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Hybrid Cavitand Capsule with Hydrogen Bonds and Metal−Ligand Coordination Bonds: Guest Encapsulation with Anion Assistance

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The rational design of molecules can produce nanoarchitectures via self-assembly. Much attention has been paid in recent years to research on self-assembled supramolecular capsules that provide an isolated nanocavity.[1] Encapsulated guest molecules can show unique behavior, e.g., stabilization of labile chemicals,[2] acceleration of chemical reactions,[3] and emergence of novel isomerisms.[4] Controllable encapsulation and release of a guest molecule still remains an important subject. A hybrid capsule constructed from several types of bonds with different strengths has advantages for controlled encapsulation because the encapsulation kinetics can be governed by association and dissociation of weaker bonds while keeping the capsule structure through the stronger bonds. Many widely investigated supramolecular capsules are composed of a functionalized C_{4v} symmetry cavitand.[1b,5−7] Reduction of the symmetry and introduction of multifunctional groups are keys to the construction of a hybrid capsule. Although some cavitands with reduced symmetry involving their metal coordinated aggregates have been reported,[8,9] multifunctional groups introduced onto the cavitand are very rare. In this paper, we report the synthesis of a C_{2v}-cavitand having both hydrogen bonding sites and metal-coordination sites. The cavitand forms a hybrid capsule in the presence of a platinum complex, and a neutral guest molecule is encapsulated with the assistance of an anion.

A C_{2v}-symmetry cavitand **1** having two octyl-ureide parts as hydrogen-bonding sites and two pyridylethynyl parts as ligands for coordination bonds was designed (Figure 1). Cavitand **1** was synthesized in six steps from a tetrabromo cavitand.[10] Preparation of a diboronic acid cavitand using Sherburn's procedure[8d] and two palladium-catalyzed cross-coupling reactions were key steps in the synthesis. The structure of cavitand **1** was confirmed by ^{1}H and ^{13}C NMR and ESI-MS spectra.

The ^{1}H NMR spectrum of a 1:1 mixture of **1** and Pt(dppp)(OTf)$_2$ (**2**) in CDCl$_3$ showed a new set of signals, indicative of a single highly symmetrical species, the hydrogen bond and metal−ligand coordination bond intermingled capsule **3** (Figure 2b vs 2a). The pyridyl α-proton (H$_a$) of **3** was shifted downfield by 0.35 ppm, and the pyridyl β-proton (H$_b$) and the inner (H$_c$) and outer (H$_d$) protons of the methylene bridge were shifted upfield by 0.37, 0.12, and 0.15 ppm, respectively, relative to those of free **1**. From DOSY experiments, the smaller diffusion coefficient of **3** ($D = (6.46 \pm 0.18) \times 10^{-10}$ m^2 s^{-1}) compared with that of **1** ($D = (8.39 \pm 0.27) \times 10^{-10}$ m^2 s^{-1}) also supports the discrete capsular structure.[11,12] The intermolecular hydrogen bond of ureide causes a broadening of the signals of the ureic N−H protons; therefore those signals could not be identified. Adding DMSO-d_6 to the CDCl$_3$ solution of **3** weakened those hydrogen bonds, leading to the appearance at 5.9 and 7.7 ppm of new signals assignable to the ureic N−H protons; however, all of the signals of **3** remained unchanged.[12] A 2:1 mixture of **1** and **2** showed sets of signals of capsule **3**, free **1**, and partially coordinated product in the ^{1}H NMR spectrum.[12] A broad and complicated ^{1}H NMR spectrum was observed in a 1:2 mixture of **1** and **2**.[12] The ^{1}H NMR spectrum of **3** in CDCl$_3$ or CD$_2$Cl$_2$ at 253 K showed a new set of signals around 0−1 ppm, which were assigned as alkyl groups of ureides by a 2D-NOESY experiment.[12] The results show that some parts of the alkyl groups of ureides penetrated into the cavity of **3**. The appearance of new signals in the upfield region relative to the original triflate signal in the ^{19}F NMR spectrum of the palladium analogue of **3** at 193 K indicated that the remaining space is filled with triflate ion.[12,13]

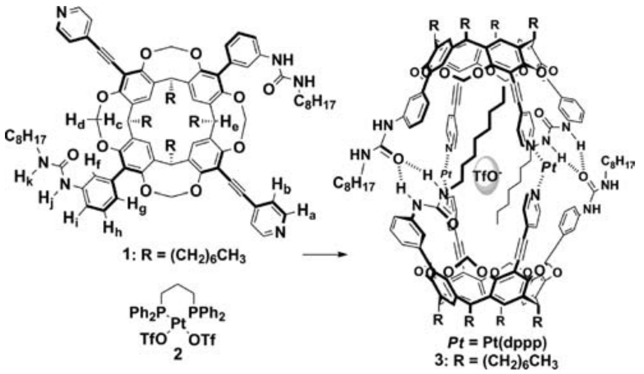

Figure 1. Structures of C_{2v}-symmetry cavitand **1** and self-assembled hybrid capsule **3**.

Encapsulation of triflate ion and penetration of alkyl chains of ureides strongly stabilized the capsular structure; consequently, encapsulation of a neutral guest molecule was not observed. We consider that encapsulation of a suitable neutral guest would be brought about by ejection of the alkyl chains from the cavity. Turning the phenyl ureide moieties is necessary for this dissolution; however, the turning would also cause dissociation of the intermolecular hydrogen bonds between the ureide groups. Addition of an appropriate anion to connect the ureide groups should compensate for the enthalpy loss and enable external guest encapsulation. New sets of signals were observed in the ^{1}H NMR spectrum concomitant with the disappearance of the signals from the penetrating alkyl groups by adding both tetrabutylammonium triflate (TBAOTf) and 4,4′-diiodobiphenyl (**4**) to the CDCl$_3$ solution of **3** (Figures 2c and 3).[14] The signals were clearly assigned by 2D-COSY and NOESY experiments.[12] Bound guest protons were observed at 6.76 and 7.51 ppm, and these were assigned as α ($\Delta\delta = -0.99$ ppm) and β ($\Delta\delta = +0.24$ ppm) to the position of iodine, respectively. The NOE correlation between a bound-guest proton and the inner proton of the methylene bridge (H$_c$) strongly indicated guest encapsulation inside the cavity. The ureide groups of the original capsule **3** were directed inward to the cavity. In contrast, these were turned outward from the cavity, accompanying anion binding to the ureide groups and neutral guest encapsulation. The highly upfield-shifted aromatic protons (H$_g$: 5.18 ppm; H$_h$: 6.14 ppm) due to the ring current effect of the cavitand support the

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conformational alteration of the capsule. The outward-pointing ureide groups are too far away to form hydrogen bonds directly, so two ureide groups are connected through one triflate ion. This proposed structure shown in Figure 3 was supported by a CPK molecular modeling study and Vilars' report.[15] Addition of PF_6^-, NO_3^-, and TsO^- ions was also effective in leading to encapsulation of **4**.[12] Titration of a $CDCl_3$ solution of **3** and excess **4** (30 equiv to **3**) with TBAOTs proved that 2 equiv of anions were necessary to complete the encapsulation.[12] A DOSY experiment on a 1:5:5 mixture of **3**, **4**, and TBAOTs showed similar diffusion coefficients ($D = (4.35 \pm 0.17) \times 10^{-10}$ m^2 s^{-1}) for the cavitand part, encapsulated **4**, and two associated TsO^- ions. Halide or acetate ions were not suitable for the encapsulation of **4** because they caused partial dissociation of the N−Pt coordination bonds.[12]

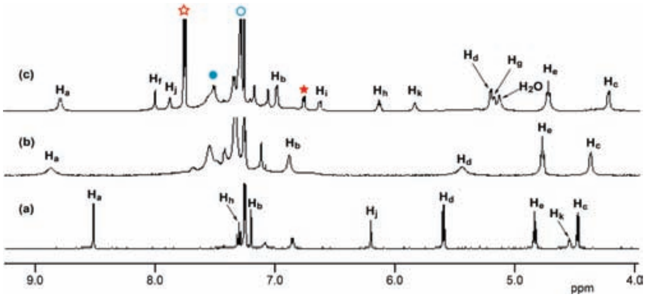

Figure 2. ^{1}H NMR spectra (600 MHz, $CDCl_3$) of (a) **1** alone at 298 K; (b) [**1**] = [**2**] = 4.5 mM at 298 K (capsule **3**); and (c) [**1**] = [**2**] = 4.5 mM and [TBAOTf] = [**4**] = 11.2 mM at 253 K.

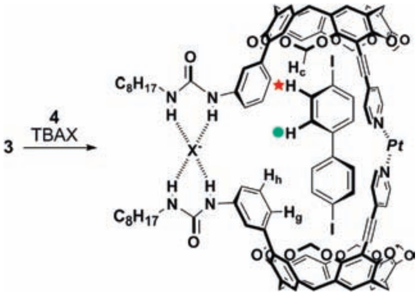

Figure 3. Structure of **4**-encapsulated hybrid capsule **3** with anion assistance.

Chemical exchange between encapsulated **4** and free **4** was confirmed by a 2D-NOESY experiment. The rate constant for guest release was estimated to be $k_{-1} = 0.038$ s^{-1} by EXSY calculation.[12,16] The guest exchange rate became fast upon addition of 20 equiv of TBAOTf ($k_{-1} = 0.064$ s^{-1}) or 70 equiv of DMSO ($k_{-1} = 0.141$ s^{-1}), although their ^{1}H NMR spectra remained almost unchanged. Metal−ligand coordination bonds strongly maintained the capsular structure of **3**, and external additives such as an anion or use of a polar solvent had an effect on the ureide moieties and accelerated the guest exchange. The type of anion influenced the rate of guest exchange. Guest exchange in the presence of $TBAPF_6$ was slightly faster than in the original TBAOTf case; the rate constants for guest release, k_{-1}, was 0.045 s^{-1}. The encapsulation complex with $TBANO_3$ reduced the guest exchange rate ($k_{-1} = 0.011$ s^{-1}). No guest exchange was observed for the TBAOTs-containing encapsulation complex on the NMR time scale.

In conclusion, we have demonstrated that multifunctionalized C_{2v}-cavitand **1** and $Pt(dppp)(OTf)_2$ (**2**) self-assemble into a hybrid capsule **3** through a hydrogen bond and metal−ligand coordination bond. Capsule **3** encapsulates a neutral guest molecule with the assistance of an anion. The kinetics of guest exchange is controllable by the amounts and/or types of anions or other influences such as the polarity of the solvent. Further studies on encapsulation by the capsule are currently underway in our laboratory.

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

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(13) Triflate ion would also be encapsulated in **3**; however, in−out exchange of triflate ions may be faster than that of the palladium analogue of **3**. Consequently, an averaged signal was observed in the ^{19}F NMR spectrum even at 193 K.
(14) The ^{1}H NMR signals of **3** in $CDCl_3$ did not change upon individual addition of **4** or TBAOTf.
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