (Fig. 2) shifted downfield by 0.014 ppm. By changing the solvent to chloroform-d_1, tetrahydrofuran-d_8, benzene-d_6, and toluene-d_8, the ^1H resonance showed averaged signals. Since the complexation induced shift was hardly observed in the ^1H NMR titration experiment, we therefore had to recourse to a ^{31}P NMR spectroscopic study at various temperatures.

The variable-temperature (VT) ^{31}P NMR spectra of **1a** were measured in toluene-d_8, ethylbenzene, and butylbenzene in the temperature range of −80–20 °C (Fig. 4). The results indicated that at lower temperatures the ^{31}P resonance signal began to show splitting, which appeared at a higher temperature for the spectrum measured in solvents of larger molecular size. This may be ascribed to the change of magnetic environment attributable primarily to the ring current effect of the phenyl rings,[12,13] caused by the restricted motion of **1a**, including the rotation of the PEt_3 moieties around the acetylide edge, subject to the size of solvent molecule.

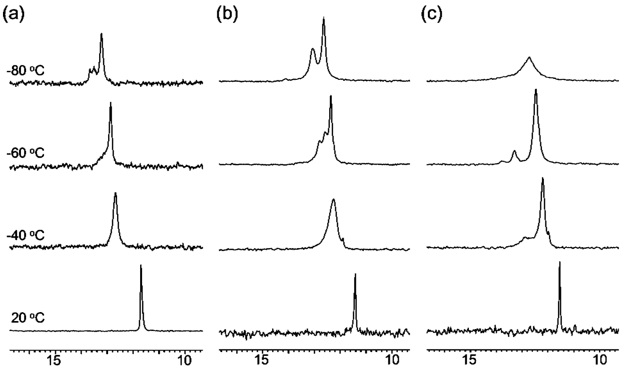


Fig. 4 VT ^{31}P NMR spectra of **1a** in (a) toluene-d_8, (b) ethylbenzene, and (c) butylbenzene.

To obtain information on the complexation of **1a** with guest molecules, we measured the diffusion coefficient (D) of **1a** in various solvents using Dynamic Light Scattering (DLS). Because this physical parameter is related to the molecular size, it would change when the macrocycle **1a** forms complexes with guest molecules.[14] The solvents used were dichloromethane, tetrahydrofuran, and *p*-dioxane as the non-aromatic solvents, and benzene, toluene, *p*-xylene, ethylbenzene, and butylbenzene as the aromatic solvents. The results are summarized in Table 1. The diffusion coefficient of **1a** in dichloromethane was 4.44×10^{-10} m^2 s^{-1} and it markedly decreased by varying the solvent. The D values of **1a** are in the range of $1.74–3.19 \times 10^{-10}$ m^2 s^{-1} for aromatic solvents (benzene, toluene, *p*-xylene, ethylbenzene, and butylbenzene). The change of D values was corroborated by the results of Pulse Gradient Spin Echo (PGSE)-NMR experiments of **1a**. The D values decreased from 4.00×10^{-10} m^2 s^{-1} (dichloromethane-d_2) to $2.64–2.93 \times 10^{-10}$ m^2 s^{-1} for the aromatic solvents.

We estimated the hydrodynamic radius (R_H) of **1a** from the obtained D value using the Stokes–Einstein equation, $D = k_BT/6\pi\eta R_H$, where k_B is the Boltzmann constant, T is the absolute temperature, and η is the viscosity of the solvent (Table 1).[15] By using DLS, the R_H values for various organic solvents were obtained (Fig. 5a). The obtained R_H values have the tendency to increase with increasing volume of the solvent molecules,[16] and the R_H values and the volume of the solvent have a linear relationship, which can be classified into two categories by the slope, non-aromatic and aromatic solvents. The tendency of the R_H values

Table 1 Physical properties of the solvents and the results of the DLS and PGSE-NMR measurements of **1a**, **1c** and **4** at 25 °C

	aromatic solvent					non-aromatic solvent		
	benzene	toluene	*p*-xylene	ethylbenzene	butylbenzene	dichloromethane	tetrahydrofuran	*p*-dioxane
intrinsic volume [cm^3 mol^{-1}][a]	71.6	85.7	99.8	99.8	128.0	49.4	62.2	68.1
viscosity [mPa s][a]	0.603	0.553	0.605	0.637	0.960	0.411	0.462	1.19
dielectric constant[b]	2.27	2.38	2.27	2.40[c]	2.36[c]	8.93	7.58	2.21
D of **1a** [m^2 s^{-1}]	2.97×10^{-10} (2.64×10^{-10})	3.19×10^{-10} (2.93×10^{-10})	2.89×10^{-10} (2.68×10^{-10})	2.72×10^{-10}	1.74×10^{-10}	4.44×10^{-10} (4.00×10^{-10})	3.83×10^{-10} (3.35×10^{-10})	1.44×10^{-10}
R_H of **1a** [nm]	1.22 (1.18)	1.24 (1.15)	1.25 (1.20)	1.26	1.31	1.20 (1.09)	1.23 (1.10)	1.27
D of **1c** [m^2 s^{-1}]	3.28×10^{-10}	3.37×10^{-10}	—[d]	2.80×10^{-10}	1.76×10^{-10}	4.27×10^{-10}	3.76×10^{-10}	1.41×10^{-10}
R_H of **1c** [nm]	1.10	1.17		1.22	1.29	1.24	1.26	1.30
D of **4** [m^2 s^{-1}]	3.18×10^{-10}	3.11×10^{-10}	2.80×10^{-10}	—[d]	1.48×10^{-10}	4.51×10^{-10}	3.83×10^{-10}	1.46×10^{-10}
R_H of **4** [nm]	1.14	1.27	1.29		1.54	1.18	1.23	1.25

[a] see Ref. 15 [b] see Ref. 21. [c] Dielectric constant at 20 °C. [d] The diffusion coefficient has not been obtained because of the lack of linearity at q^2 *vs.* Γ plots. The results of the PGSE-NMR are shown in parentheses.

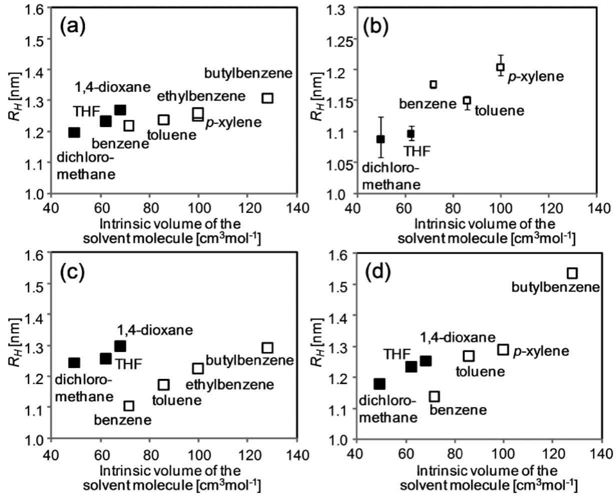
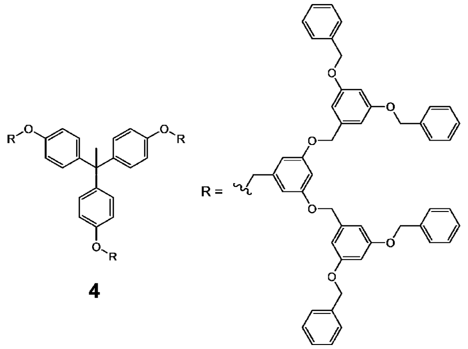


Fig. 5 (a) Plots of R_H values of **1a** obtained by DLS measurements *versus* the intrinsic volumes of the solvent molecule. (b) Plots of R_H values of **1a** obtained by PGSE-NMR measurements *versus* the intrinsic volumes of the solvent molecule. The error bar is the average of 12 to 15 experiments. (c) Plots of R_H values of **1c** obtained by DLS measurements *versus* the intrinsic volumes of the solvent molecule. (d) Plots of R_H values of dendrimer **4** obtained by DLS measurements *versus* the intrinsic volumes of the solvent molecule. Black squares: non-aromatic solvents, white squares; aromatic solvents.

was corroborated by the results of the PGSE-NMR measurements (Fig. 5b). The R_H value increased by 1.11 times by changing the volume of the solvent from 49.4 cm^3 mol^{-1} (dichloromethane) to 99.8 cm^3 mol^{-1} (*p*-xylene). A similar tendency was observed for macrocycle **1c** (Fig. 5c). Macrocycle **1c** has a similar tetrahedral structure, but is composed of platinum atoms coordinated by P(*i*-Pr)$_3$ ligands. These results suggested that macrocycles **1a** and **1c** could form host–guest complexes between the macrocycle and the solvent molecules. To confirm this host–guest complexation of **1a** and **1c** with the solvent molecules, we compared them with the open-type host molecule **4**, so called the second generation of the Fréchet-type poly(benzyl ether) dendrimer (Fig. 6).[17] Estimated R_H values from the results of the DLS measurements indicated that the dendrimer **4** has the tendency to increase its volume according to the increasing size of the solvent molecule (Fig. 5d).



4

Fig. 6 Structure of the dendrimer **4**.

These results showed that the host–guest complexation between the dendrimer **4** and the solvent molecules was observed as swelling in solution. Thus, the swelling observed for **1a** and **1c** indicated that both macrocycles are capable of forming host–guest complexes with solvent molecules. The host–guest complexation of macrocycles **1a** and **1c** with solvent molecules may be achieved by weak interactions, which can be classified into two categories according to the chemical properties of the solvent, aromatic and non-aromatic solvents. For the non-aromatic solvents, the dipole of the solvent may play an important role, while for the aromatic solvents, π–π and CH–π interactions due to the aromatic character of the solvent may be responsible.[18]

As shown in Fig. 5a, the plot of the R_H values of **1a** against the intrinsic volumes of the non-aromatic solvents displays a steeper slope than that of the aromatic solvents. However, the opposite trend was observed for **1c** (Fig. 5c). Presumably, macrocycle **1c** could interact with the aromatic solvent more effectively than macrocycle **1a** *via* a CH–π interaction. Since **1c** has more aliphatic P(*i*-Pr)$_3$ ligands instead of PEt$_3$ ones, the CH–π interaction may be more effective in the complexation than that of **1a**, leading to the steeper slope for the aromatic solvents. A similar explanation may be applied to **4**, the slope was steeper for aromatic solvents than that for non-aromatic solvents (Fig. 5d), which may be induced by the π–π interaction between the phenyl rings of the dendrimer and the solvent molecules.[19] Further study is needed to account for these phenomena.[20]

In summary, we have found that giant macrocycles **1a** and **1c** can form complexes with guest solvent molecules. The complexation leads to swelling of the macrocycles in solution. The size expansion of the macrocycle was observed with increasing volume of the solvent molecule as evidenced by a decrease in the diffusion coefficients. These results showed that the swelling could be generated for macrocycles **1a** and **1c** as well as for a divergent system of polymeric materials even though the macrocycles have a closed-structure. These observations may originate from the giant-sized structure and the flexibility of the macrocycles.[11] With respect to the host–guest complexation of the macrocycles, the R_H value also depends on the chemical properties of the solvent. The size expansion of the macrocycle **1a** is more sensitive to the non-aromatic solvents than that of the aromatic solvents, while the reverse tendency was observed for **1c** and **4**. Further investigation is required to clarify these observations. The study on the adsorptive properties of the macrocycles may give insight into the interrelated factors between the macrocycle and the guest molecules, and this study is in progress.

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7 $C_{205}H_{292}N_{16}OP_{12}Pt_6$, $M = 4538.89$, triclinic, $a = 21.913(3)$, $b = 23.156(3)$, $c = 23.850(4)$ Å, $U = 11350(3)$ Å^3, $T = 133$ K, space group $P\bar{1}$(# 2), $Z = 2$, 51700 reflections measured, 36467 unique ($R_{int} = 0.0540$). The final residuals for $I > 2\sigma(I)$ were $R_1 = 0.0888$, w$R_2 = 0.2755$ (GOF = 1.031). Data are summarized in the supporting information‡ and crystallographic data for the structural analysis of **1a** has been deposited within the Cambridge Crystallographic Data Center (CCDC) as 795885.

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11 In addition to the rotation of the PEt_3 moieties around the platinum acetylide edge, clockwise and counterclockwise inversion between two C_3 conformers of the $N(CH_2CH_2N)_3$ moieties exists, as is supported by VT ^1H NMR spectra (Figs. *S*8 and *S*11). This inversion process is expected to be fast at room temperature and slow down below at −60 °C. Furthermore, the rotation of the Pt–P bond also exists.[6].

12 The splitting of the ^{31}P resonance may be ascribed to the restricted rotation of the PEt_3 moieties around the platinum acetylide edge. When the rotation is restricted, the PEt_3 moieties locate inside and outside of the cavity and different chemical shifts are expected. The other one is the rotation of the *para*-substituted benzene rings around the acetylide edge. This rotation may affect the magnitude of the π-conjugation through the acetylide axis, and cause the PEt_3 moieties in different magnetic environment.

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18 CH–π and π–π interactions are expected to exist as one of the host–guest interactions for aromatic solvents because the macrocycle **1** has aromatic and aliphatic moieties in its structure. For non-aromatic solvents, dipole–dipole interactions may become important due to their higher molecular dipoles than those of aromatic solvents.

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