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Structural Alteration of Hybrid Supramolecular Capsule Induced by Guest Encapsulation

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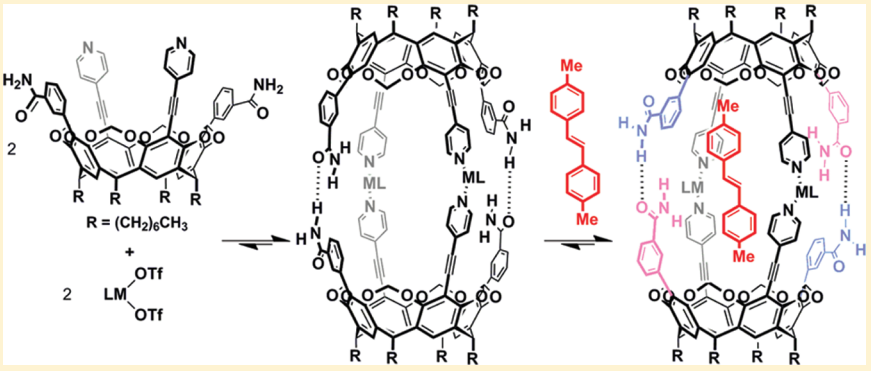
Supporting Information

ABSTRACT:



Heterofunctionalized C_{2v} symmetrical cavitand **1** with 4-pyridylethynyl and 3-carbamoylphenyl groups in alternating arrangement was designed and synthesized. A 1:1 mixture of the cavitand **1** and a *cis*-coordinated palladium(II) or platinum(II) complex self-assembled into a hybrid supramolecular capsule via both metal−ligand coordination bonds and hydrogen bonds. Formation of the capsular assembly was confirmed by NMR spectroscopy and mass spectrometry. The hybrid capsule encapsulated the appropriate guest, the molecular sizes of which fit the size of the capsular cavity. Structural alteration of the hybrid capsule was induced by the guest encapsulation. A C_{2h} structure for the encapsulation complex was assigned by 2D NMR spectra analysis. Thermodynamic and kinetic properties of the guest encapsulation were investigated. The kinetics of in/out guest exchange was strongly influenced by hydrogen bonding in the hybrid capsule.

INTRODUCTION

Self-assembly is a smart approach to access nanoscale architecture. Spontaneous assembly of well-designed units enables the construction of complicated structures, whereas it is often difficult to build them via the classical covalent approach.[1] Capsular structures with isolated nanoscale cavities are interesting targets for the creation of discrete assemblies. To date, varieties of molecular capsules have been reported using noncovalent interactions as the attractive forces.[2] Encapsulated guest molecules inside the isolated cavity sometimes show unique behavior that is different from the bulk phase. For example, acceleration of reaction and stabilization of labile guest molecules can be achieved by encapsulation.[3] To create a supramolecular capsule, the cavitand[4] derived from calix[4]resorcinarene is one of the most useful platforms. The cavitand originally possesses the exact size of the cavity, and it is possible to introduce adequate functional groups at the upper rim to conduct self-assembly while controlling their orientation. The creation of many cavitand-based capsular assemblies through hydrogen bonds,[5] metal−ligand coordination bonds,[6] and other interactions[7] has been achieved. We have developed a hybrid supramolecular capsule assembled by a C_{2v} symmetrical cavitand bearing pyridylethynyl and phenylureido groups and a *cis*-coordinated platinum(II) complex via both metal−ligand coordination bonds and hydrogen bonds.[8]

The dynamics of a guest molecule encapsulated in the isolated nanospace of a supramolecular capsule are restricted. The restriction results in novel isomerisms characteristic of encapsulation complexes.[9−11] Rebek and co-workers reported social isomers and constellational isomers in multimolecular encapsulation.[9] These isomers originate from restriction on the tumbling of an unsymmetrical guest molecule along the long axis and/or change in their arrangement relative to each other. Unsymmetrical guest encapsulation in the unsymmetrical heterodimeric capsule and restriction of guest tumbling along the long axis causes orientational isomers.[10] Furthermore, the symmetry of the capsule is reduced as a consequence of restricting not only vertical tumbling but also horizontal rotation of the guest motion.[11] Although much attention has been paid to controlling the guest dynamics, the restriction of capsular dynamics in encapsulation complexes

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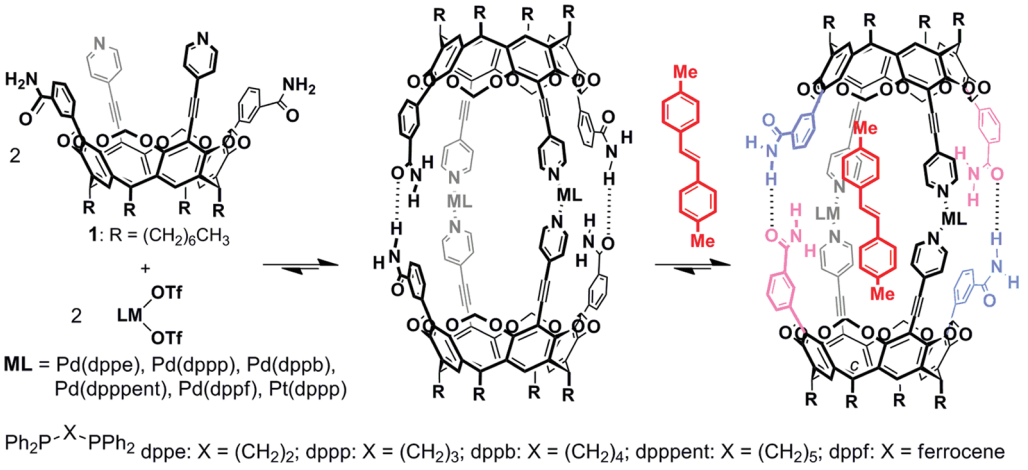
Scheme 1. Hybrid Capsular Formation of Cavitand 1 and Metal Complex and the Guest Encapsulation

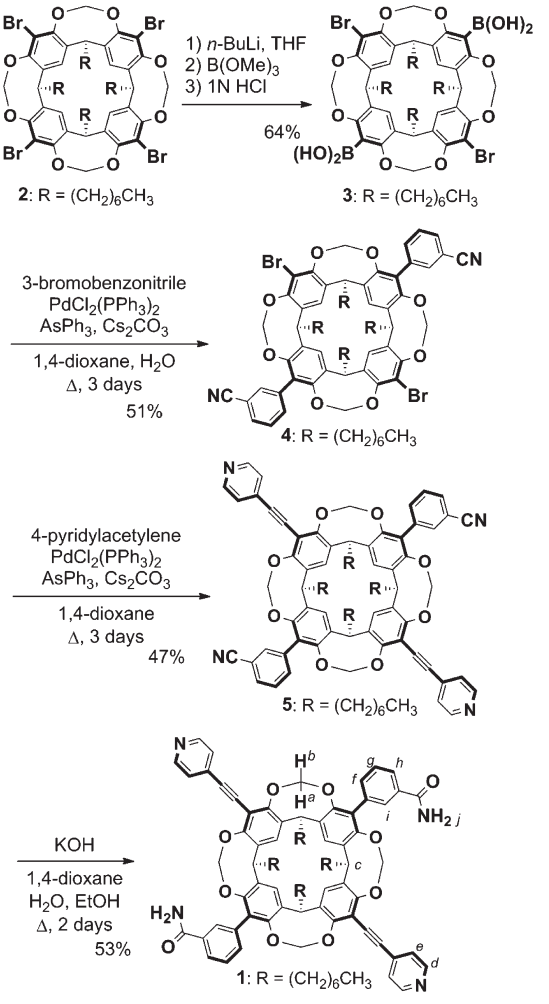


has been rarely reported.[12] Guest encapsulation leading to structural alteration of capsular assembly is an interesting subject because the alteration is induced by weak van der Waals interactions. Here, we report (1) the synthesis of a heterofunctionalized C_{2v} symmetrical cavitand **1** with 4-pyridylethynyl and 3-carbamoylphenyl groups in alternating arrangement at the upper rim, (2) self-assembly of **1** and a *cis*-coordinated palladium(II) or platinum(II) complex into a hybrid capsule via both metal−ligand coordination bonds and hydrogen bonds, and (3) structural alteration of the hybrid capsule induced by guest encapsulation (Scheme 1).

RESULTS AND DISCUSSION

Synthesis of C_{2v} Cavitand 1. The cavitand **1** with C_{2v} symmetry was designed to construct a hybrid supramolecular capsule by both metal−ligand coordination bonds and hydrogen bonds. The cavitand **1** has two 4-pyridylethynyl groups as ligands for metal−ligand coordination and two 3-carbamoylphenyl groups for the hydrogen bonding in alternating arrangement at the upper rim. The tetrabromo cavitand[13] **2** was converted into cavitand **1** using palladium-catalyzed cross-coupling reactions twice as key steps (Scheme 2). C_{4v} tetrabromo cavitand was converted into C_{2v} symmetrical dibromo-diboronic acid cavitand **3** using a modification of Sherburn's procedure.[14] The Suzuki−Miyaura cross-coupling of cavitand **3** with 3-bromobenzonitrile resulted in two benzonitriles being introduced into cavitand **4** in 51% yield. Subsequent Sonogashira-type cross-coupling of cavitand **4** with 4-ethynylpyridine afforded cavitand **5** in 47% yield.[15] Use of typical Sonogashira coupling conditions in the presence of copper salts was not effective in affording **5** because of preferential progress of the homocoupling reaction of 4-ethynylpyridine. Hydrolysis of nitrile groups under basic conditions afforded C_{2v} symmetrical di(4-pyridylethynyl)-di(3-carbamoylphenyl) cavitand **1** in 53% yield. Surprisingly, the alkaline hydrolysis did not produce a carboxylate as a product. The structure of **1** was confirmed by NMR, mass, and IR spectra. The ^{1}H NMR spectrum of **1** in $CDCl_3$ showed a symmetrical species (Figure 1a). The signal of the α-protons of the pyridyl nitrogen (H^d) was observed at 8.53 ppm. The inner and outer protons of the methylene bridges (H^a and H^b) and methine protons (H^c) appeared at 4.44, 5.56, and 4.85 ppm, respectively. Broad singlet signals appearing at 5.59 and 6.11 ppm were assigned as

Scheme 2. Synthesis of C_{2v} Symmetrical Cavitand 1



amide protons (H^j), because these signals disappeared upon addition of a small amount of D_2O.

Capsular Formation via Self-Assembly of Cavitand 1 and Metal Complexes. A metal−ligand coordination bond between pyridylethynyl groups of the cavitand **1** and *cis*-coordinated

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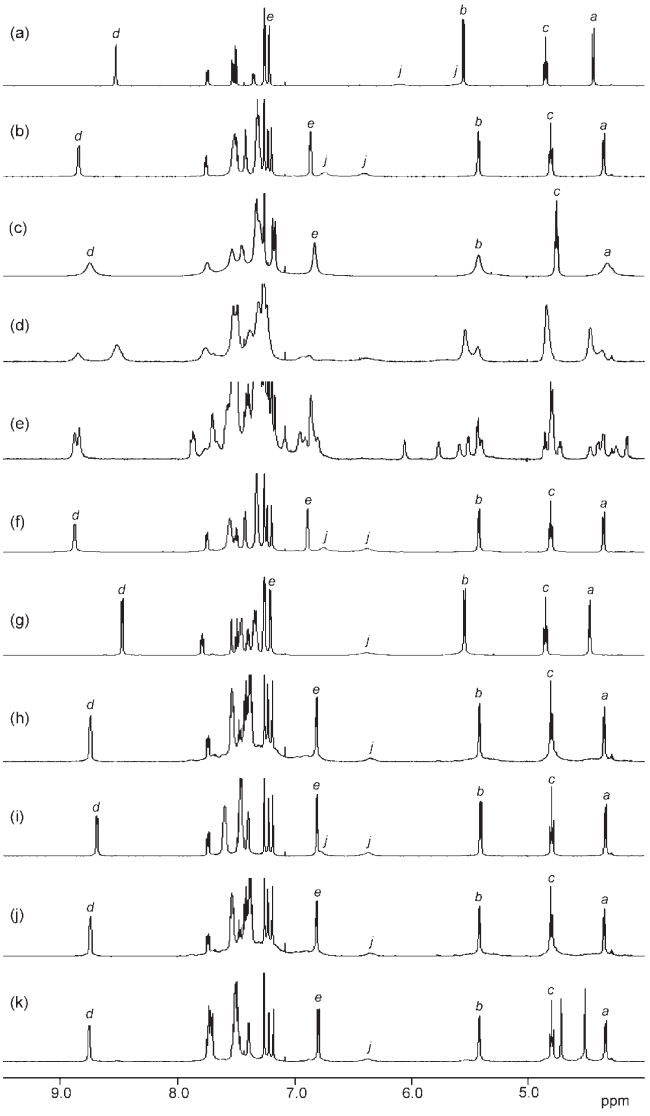


Figure 1. ^{1}H NMR spectra (600 MHz, $CDCl_3$) of (a) **1** alone at 298 K; (b) [**1**] = [Pd(dppp)$(OTf)_2$] = 4 mM at 298 K; (c) [**1**] = [Pd(dppp)-$(OTf)_2$] = 4 mM at 243 K; (d) [**1**] = 8 mM and [Pd(dppp)$(OTf)_2$] = 4 mM at 298 K; (e) [**1**] = 4 mM and [Pd(dppp)$(OTf)_2$] = 6 mM at 298 K; (f) [**1**] = [Pt(dppp)$(OTf)_2$] = 4 mM at 298 K; (g) [**1**] = [Ni(dppp)$(OTf)_2$] = 4 mM at 298 K; (h) [**1**] = [Pd(dppe)$(OTf)_2$] = 4 mM at 298 K; (i) [**1**] = [Pd(dppb)$(OTf)_2$] = 4 mM at 298 K; (j) [**1**] = [Pd(dpppent)$(OTf)_2$] = 4 mM at 298 K; and (k) [**1**] = [Pd(dppf)$(OTf)_2$] = 4 mM at 298 K.

divalent group 10 metal complexes formed discrete aggregates spontaneously. Consequently, the approaching 3-carbamoylphenyl groups are easily connected through hydrogen bonds (Scheme 1). A 1:1 mixture of cavitand **1** and Pd(dppp)$(OTf)_2$ [dppp = 1,3-bis(diphenylphosphino)propane] in $CDCl_3$ showed a highly symmetrical ^{1}H NMR spectrum, suggesting capsular assembly (Figure 1b). Pyridyl−palladium coordination bond formation caused a downfield shift of the α-protons of the pyridyl nitrogen (H^d: δ = 8.85 ppm; $\Delta\delta$ = +0.32 ppm) and an upfield shift of the β-protons of the pyridyl nitrogen (H^e: δ = 6.87 ppm; $\Delta\delta$ = −0.35 ppm). The signals of the inner and outer protons of the methylene bridges (H^a and H^b) and methine protons (H^c) were shifted upfield by 0.09, 0.13, and 0.04 ppm, respectively, relative to those of cavitand **1** alone. Hydrogen-bond formation between

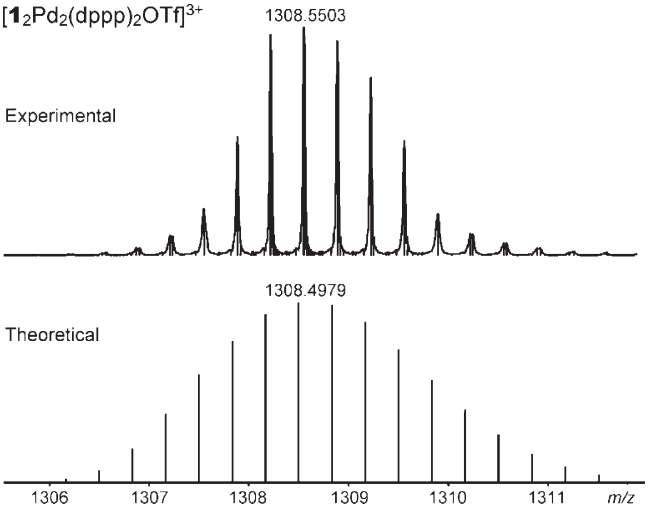


Figure 2. ESI-FT-ICR MS spectrum of [$\mathbf{1}_2Pd_2(dppp)_2(OTf)_4$].

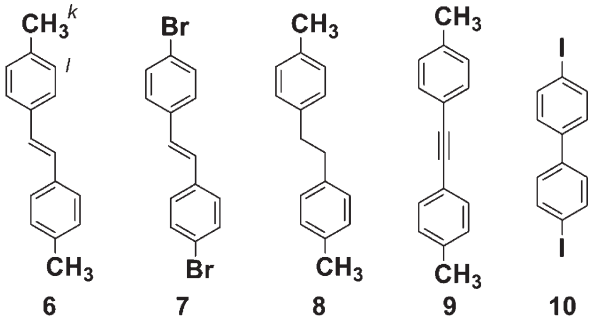
amide groups of two molecules of **1** caused a downfield shift of the amide protons (H^j: $\Delta\delta$ = +0.82, +0.63 ppm). Signals observed in the ^{1}H NMR spectrum were assigned by ^{1}H−^{1}H COSY and NOESY measurements (Figures S1 and S2). The 1:1 mixture of **1** and Pd(dppp)$(OTf)_2$ at 243 K showed a ^{1}H NMR spectrum similar to that at 298 K (Figure 1c vs b). The electron spray ionization (ESI) Fourier transform ion cyclotron resonance mass spectrum (FT-ICR-MS) of the mixture showed a trivalent molecular ion peak of the capsular assembly {[$\mathbf{1}_2Pd_2$-$(dppp)_2OTf]^{3+}$} at m/z 1308.5503 (theoretical: 1308.4979) (Figure 2). These results strongly support the formation of supramolecular capsule [$\mathbf{1}_2Pd_2(dppp)_2(OTf)_4$]. The ratio of cavitand **1** to Pd(dppp)$(OTf)_2$ was important for the formation of the capsular assembly. A 2:1 mixture of cavitand **1** and Pd(dppp)-$(OTf)_2$ in $CDCl_3$ indicated coexistence of the capsular assembly and free cavitand **1**, and their relatively fast exchange caused signal broadening in the ^{1}H NMR spectrum (Figure 1d). Capsular assembly and unidentified assemblies are produced in a 2:3 mixture of cavitand **1** and Pd(dppp)$(OTf)_2$ in $CDCl_3$ (Figure 1e). Quantitative capsule formation was identified in a 1:1 mixture of cavitand **1** and Pt(dppp)$(OTf)_2$, and the ^{1}H NMR spectrum was similar to that of [$\mathbf{1}_2Pd_2(dppp)_2(OTf)_4$] (Figure 1f). On the other hand, a mixture of **1** and Ni(dppp)$(OTf)_2$ did not form a capsule (Figure 1g). The cavitand signals in the ^{1}H NMR spectrum of this mixture coincided with those of cavitand **1** alone.

Next, we paid attention to bidentate phosphine ligands on the metal center. Dalcanale and co-workers investigated the capsular assembly of a tetracyano cavitand and various metal complexes.[6a,16] Four molecules of Pd(dppp)$(OTf)_2$ and two molecules of the tetracyano cavitand self-assemble into a capsular structure; however, Pd(dppe)$(OTf)_2$ [dppe = 1,2-bis(diphenylphosphino)ethane] and Pd(dppb)$(OTf)_2$ [dppb = 1,4-bis(diphenylphosphino)butane] did not converge into discrete structures. The P−Pd−P angles of Pd(dppe)Cl_2, Pd(dppp)Cl_2, and Pd(dppb)Cl_2 based on their crystal structures were 85.8°, 90.6°, and 94.3°, respectively.[17] Consequently, the Cl−Pd−Cl angles also changed, although the ratio was small. Values of the Cl−Pd−Cl angle of Pd(dppe)Cl_2, Pd(dppp)Cl_2, and Pd(dppb)Cl_2 were 94.2°, 90.8°, and 89.6°, respectively. These angles are similar to the angles in RCN−Pd−NCR. Slight differences between these angles were strikingly reflected in their assemblies because of the rigid structure of

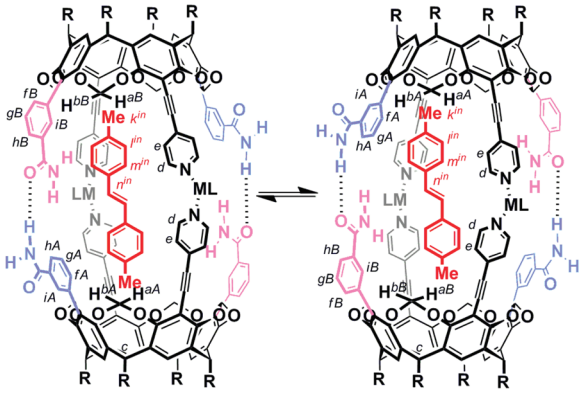
the tetracyano cavitand. In contrast, all mixtures of **1** and palladium complexes {Pd(dppe)(OTf)$_2$, Pd(dppp)(OTf)$_2$, Pd(dppb)(OTf)$_2$, Pd(dpppent)(OTf)$_2$, [dpppent = 1,5-bis(diphenylphosphino)-pentane], and Pd(dppf)(OTf)$_2$ [dppf = 1,1′-bis(diphenylphosphino)ferrocene]} suggested the formation of capsular assemblies. Downfield shifts of the α-protons of the pyridyl nitrogen and upfield shifts of the β-protons of the pyridyl nitrogen in ^{1}H NMR spectra were characteristic of pyridyl−palladium coordination bond formation (Figure 1h−k). The pyridylethynyl group on cavitand **1** would be more or less flexible enough to form a coordination bond with those palladium complexes at different angles.

Guest Encapsulation and Structural Analysis. Cavities formed by capsular assembly of cavitand **1** and palladium or platinum complexes must be sizable to encapsulate guest molecules (Chart 1). It was found that *trans*-4,4′-dimethyl stilbene (**6**) is an appropriate guest for the hybrid capsule [**1**$_2$Pd$_2$(dppp)$_2$-(OTf)$_4$]. The ^{1}H NMR spectrum of a 1:10 mixture of [**1**$_2$Pd$_2$-(dppp)$_2$(OTf)$_4$] and **6** in $CDCl_3$ at 298 K showed new sets of signals, assignable to {**6**@[**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$]} (Figure 3a). The ^{1}H NMR signals of encapsulated and free guests were independently observed, indicating that the exchange of guests in and out of the capsule is slow on the NMR time scale. The methyl groups of encapsulated **6** showed a large upfield shift (H^k: $\delta = -1.54$ ppm; $\Delta\delta = -3.90$ ppm) because of the aromatic ring current effect of the cavity end of the cavitand. Aromatic protons at the 3,3′ and 5,5′ positions of encapsulated **6** also showed an upfield shift (H^l: $\delta = 6.10$ ppm; $\Delta\delta = -1.06$ ppm). In contrast to the sharp signals of encapsulated guest, ^{1}H NMR signals of cavitands of the encapsulation complex (H$^{a,b(encap.)}$) were broadened at 298 K. These broadened signals started to split when the temperature of the sample decreased; however, signals of the encapsulated guest remained almost unchanged. The fraction of encapsulation complex increased at lower temperature (vide infra). The ^{1}H NMR spectrum of a 4 mM $CDCl_3$ solution of [**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] in the presence of 10 equiv of **6** at 243 K showed only encapsulation complex {**6**@[**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$]} and free **6** (Figure 3b). Most of the protons of the cavitand were split into two sets of signals. In marked contrast, signals of the capsule in the absence of **6** did not split into two sets of signals even at 243 K (Figure 1b vs c). There are two possible explanations for these splittings. One is that two cavitands forming a capsular assembly (upper and lower) become nonequivalent, wherein the encapsulated guest should be desymmetrized. The other is that the structure of the cavitand itself is altered, but the upper and lower cavitands are equivalent. In this case, the encapsulated guest would maintain the symmetry. In fact, ^{1}H NMR signals of encapsulated **6** maintained their symmetry even at lower temperature. Consequently, structural alteration of the encapsulation complex is caused by desymmetrization of the cavitand itself. A C_{2h} symmetrical structure for the encapsulation complex, because of rotational regulation of the aromatic rings of 3-carbamoylphenyl groups, was identified by the following experiments (Scheme 3). Full structural analysis of this encapsulation complex was performed by ^{1}H−^{1}H COSY and NOESY experiments at 243 K. The ^{1}H−^{1}H COSY spectrum enabled the assignment of the combinations of splitting patterns of the inner and outer protons of methylene bridges (H^{aA}−H^{bA} and H^{aB}−H^{bB}) as shown in Figure S3. Aromatic protons of H^{fA}, H^{gA}, and H^{hA} were also identified by correlations in the ^{1}H−^{1}H COSY spectrum. The ^{1}H−^{1}H NOESY spectrum provided much structural information (Figure S4). NOE correlations between methyl groups of guest molecule **6** at −1.65 ppm (H$^{k\text{-}in}$) and protons of the methylene bridges (H^{aA}, H^{aB}, H^{bA}, and H^{bB}) strongly supported

Chart 1. Structure of Guest Molecules



Scheme 3. Structure of C_{2h} Symmetrical Guest Encapsulated Hybrid Capsule



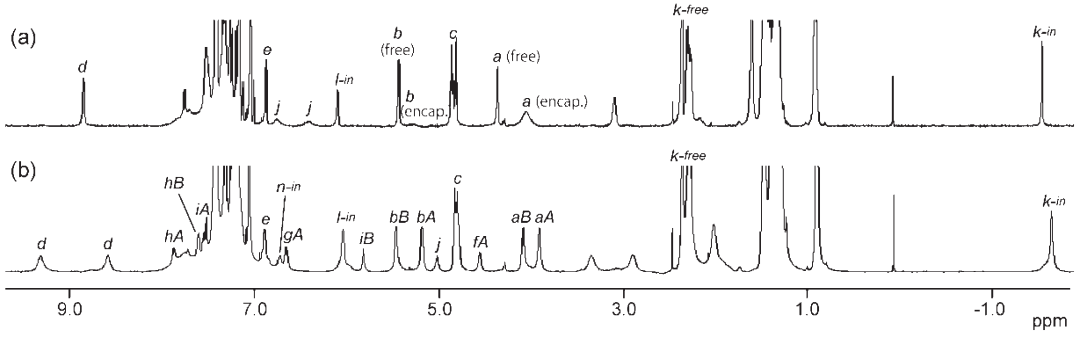


Figure 3. ^{1}H NMR spectra (600 MHz, $CDCl_3$) of [**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] = 4 mM and [**6**] = 40 mM at (a) 298 K, and (b) 243 K.

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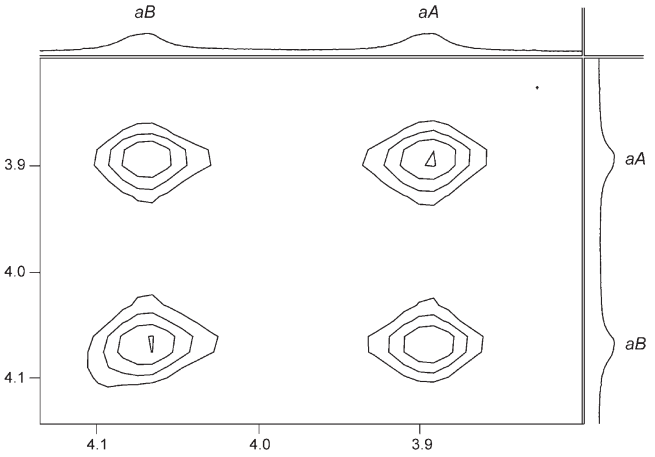

Figure 4. ^{1}H−^{1}H NOESY spectrum of **6**@**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$ (600 MHz, $CDCl_3$, 243 K, mixing time 0.5 s).

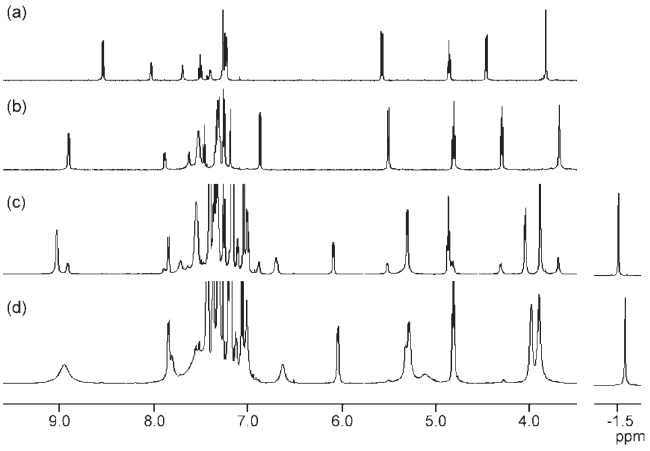

Figure 5. ^{1}H NMR spectra (600 MHz, $CDCl_3$) of (a) **11** alone at 298 K; (b) [**11**] = [Pd(dppp)(OTf)$_2$] = 8 mM at 298 K. (c) [**11**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] = 4 mM and [**6**] = 40 mM at 298 K; at (d) [**11**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] = 4 mM and [**6**] = 40 mM at 243 K.

the encapsulation. Similar NOE correlations between encapsulated guest and cavitand were observed between aromatic protons ($H^{l\text{-}in}$) and methylene bridge (H^{aA}, H^{aB}, H^{bA}, and H^{bB}), or olefinic protons ($H^{n\text{-}in}$) and N−H protons of the 3-carbamoylphenyl groups (H^{j}). The aromatic protons of H^{fA}, H^{fB}, H^{iA}, and H^{iB} appeared at 4.55, 7.23, 7.51, and 5.82 ppm, respectively. Upfield shifts of H^{fA} and H^{iB} indicated that these protons are directed toward the inside of the cavity. NOE correlations of H^{aA}−H^{fA}, H^{bA}−H^{fA}, H^{aB}−H^{iB}, and H^{bB}−H^{iB} supported this assignment. To summarize these assignments, the C_{2h} structure of the encapsulation complex {**6**@[**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$]} shown in Scheme 3 was confirmed. Exchange cross-peaks between H^{aA} and H^{aB} were observed in the ^{1}H−^{1}H NOESY spectrum, originating from the interconversion of the C_{2h} capsule (Figure 4). The rate of the chemical exchange (k value of H^{aA}−H^{aB}) was determined to be 2.44 s^{-1} at 243 K by EXSY analysis. The calculated $\Delta G^{\ddagger}$ of 13.7 kcal/mol corresponds to the activation barrier for the interconversion resulting from rotation of the 3-carbamoylphenyl groups, as shown in Scheme 3. Structurally similar guest molecules, such as *trans*-4,4′-dibromo stilbene (**7**), 1,2-di-*p*-tolylethane (**8**), and 1,2-di-*p*-tolylethyne (**9**), also encapsulated in the hybrid capsule [**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] (Figure S5). Those encapsulation complexes again showed structural regulation, and splits of cavitand protons were observed at lower temperature. A 1:5 mixture of [**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] and 4,4′-diiodobiphenyl (**10**) showed broad signals in the ^{1}H NMR spectrum at 298 K (Figure S5). Because the length along the long axis of **10** is shorter than those of the other guest molecules (**6**−**9**), the exchange between encapsulated **10** and free **10** would be faster than the NMR time scale. The ^{1}H NMR spectrum at 243 K showed encapsulation complex [**10**@**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$], free capsule [**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$], and free guest (**10**) as independent signals (Figure S5). In addition, the encapsulation complex [**10**@**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] at lower temperature was assigned to the C_{2h} structure similar to other encapsulation complexes as mentioned above. The encapsulation complex {**10**@[**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$]} was detected in the FT-ICR-MS as a tetravalent molecular ion peak at m/z 1045.63 (theoretical 1045.60) (Figure S6).

Non-Hydrogen-Bonding Capsular Assembly. An encapsulation experiment using a supramolecular capsule constructed from only metal−ligand coordination bonds to prove the effect of hydrogen bonds for the structural regulation of the hybrid capsule was performed. C_{2v} cavitand **11** with two pyridylethynyl groups and two methyl benzoates served as a contrasting compound to **1**; it lacked hydrogen-bonding ability. Cavitand **11** was synthesized by two palladium-catalyzed cross-coupling reactions of C_{2v} symmetrical dibromo-diboronic acid cavitand **3** (Figure 5a and Supporting Information). A 1:1 mixture of **11** and Pd(dppp)(OTf)$_2$ in $CDCl_3$ showed highly symmetrical ^{1}H NMR signals, corresponding to capsular assembly [**11**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] (Figure 5b). This means that the capsular structure of [**11**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] was constructed only by metal−ligand coordination bonds (Scheme 4). The coordination bonding capsule [**11**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] could encapsulate **6** in the same way as the hybrid capsule [**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] (Figure 5c). For instance, in the ^{1}H NMR spectrum at 298 K, the methyl groups of encapsulated **6** showed an upfield shift (δ = −1.52 ppm; $\Delta\delta$ = −3.88 ppm) because of the ring current effect of the cavitand. Encapsulation complex {**6**@[**11**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$]} maintained its symmetry in the ^{1}H NMR spectrum, even at lower temperature (Figure 5d). The difference between [**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] and [**11**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] clearly indicates the importance of the hydrogen bond for structural alteration of the hybrid capsule through guest encapsulation.

Thermodynamic and Kinetic Properties of Guest Encapsulation. A 1:1 mixture of capsule [**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] and guest **6** showed the encapsulation complex {**6**@[**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$]} and free capsule as separate ^{1}H NMR signals. The binding constant (K) at 263 K, determined from the integration ratios, was estimated to be 214 M^{-1} (K = 76 M^{-1} at 298 K). Variable temperature (VT) NMR data and van't Hoff plot provided the thermodynamic data of the encapsulation (Figure S7). Negative values for both $\Delta H°$ (−3.74 kcal/mol) and $\Delta S°$ (−3.68 cal/mol·K) indicated the exothermic enthalpy driven encapsulation nature of the process. The thermodynamic properties of guest encapsulations are summarized in Table 1. Binding constants of [**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] with other guest molecules (**7**−**10**) were smaller than that with **6**. A slight alteration in size and shape of guest molecules influenced the thermodynamic stabilities of the encapsulation complexes. To our surprise, the binding constants of [**11**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] with **6** were similar to that of [**1**$_2$Pd$_2$(dppp)$_2$(OTf)$_4$] with **6** (K = 192 M^{-1} at 263 K;

Scheme 4. Self-Assembly of Cavitand 11 and Pd(dppp)(OTf)$_2$ and Guest Encapsulation

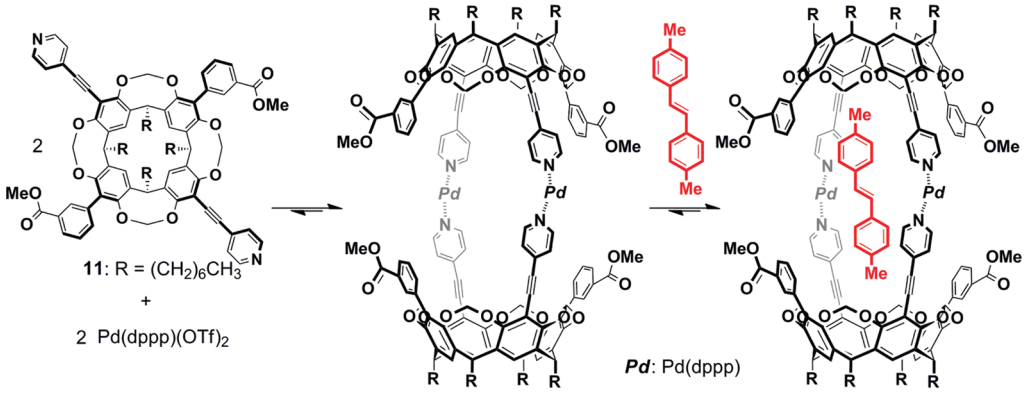

Table 1. Thermodynamic Properties of Guest Encapsulation: Equilibrium Constant between Guest Filled and Free Capsules (K, M^{-1}) and Corresponding Values of Free Energy ($\Delta G°$, kcal/mol), Enthalpy ($\Delta H°$, kcal/mol), and Entropy ($\Delta S°$, cal/mol·K)[a]

capsule	guest	T (K)	K[b]	ΔG_0[c]	ΔH_0[d]	ΔS_0[d]
$\mathbf{1}_2Pd_2(dppp)_2(OTf)_4$	**6**	263	214 ± 5	−2.80 ± 0.01	−3.74 ± 0.06	−3.68 ± 0.29
$\mathbf{1}_2Pd_2(dppp)_2(OTf)_4$	**7**	263	96.5 ± 3	−2.39 ± 0.02	−4.14 ± 0.09	−6.65 ± 0.29
$\mathbf{1}_2Pd_2(dppp)_2(OTf)_4$	**8**	263	39.5 ± 2	−1.91 ± 0.02	−6.08 ± 0.04	−15.9 ± 0.10
$\mathbf{1}_2Pd_2(dppp)_2(OTf)_4$	**9**	263	14.0 ± 1	−1.39 ± 0.01	−3.23 ± 0.14	−7.07 ± 0.63
$\mathbf{1}_2Pd_2(dppp)_2(OTf)_4$	**10**	263	65.5 ± 1	−2.15 ± 0.03	−2.19 ± 0.20	−0.75 ± 0.06
$\mathbf{11}_2Pd_2(dppp)_2(OTf)_4$	**6**	263	192 ± 1	−2.75 ± 0.01	−4.83 ± 0.16	−7.98 ± 0.68

[a] Average of two runs. [b] K = [guest filled capsule]/[free capsule][guest]. [c] $\Delta G° = -RT \ln K$. [d] $\Delta G° = \Delta H° - T\Delta S°$.

$K = 56$ M^{-1} at 298 K). This means that hydrogen bonding of the hybrid capsule has only a small influence on the thermodynamics of the guest encapsulation. The exchange rate constants of guest molecule were calculated from ^{1}H−^{1}H NOESY spectra. Values of the rate constant (k_{-1}) and activation energy ($\Delta G_{-1}^{\ddagger}$) for the release of encapsulated **6** from [$\mathbf{1}_2Pd_2(dppp)_2(OTf)_4$] or [$\mathbf{11}_2Pd_2(dppp)_2(OTf)_4$] at 298 K were determined by EXSY analyses (Figures S8 and S9). The release rate constant (k_{-1}) of guest **6** from the hybrid capsule [$\mathbf{1}_2Pd_2(dppp)_2(OTf)_4$] was 0.034 s^{-1}. On the other hand, the release rate constant (k_{-1}) of guest **6** from the capsule that lacked hydrogen-bonding ability [$\mathbf{11}_2Pd_2(dppp)_2(OTf)_4$] was 5 times faster (0.173 s^{-1}). Approximately 1 kcal/mol difference existed in their activation energies (19.4 kcal/mol for [$\mathbf{1}_2Pd_2(dppp)_2(OTf)_4$], 18.5 kcal/mol for [$\mathbf{11}_2Pd_2(dppp)_2(OTf)_4$]). Hydrogen bonding of the hybrid capsule strongly influenced the kinetics of in/out guest exchange.

CONCLUSIONS

We have demonstrated that 4-pyridylethynyl and 3-carbamoylphenyl bound C_{2v} symmetrical cavitand and divalent palladium complexes self-assemble into a hybrid supramolecular capsule via both metal−ligand coordination bonds and hydrogen bonds. Encapsulations of appropriate guest molecules were identified. Structural alteration of the hybrid capsule was observed through guest encapsulation. The C_{2h} structure of the encapsulation complex was confirmed by NMR analysis. The hydrogen bonding of the hybrid capsule has only a small influence on the thermodynamic properties of guest encapsulation. In marked contrast, the kinetic properties of guest encapsulations change, depending on the presence or absence of hydrogen-bonding moieties in the capsule.

EXPERIMENTAL SECTION

General. Chemicals and solvents required were obtained from commercial suppliers. ^{1}H, ^{13}C, and 2D NMR spectra were recorded on a JEOL JNM-ECA600 spectrometer. Mass spectra were measured on a JMS-T100LC AccTOF (JEOL) or a solariX FT-ICR-MS (Bruker Daltonik GmbH) spectrometer.

*Dibromo-bis(3-cyanophenyl) Cavitand (**4**).* A mixture of cavitand **3** (3.50 g, 2.98 mmol), 3-bromobenzonitrile (2.17 g, 11.9 mmol), $PdCl_2(PPh_3)_2$ (544 mg, 0.77 mmol), $AsPh_3$ (913 mg, 2.98 mmol), and Cs_2CO_3 (7.77 g, 23.8 mmol) in 1,4-dioxane (90 mL) and H_2O (9.0 mL) was refluxed for 3 days under an argon atmosphere. The reaction mixture was concentrated under reduced pressure, and then H_2O and EtOAc were added. The separated organic layer was washed with H_2O and brine successively and dried over Na_2SO_4. After removal of solvent, the crude mixture was purified by column chromatography (SiO_2 EtOAc/hexane = 1/20). The desired product **4** was obtained as a pale yellow solid (1.96 g, 51% yield).

Mp 129 °C; ^{1}H NMR ($CDCl_3$) δ 0.90 (t, J = 6.9 Hz, 12H), 1.28−1.46 (m, 40H), 2.25−2.29 (m, 8H), 4.28 (d, J = 7.6 Hz, 4H), 4.84 (t, J = 8.2 Hz, 4H), 5.58 (d, J = 7.6 Hz, 4H), 7.16 (s, 2H), 7.23 (s, 2H), 7.28 (d, J = 7.6 Hz, 2H), 7.40 (s, 2H), 7.53 (d, J = 7.9 Hz, 2H), 7.65 (d, J = 7.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 14.25, 22.80, 27.96, 29.50, 29.84, 30.24, 31.99, 37.50, 99.50, 112.77, 113.33, 118.59, 119.12, 121.16, 127.90, 129.21, 131.27, 133.64, 134.14, 135.47, 138.88, 139.39, 152.31, 152.46; HRMS (ESI, M + Na$^+$) calcd for $C_{74}H_{84}Br_2N_2NaO_8$: 1309.4492; found 1309.4518.

*Bis(4-pyridylethynyl)-bis(3-cyanophenyl) Cavitand (**5**).* A mixture of cavitand **4** (1.24 g, 0.96 mmol), 4-pyridylacetylene (595 mg, 5.77 mmol), $PdCl_2(PPh_3)_2$ (202 mg, 0.29 mmol), and $AsPh_3$ (295 mg, 0.96 mmol) in 1,4-dioxane (32 mL) was refluxed for 3 days under an argon atmosphere. After the same treatment described above, the crude mixture was

purified by column chromatography (SiO_2 EtOAc/hexane = 1/2). The desired product **5** was obtained as a pale yellow solid (602 mg, 47% yield).

Mp 258−259 °C; ^{1}H NMR ($CDCl_3$) δ 0.91 (t, J = 6.9 Hz, 12H), 1.32−1.47 (m, 40H), 2.24−2.35 (m, 8H), 4.39 (d, J = 6.9 Hz, 4H), 4.85 (t, J = 7.9 Hz, 4H), 5.61 (d, J = 6.9 Hz, 4H), 7.23 (d, J = 6.2 Hz, 4H), 7.25 (s, 2H), 7.26 (s, 2H), 7.29 (d, J = 7.6 Hz, 2H), 7.40 (s, 2H), 7.54 (t, J = 7.6 Hz, 2H), 7.66 (d, J = 7.6 Hz, 2H), 8.56 (d, J = 6.2 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 14.25, 22.80, 27.96, 29.50, 29.83, 30.05, 31.73, 31.99, 36.92, 85.62, 94.86, 99.44, 112.22, 112.77, 118.61, 121.00, 121.37, 125.58, 127.94, 129.30, 130.90, 131.28, 133.55, 135.55, 138.58, 138.97, 150.00, 152.49, 155.77; HRMS (ESI, M + Na^+) calcd for $C_{88}H_{92}N_4NaO_8$: 1355.6813; found 1355.6832.

*Bis(4-pyridylethynyl)-bis(3-carbamoylphenyl) Cavitand (**1**).* A mixture of cavitand **5** (630 mg, 0.47 mmol) and KOH (2.65 g, 47.2 mmol) in 1,4-dioxane (13 mL), H_2O (6.0 mL), and EtOH (4.0 mL) was refluxed for 2 days under an argon atmosphere. After the same treatment described above, the crude mixture was recrystallized from EtOH. The desired product **1** was obtained as a pale yellow solid (340 mg, 53% yield).

Mp 151−152 °C; ^{1}H NMR ($CDCl_3$) δ 0.91 (t, J = 7.2 Hz, 12H), 1.29−1.49 (m, 40H), 2.25−2.35 (m, 8H), 4.44 (d, J = 6.9 Hz, 4H), 4.85 (t, J = 7.9 Hz, 4H), 5.67 (d, J = 6.9 Hz, 4H), 5.59 (brs, 2H), 6.11 (brs, 2H), 7.22 (d, J = 5.5 Hz, 4H), 7.25 (s, 2H), 7.26 (s, 2H), 7.35 (d, J = 7.6 Hz, 2H), 7.51 (t, J = 7.6 Hz, 2H), 7.53 (s, 2H), 7.75 (d, J = 7.6 Hz, 2H), 8.53 (d, J = 5.5 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 14.27, 22.82, 28.02, 29.53, 29.87, 30.11, 32.01, 36.92, 85.98, 94.64, 99.49, 112.19, 120.32, 121.41, 125.62, 126.11, 128.72, 129.02, 129.33, 131.12, 133.11, 135.03, 138.54, 138.66, 149.92, 152.62, 155.79, 159.73, 168.64; HRMS (ESI, M + Na^+) calcd for $C_{88}H_{96}N_4NaO_{10}$: 1391.7024; found 1391.7010.

■ ASSOCIATED CONTENT

Supporting Information. Synthetic procedures and spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

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