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Encapsulation of Cationic Ruthenium Complexes into a Chiral Self-Assembled Cage

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A chiral supramolecular assembly encapsulates the two cationic ruthenium sandwich complexes $[\mathrm{CpRu}(\eta^6\text{-}\mathrm{C_6H_6})]^+$ and $[\mathrm{CpRu}(p\text{-cymene})]^+$. The host–guest complexes $\mathrm{K_{11}}[\mathrm{CpRu}(\eta^6\text{-}\mathrm{C_6H_6}) \subset \mathrm{Ga_4L_6}]$ (**2**) and $\mathrm{K_{11}}[\mathrm{CpRu}(p\text{-cymene}) \subset \mathrm{Ga_4L_6}]$ (**3**) were characterized by one- and two-dimensional NMR techniques as well as by electrospray mass spectrometry. Encapsulation of the prochiral complex $[\mathrm{CpRu}(p\text{-cymene})]^+$ by the chiral host renders enantiotopic protons diastereotopic as evidenced by ^{1}H NMR spectroscopy.

The control of reactivity at a catalytic metal center is often achieved by tailoring the ligands coordinated to the metal. Sophisticated chiral ligands or chiral additives can be utilized to achieve stereocontrol in metal catalyzed transformations.[1,2] However, another way to achieve stereocontrol is to regulate the secondary coordination sphere by using the well-defined environment of a chiral supramolecular host. Thus the encapsulation of transition metal catalysts can lead to a new class of molecular reactors with catalytic properties determined by both catalyst and host. For example, enantioselective reactions could be envisioned to proceed with an achiral catalyst inside a chiral cavity. The use of supramolecular structures as molecular reaction vessels for organic transformations has been reported,[3−6] and only recently a few papers on encapsulation of organometallic complexes into preformed cavities have been published.[7−10]

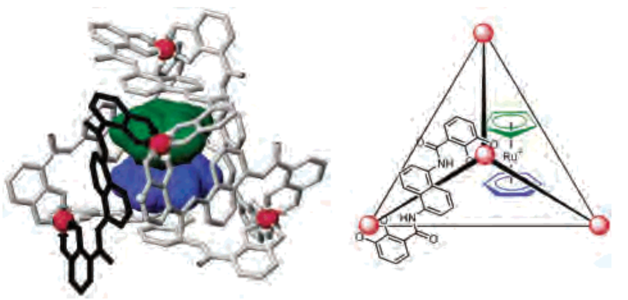

Figure 1. View down the 3-fold axis of the $\mathrm{Ga_4L_6}$ tetrahedral assembly, encapsulating $[\mathrm{CpRu}(\eta^6\text{-}\mathrm{C_6H_6})]^+$. Six bis-bidentate catechol amide ligands span the edges of the tetrahedron, and the $\mathrm{Ga^{3+}}$ atoms are located on the vertices (red spheres). Left: CAChe model, energy minimized (MM3) with one ligand highlighted in black. Right: Schematic; five of the six ligands are drawn as lines for clarity.

In pursuing encapsulated organometallic chemistry it is necessary to identify suitable substrates whose reactivity, size, and shape are compatible with the supramolecular assembly. Cationic ruthenium catalysts are used for a wide variety of C−C bond formation reactions. Examples of such reactions include alkene−alkyne coupling and formation of 1,3-dienes from allenes.[11] Since $\mathrm{Cp_2Fe^+}$ and $\mathrm{Cp_2Co^+}$ were found to encapsulate in the $\mathrm{M_4L_6}$ assembly,[12] we turned our attention to similarly hydrophobic cationic ruthenium complexes. Here we report the encapsulation of the organometallic complexes $[\mathrm{CpRu}(\eta^6\text{-}\mathrm{C_6H_6})]^+$ (Figure 1) and $[\mathrm{CpRu}(p\text{-cymene})]^+$ into a chiral host, constructed from achiral components.

The host−guest chemistry of tetrahedral $\mathrm{M_4L_6}$ assemblies ($\mathrm{M} = \mathrm{Ga^{3+}}, \mathrm{Al^{3+}}, \mathrm{Fe^{3+}}$; L = 1,5-bis(2′,3′-dihydroxybenzamido)naphthalene), composed of simple metal and ligand components, has been investigated.[13] The hosts are water soluble but have hydrophobic cavities into which they can

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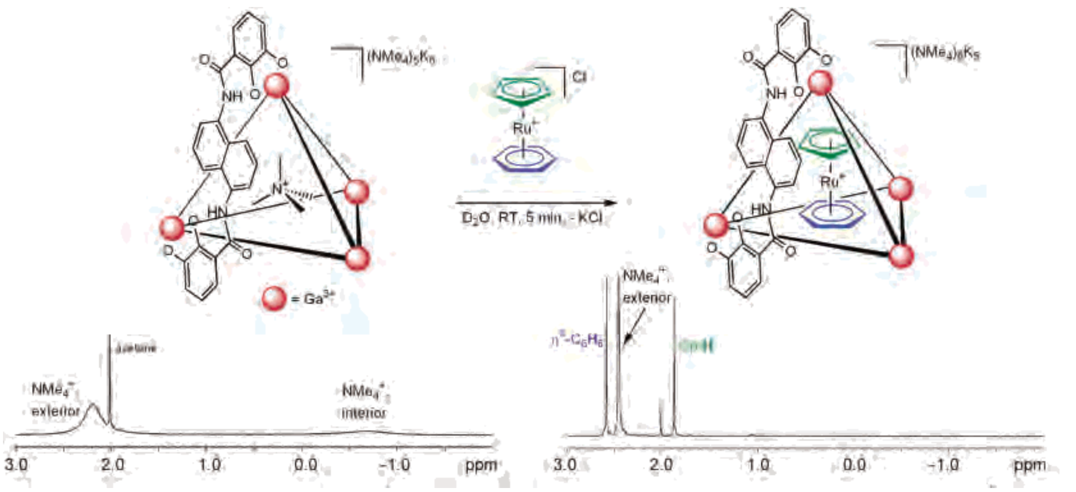

Figure 2. Guest exchange reaction of NMe_4^+ for $[CpRu(\eta^6\text{-}C_6H_6)]^+$. Left: $K_6(NMe_4)_5[NMe_4 \subset Ga_4L_6]$ before the addition of $[CpRu(\eta^6\text{-}C_6H_6)]^+$. Right: Five minutes after the addition of $[CpRu(\eta^6\text{-}C_6H_6)]^+$; the guest exchange is complete.[16]

bind a variety of cationic guest molecules. The strength of guest binding strongly depends on the size of the guest; NMe_4^+ for example has a low binding constant and is easily replaced by other alkylammonium cations.[14] The weak binding is reflected in the ^1H NMR spectrum of $K_6(NMe_4)_5[NMe_4 \subset Ga_4L_6]$ (**1**; $\subset$ indicates that 1 equiv of NMe_4^+ is encapsulated in the cavity). Due to fast chemical exchange two very broad signals for the NMe_4 protons at 2.21 ppm and −0.70 ppm for exterior and interior NMe_4^+ are displayed, respectively (Figure 2, left).

When 1 equiv of $[CpRu(\eta^6\text{-}C_6H_6)]Cl$ was added to an aqueous solution of **1**, an exchange reaction took place within minutes which was readily apparent in the ^1H NMR spectrum.[15] The signal of the interior NMe_4^+ disappeared, while two new signals for the encapsulated ruthenium complex were observed at 2.60 ppm ($\eta^6\text{-}C_6H_6$) and 1.89 ppm (Cp-H) (Figure 2, right). These signals are shifted significantly to higher field compared to the unencapsulated complex, for which the corresponding signals are displayed at 6.04 and 5.29 ppm.

This upfield shift is indicative of encapsulation and can be attributed to shielding of the naphthalene moiety of the host assembly, illustrating that the guest molecule is in close contact with the host. Further addition of $[CpRu(\eta^6\text{-}C_6H_6)]Cl$ does not lead to an increase of the signals assigned to the encapsulated guest. Instead, two new signals are observed at higher field (4.93 and 4.58 ppm), corresponding to $[CpRu(\eta^6\text{-}C_6H_6)]^+$, which is presumably ion paired to the exterior of the assembly.

Rather than exchanging NMe_4^+ for the ruthenium sandwich complexes, the host assembly can also be synthesized in the presence of these cationic organometallic complexes. Combining 6 equiv of the ligand, 4 equiv of $Ga(acac)_3$, and 1 equiv of sandwich complex in the presence of KOH resulted in the formation of the desired products ($K_{11}[CpRu(\eta^6\text{-}C_6H_6) \subset Ga_4L_6]$, **2**; $K_{11}[CpRu(p\text{-cymene}) \subset Ga_4L_6]$, **3**) as yellow powders in very good yields (93% and 87% respectively).

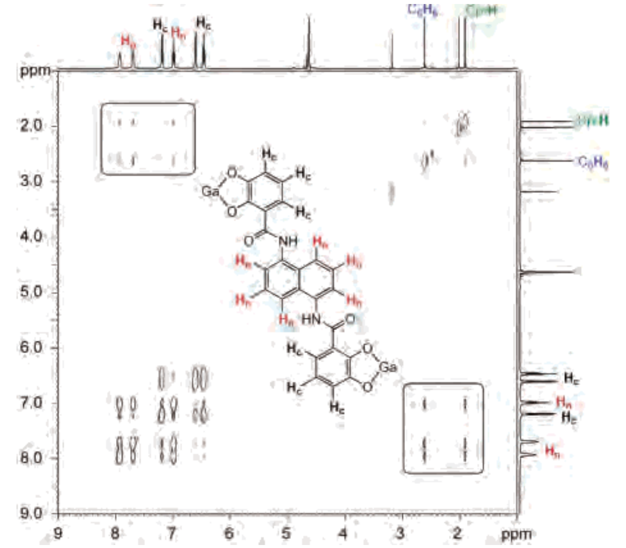

Figure 3. 2D-Gradient NOESY spectrum of **2** illustrating the close proximity of the guest molecule to the naphthalene portion of the ligand backbone (HDO cross-peak deleted for clarity).

Additional evidence for encapsulation is shown in the 2D-NOESY spectrum of **2** (Figure 3). The resonances at 7.91, 7.67, and 6.97 ppm correspond to the naphthalene protons in the ligand backbone (H_n). The cross-peaks between only these resonances and the Cp-H and C_6H_6 resonances of the guest molecule strongly indicate encapsulation.

To probe the effect of the chiral environment on an encapsulated organometallic species, a $[CpRu(p\text{-cymene})]^+$ complex was employed. A significant feature of the corresponding host−guest complex (**3**) is revealed in the ^1H NMR spectrum (Figure 4). The M_4L_6 assemblies contain four metal centers, each of which can adapt either a Δ or Λ configuration. It has been established that only homochiral isomers of the assemblies form, i.e., each assembly is either $\Delta,\Delta,\Delta,\Delta$- or $\Lambda,\Lambda,\Lambda,\Lambda$-configured and does not racemize.[17] Each individual cluster is therefore chiral and the $\Delta,\Delta,\Delta,\Delta$- and $\Lambda,\Lambda,\Lambda,\Lambda$-assemblies are enantiomers. The isopropyl sub-

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(15) $K_6(NMe_4)_5[NMe_4 \subset Ga_4L_6]$ (21.0 mg, 5.93 μmol) was dissolved in 600 μL of D_2O and the solution transferred to an NMR tube. $[CpRu(\eta^6\text{-}C_6H_6)]Cl$ (1.66 mg, 5.93 μmol) was added, and the solution was shaken. The ^1H NMR spectrum was recorded 5 min after the addition.

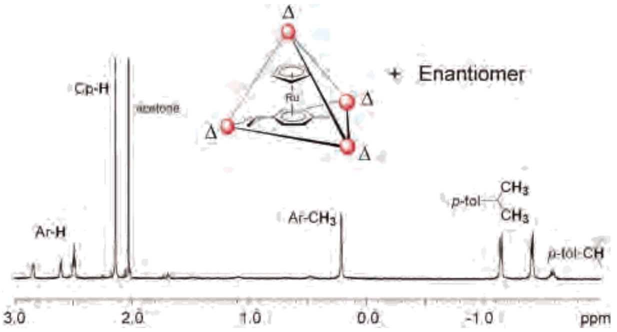

Figure 4. ^1H NMR spectrum of **3**, showing the effect of encapsulation on the prochiral ruthenium complex.

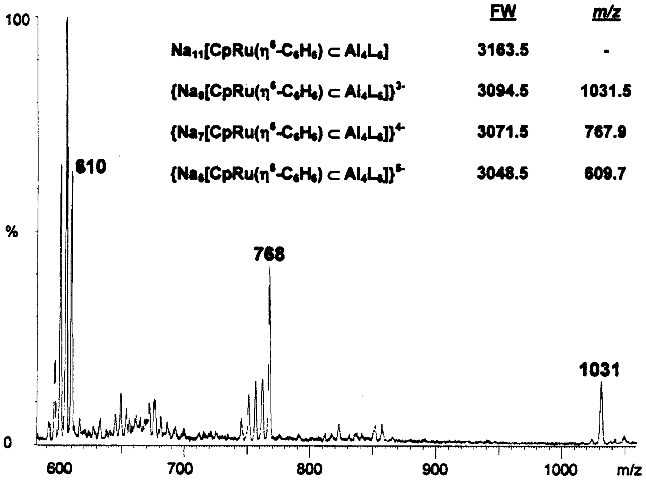

Figure 5. ES(−) mass spectrum of **4**, displaying peaks for the 3^-, 4^-, and 5^- charged complexes.

stituent of the *p*-cymene moiety contains two enantiotopic methyl groups. Upon encapsulation into the chiral cavity these two methyl groups become diastereotopic and distinguishable by ^1H NMR. Two separate signals for the isopropyl methyl groups at −1.15 and −1.41 ppm as well as four separate resonances for the aromatic protons are displayed.

Another important characterization method for these high molecular weight species is mass spectrometry. Under basic conditions, we are able to observe peaks in the electrospray mass spectrum that correspond to the 3^-, 4^-, and 5^- charge states of the host−guest complex. To simplify the isotope distribution patterns, the analogous assemblies, using aluminum and sodium rather than gallium and potassium (both ^{27}Al and ^{23}Na have 100% natural abundance), were synthesized. The products $Na_{11}[CpRu(\eta^6\text{-}C_6H_6) \subset Al_4L_6]$ (**4**) and $Na_{11}[CpRu(p\text{-cymene}) \subset Al_4L_6]$ (**5**) were obtained in good yields, and the mass spectrum of **4** is shown in Figure 5. In addition to the peaks for the 3^-, 4^-, and 5^- charged species a number of peaks of lower molecular weight occur due to H^+/Na^+ exchange. It is significant to note that exchange of $[CpRu(\eta^6\text{-}C_6H_6)]^+$ or $[CpRu(p\text{-cymene})]^+$ for other cations is not observed. Strong binding of these organometallic species within the host cavity renders them an integral assembly component. These data are consistent with the assignment of these materials as tetrahedral M_4L_6 assemblies containing encapsulated ruthenium sandwich complexes.

Attempts to photolyze the encapsulated sandwich complexes in the presence of acetonitrile to yield the catalytically active $[CpRu(MeCN)_3]^+$ only led to recovery of starting material. Whereas the free sandwich complexes readily undergo this transformation,[18] the encased molecules exhibit a different chemical reactivity and appear to be protected from the outside chemical environment.

In expanding the range of organometallic complexes able to encapsulate into the M_4L_6 assemblies described here, the high affinity of the sandwich complexes discussed above for the cavity encouraged us to explore the catalytically active and similarly hydrophobic compounds of the general formula CpRu(diene)Cl. Current investigations in our laboratories with these complexes are underway.

In summary, progress has been made toward the development of organometallic catalysis encapsulated within supramolecular structures. Two organometallic ruthenium complexes, $[CpRu(\eta^6\text{-}C_6H_6)]^+$ and $[CpRu(p\text{-cymene})]^+$, were encapsulated and their reactivity is altered by encapsulation. Due to incorporation of the achiral $[CpRu(p\text{-cymene})]^+$ into a chiral host, the enantiotopic methyl protons become diastereotopic. Future challenges will include identification of a system in which encapsulation does not lead to reduced guest reactivity, but allows for stoichiometric and catalytic reactions to take place inside the chiral vessel. Further, a chiral host might mediate asymmetric transformations with an achiral encapsulated catalyst.

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Supporting Information Available: Experimental procedures and characterization for **2**, **3**, **4**, and **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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