Anion Recognition

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Inclusion of Anionic Guests inside a Molecular Cage with Palladium(II) Centers as Electrostatic Anchors**

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Anion recognition and binding play an important role in biological processes, such as ATP metabolism and transmembrane transport of anions to regulate osmotic pressure in the cell. Furthermore, anion recognition has emerged to be a major area of supramolecular chemistry, as exemplified by systems such as selective anion sensors and anion-templated molecular architectures.[1]

In supramolecular assemblies such as nanoscopic cages and capsules,[2] metal ions often act as 'glue' for the spontaneous but directed assembly of organic building blocks.[3] In some cases, coordinatively labile sites of metal centers provide a platform for direct binding to guest species through ligand-exchange reactions.[1] In contrast, positively charged metal complexes can also interact with anionic species through pure electrostatic interactions.

Accordingly, the precise positioning of such metal centers within molecular assemblies that have a hollow space would allow for specific attractive interactions with anionic guest molecules. In the system presented herein, two Pd^{II} ions are bound by four bis(monodentate) ligands to give stable square-planar complexes of the d^8 Pd^{II} ions. The two Pd^{II} centers are spaced 1.7 nm apart and are directly linked by the rigid, banana-shaped ligands, thus allowing this construct to quantitatively bind one dianionic guest by coulombic interactions (Figure 1 a).[4]

The synthesis of the ligands is based on consecutive cycloaddition reactions to build up the backbone structure **3** from norbornene **1** and oxadiazole **2**, as reported by Warrener et al. (Figure 1 b).[5] A further Diels–Alder reaction with subsequent oxidative aromatization provided tetraester **4**, which was converted to ligand **5** in high yield. Upon heating the ligand with $[Pd(CH_3CN)_4](BF_4)_2$ in acetonitrile, the cage compound **6** formed quantitatively, as shown by the ESI mass spectrum and the NMR spectra (Figure 3 and the Supporting Information). In the ^1H NMR spectrum, two of the four pyridine signals are shifted downfield, as can be assumed for the complexation of the double positively charged Pd^{II} ions,

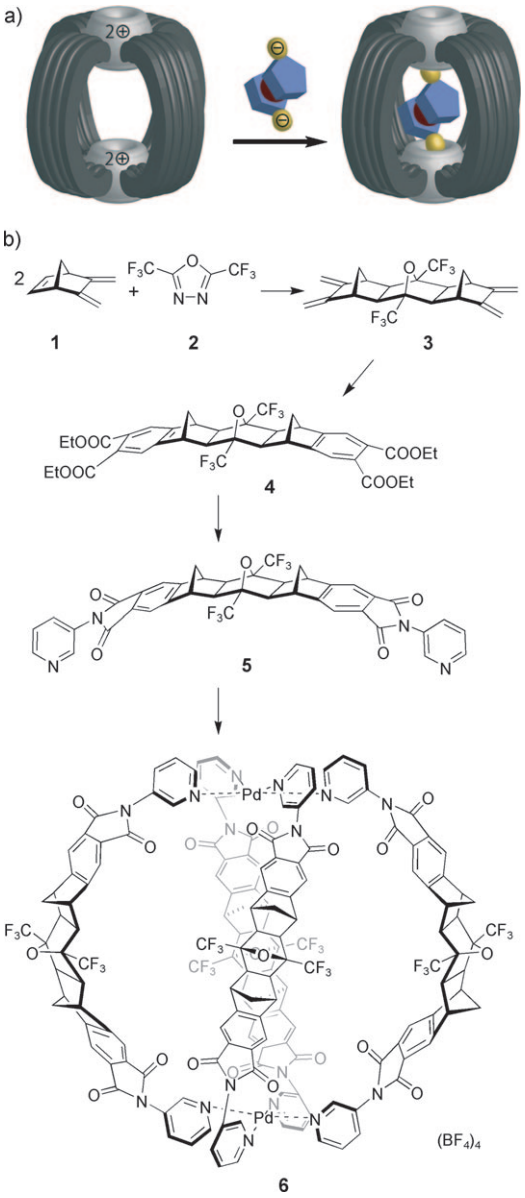

Figure 1. a) Representation of the binding of a guest, 1,1′-ferrocene bis(sulfonate), inside the cage formed by two Pd^{II} centers (light gray) and four rigid, banana-shaped ligands (dark gray). b) Synthesis of cage **6** (see the Supporting Information).

and two resonances are shifted upfield, which is most likely due to the position of these protons relative to the aromatic planes of the neighboring pyridine rings. An EXSY NMR experiment with a 1:4 mixture of the cage and the free ligand at 293 K showed no cross-peaks between the corresponding

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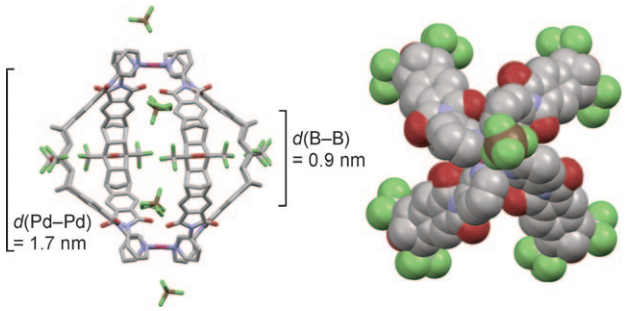

Figure 2. Side view (left) and space-filling model of the top view (right) of the crystal structure of **6**. Solvent molecules are omitted for clarity. C gray, O red, N blue, F green, Pd fuchsia, B brown.

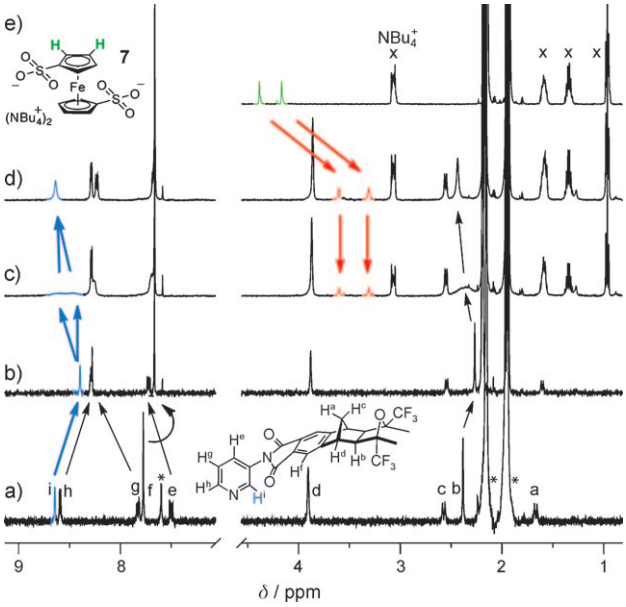

Figure 3. ^{1}H NMR spectra (500 MHz, CD_3CN, 293 K) of a) ligand **5**, b) cage **6**, c) **6** with 0.5 equiv **7**, d) **6** with 1 equiv **7**, and e) **7**. * = water and solvent.

signals of the coordinated and uncoordinated ligands; thus a slow exchange of the free and bound ligands can be anticipated (see the Supporting Information). The hydrodynamic radius of the molecule in solution was estimated to be about 1.1 nm (diffusion coefficient $D = 5.0 \times 10^{-10}\ m^2 s^{-1}$) by ^{1}H DOSY NMR spectroscopy, which is in good agreement with the structure of the 2 nm ball-shaped cage determined by single-crystal X-ray analysis (Figure 2).

The number and multiplicity of the signals in the solution ^{1}H NMR spectrum indicate a D_{4h} cage symmetry, which is probably the averaged result of a fast flipping mechanism between two degenerated conformations, each with C_{4h} symmetry. In the crystal, all of the cages are fixed in this C_{4h} symmetry. The stiff, banana-shaped structure of the ligands, which assembles around the two metal ions, generates a hollow space that is amenable to guest incorporation through the four large portals. Each metal ion is flanked by two counteranions. In total, two BF_4^- ions are located inside the cavity (two different arrangements were found in the solid state, see the Supporting Information) and two outside the cage. We found that the inner counterions can be selectively and quantitatively exchanged in solution by guest molecules that contain two negatively charged sulfonate groups at a suitable distance that matches the BF_4^-–BF_4^- distance found inside one of the two cages in the unit cell (d(B–B) = 0.9 nm). A screening of possible guests by molecular modeling studies yielded the known compound 1,1′-ferrocene bis(sulfonate) **7** as a potential candidate, which showed a maximal S–S distance of 0.8 nm.[6] Indeed, upon titration of a 0.70 mM solution of the cage compound **6** in CD_3CN with a solution of bis(tetrabutylammonium)-1,1′-ferrocene bis(sulfonate) **7**, the signals of the cage shift until one equivalent of the guest is added (Figure 3).

Most indicative is the signal at $\delta = 8.41$ ppm, which corresponds to the inward-pointing hydrogen atoms attached to the pyridine rings (H^i, blue in Figure 3). After 0.5 equivalents of the guest molecule were added, this signal split up into two broadened resonances, which indicated uptake of the guest inside half of the available cage molecules. The signal broadening might indicate an exchange between the 'filled' and the 'empty' cages on the NMR timescale.

Upon addition of one equivalent of 1,1′-ferrocene bis(sulfonate), the inclusion complex was quantitatively formed, as indicated by the sharpening of the signals in the NMR spectrum. Additionally, the guest signals were identified in the NMR spectrum at $\delta = 3.31$ and 3.60 ppm (Figure 3, red), and thus undergo a significant upfield shift with respect to the signals of the free guest molecule ($\delta = 4.17$ and 4.39 ppm, Figure 3, green) at the same concentration because of the magnetic shielding of the surrounding cage structure.[7] A comparison of the ^{1}H DOSY NMR spectra of the free and encapsulated guest likewise supports the quantitative formation of the inclusion complex (see the Supporting Information).

Finally, the redox potential of the ferrocene guest **7** was probed in a cyclic voltammetry experiment. The encapsulated guest molecule shows an anodic shift of 37 mV for $E_{1/2}(Fe^{II/III})$ with respect to free 1,1′-ferrocene bis(sulfonate), thus implying that the reduced state of the guest **7** is stabilized when it is included within the cage (Figure 4). The observation of an anodic shift is in good agreement with a previous report on the interaction of **7** with a cationic polymer,[8] and a similar encapsulation study by Fujita and co-workers.[7a] The result

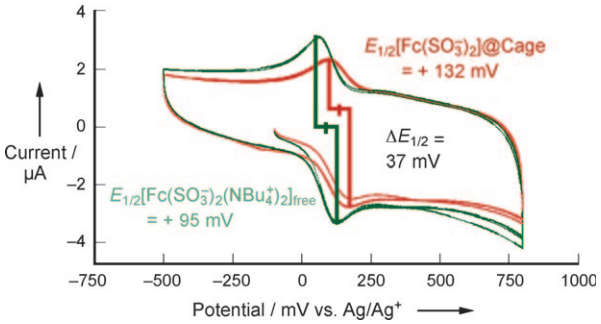

Figure 4. Cyclic voltammograms of the free (green) and encapsulated guest (red) at 293 K, 0.15 mM, 0.1 M TBAP, scan rate 0.1 Vs^{-1}.

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can be explained by the electron-withdrawing effect of the positively charged Pd^{II} complexes that make up the cage.

The system presented here is topologically similar to the so-called molecular gyroscopes.[9] We believe that the binding principle that underlies our system will prove versatile in different areas of nanoassembly since the ligand synthesis is simple, the formation of the cage is spontaneous and quantitative under the given conditions, a template is not required, and the aromatic sulfonate guests are easily accessible. The binding of the guest molecules has proven to be quick, quantitative, and easily observable by NMR spectroscopy and mass spectrometry.

We imagine that our system will be useful for the construction of higher-order functional nanoassemblies in which various building blocks that contain multiple anionic groups can be joined in a controlled manner. Currently, we are extending this binding mode to generate rotaxanes and higher-order aggregates of individual cage molecules.

Experimental Section

Cage compound **6** was prepared in quantitative yield by heating a mixture of the ligand **5** (2.1 mg, 2.8 μmol) and a solution of $[Pd(CH_3CN)_4](BF_4)_2$ (1.4 μmol, 93 μL of a 15 mM stock solution in CD_3CN) in CD_3CN (930 μL) at 70 °C for 30 min in a closed vial to yield 1.0 mL of a 0.70 mM solution of **6**. Single crystals suitable for X-ray crystallographic analysis were grown from this solution by slow evaporation of the solvent. CCDC 729445 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

The host–guest complex was formed by titrating a solution of the guest 1,1′-ferrocene bis(sulfonate) **7** (8.75 mM) in CD_3CN into 500 μL of a 0.70 mM solution of cage **6** in CD_3CN in an NMR tube. The NMR spectra were recorded immediately after briefly shaking the solution.

The cyclic voltammograms were measured at a concentration of 0.15 mM analyte and 0.1M tetra(*n*-butyl)ammonium perchlorate (TBAP) in CH_3CN with a scan rate of 0.1 Vs^{-1} (ALS-CH Instruments, Model 630 A). The formation of the host–guest complex under the conditions required for the electrochemical analysis was confirmed by ^1H NMR spectroscopy.

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