Host–Guest Systems

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Stabilization of Reactive Organometallic Intermediates Inside a Self-Assembled Nanoscale Host**

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Molecular container compounds provide a new space for reaction chemistry, both literally and figuratively, through the encapsulation of smaller guest molecules.[1] The environment of the host interior may be very different from that of the exterior surroundings, resulting in novel patterns of reactivity. In effect, the energetic landscape within a host may be significantly altered from that of the bulk solution, so that what is "unstable" in solution may become "stable" and vice versa. The stabilization of reactive species within the narrow confines of a host cavity is an intriguing functional property of covalent and self-assembled hosts and has been observed in a number of different systems. Both kinetic and thermodynamic factors can contribute to this stabilization: the tight host portals may kinetically inhibit guest escape and subsequent reactivity, or strong host–guest binding may stabilize an otherwise reactive structure.[2] Cram and Warmuth have used hemicarcerands to isolate the highly unstable intermediates cyclobutadiene, *o*-benzyne, and cycloheptatetraene by preventing them from dimerization or reaction with bulk-phase species.[3–5] Fujita and co-workers observed the formation of an otherwise nonisolable cyclic silanol trimer within the cavity of their M_6L_4 supramolecular host.[6,7] Rebek et al. were able to inhibit homolytic bond cleavage of benzoyl peroxide by encapsulation, even at elevated temperatures for prolonged periods of time.[8] All of these examples involved reactive organic species. Herein, we report the stabilization of reactive organometallic intermediates in aqueous solution through molecular encapsulation. This result augurs well for the further development of encapsulated organometallic chemistry.

Over the past years, we have investigated the properties and utilities of an M_4L_6 tetrahedral assembly constructed from metal and ligand components.[9,10] In this structure, the metal atoms are located on the vertices of the tetrahedron and the six bis(bidentate) catechol amide ligands span the edges (Figure 1). The tetrahedron assembles exclusively as the homochiral stereoisomer (that is, ΔΔΔΔ or ΛΛΛΛ), with its chirality generated by the tris(bidentate) chelation of each of the four metal centers. The metal–ligand assembly has provided rich host–guest chemistry; it can bind a large variety of monocationic guest molecules, which range from simple alkyl ammonium ions[11,12] to cationic organometallic species, into its hydrophobic cavity.[13] Among the organometallic complexes encapsulated by the supramolecular host are ruthenium sandwich complexes and half-sandwich complexes of the general formula $[Cp/Cp^*Ru(diene)(H_2O)]^+$ (Cp = cyclopentadiene, Cp* = pentamethylcyclopentadiene).[14,15] The tetrahedron has also demonstrated its ability to stabilize reactive organic intermediates: a water-sensitive cationic phosphane–acetone adduct—previously synthesized only under anhydrous conditions—was stabilized in aqueous solution for several weeks.[16,17]

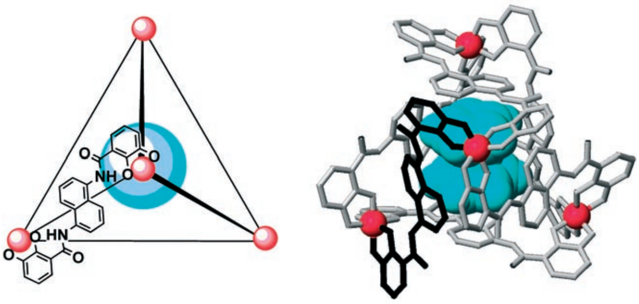

Figure 1. Left: A schematic representation of the $[G\subset M_4L_6]$ supramolecular tetrahedral assembly, with a view down the C_3 axis. One ligand is drawn and the other ligands are represented as sticks for clarity. Right: CAChe model of $[CpRu(\eta^6\text{-}C_6H_6)\subset Fe_4L_6]^{11-}$, with the guest molecule shown in a space-filling view; the hydrogen atoms are omitted for clarity.

The high binding affinity of half-sandwich complexes in the M_4L_6 host prompted us to investigate the structurally related [CpRuCl(cod)] (cod = 1,5-cyclooctadiene), a catalyst employed in many C–C bond-forming reactions, as a guest precursor.[18] In polar media, this complex should undergo halide dissociation to form the cationic solvated species. Under the previously established biphasic reaction conditions,[15] an organometallic complex could be quantitatively encapsulated; however, to our surprise the resulting product did not appear to be $[CpRu(cod)(H_2O)\subset Ga_4L_6]^{11-}$. The ^1H NMR spectrum of the host–guest complex displays an apparent doubling of all expected signals (Figure 2).[19] For example, two resonances for the encapsulated Cp fragment at $\delta = 2.07$ and 2.04 ppm are detected; also, all the signals for the cod moiety of the guest molecule are displayed twice. The 2D TOCSY spectrum reveals that two different species with 12 cod resonances each are encapsulated, in an approximate 1:1 ratio, as two independent spin systems are observed (see the

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Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

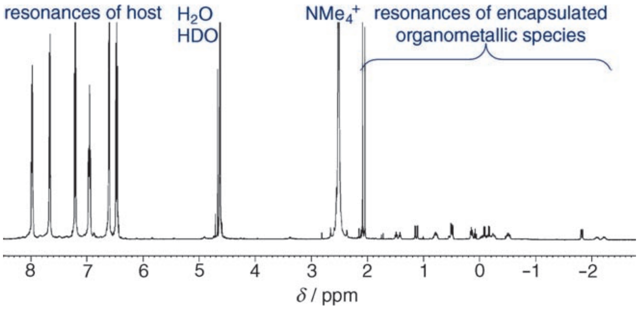


Figure 2. ^{1}H NMR spectrum of $[\mathbf{1}\subset Ga_4L_6](NMe_4)_5K_6$.

Supporting Information). In addition, the electrospray mass spectrum did not corroborate the formation of $[CpRu(cod)(H_2O)\subset Ga_4L_6]^{11-}$ either. Only peaks that correspond to the host–guest complex $[CpRu(cod)\subset Ga_4L_6]^{11-}$ were observed, implying that the metal–ligand assembly incorporated merely the desolvated $[CpRu(cod)]^+$ fragment. Although no such 16-e^- species has been isolated previously, the cluster cavity is known to stabilize reactive species that would not be able to exist outside of the assembly,[16] and the supramolecular structure might function as a very large and non-coordinating counterion.

To explore this possibility, we attempted to prepare the complex $[CpRu(cod)]BF_4$ by treating $[CpRuCl(cod)]$ with $AgBF_4$ in CH_2Cl_2. Unexpectedly, the dominant reaction product turned out to be the novel complex [CpRu(*cis*-1,3,7-octatriene)]BF_4 (**1**-BF_4). This compound showed a complex ^{1}H NMR spectrum with one Cp resonance and 12 different cod signals (Figure 3, top). When the spectrum of **1**-BF_4 is compared with the spectrum of the previously isolated host–guest complex (Figure 3, bottom), it becomes apparent that **1** is the encapsulated guest. Each resonance of **1** is displayed twice in the spectrum of the host–guest complex, confirming that **1** is chiral and its placement into the chiral cavity leads to the formation of two diastereomeric host–guest species.

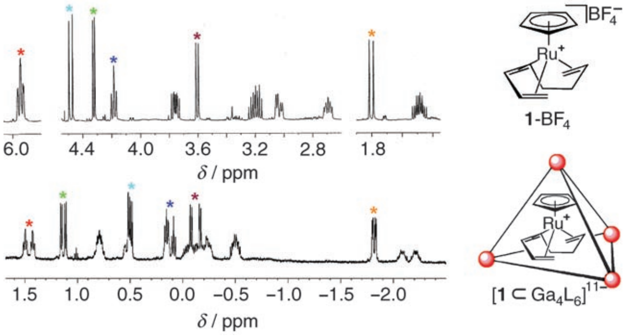


Figure 3. Comparison of the ^{1}H NMR spectra of **1**-BF_4 (top) and $[\mathbf{1}\subset Ga_4L_6](NMe_4)_5K_6$ (bottom). Encapsulation of the chiral ruthenium complex **1** into the chiral cavity leads to the formation of two diastereomers in a 1:1 ratio. Selected resonances are highlighted to illustrate the doubling of signals.

The structure of **1**-BF_4 was elucidated by performing a number of NMR experiments. An HMQC–HMBC sequence defined the C–C bond connectivities and gave evidence for the presence of four =CH- groups and four -CH_2- groups. The final structure of **1**-BF_4 was assigned through coupling-constant analysis (see the Supporting Information) in combination with 2D TOCSY and 2D NOESY NMR studies.[20] Compound **1**-BF_4 is stable for approximately 20 h at room temperature in CD_2Cl_2. Addition of water to the organic solution resulted in fast and irreversible decomposition.[21] The major decomposition product was identified as the cyclooctatriene complex [CpRu(1,3,5-cyclooctatriene)]BF_4, the hexafluorophosphate analogue of which has been reported previously.[22] Importantly, this decomposition does not occur when the complex is encapsulated. Inside the metal–ligand assembly, this reactive intermediate is stable for several weeks at room temperature in aqueous solution. It is protected from the outside chemical environment and sheltered from possible reaction channels that lead to decomposition.

The Cp* analogue of **1** was reported by Itoh and coworkers.[23] They obtained [Cp*Ru(*cis*-1,3,7-octatriene)]OTf (Tf = trifluoromethanesulfonyl) through treatment of [Cp*RuCl(butadiene)] with AgOTf in the presence of excess butadiene and found that addition of CO (one atm) to [Cp*Ru(*cis*-1,3,7-octatriene)]OTf led to the formation of the carbonyl complex [Cp*Ru(cod)(CO)]OTf.[23,24] Complex **1**-BF_4 reacted with CO in CH_2Cl_2 in a similar fashion to yield $[CpRu(cod)(CO)]BF_4$ (**2**-BF_4) as a pale-yellow solid. This carbonyl complex possesses a strong characteristic C=O stretch in the IR spectrum at $\nu = 2023\ cm^{-1}$ and has previously been described by Crocker et al.[25] Compound **2**-BF_4 was encapsulated in water, and the resulting host–guest complex $[\mathbf{2}\subset Ga_4L_6]^{11-}$ reveals the typical upfield shift in the ^{1}H NMR spectrum for the guest and inclusion into the asymmetric cavity: 12 separate signals are displayed for the cod moiety of the Ru complex. In addition, the IR spectrum shows a strong C=O stretch at $\nu = 2026\ cm^{-1}$, confirming encapsulation of the carbonyl complex. More interestingly, the host–guest complex $[\mathbf{2}\subset Ga_4L_6]^{11-}$ could also be generated from $[\mathbf{1}\subset Ga_4L_6]^{11-}$ in water through the addition of CO. This transformation was monitored by ^{1}H NMR spectroscopy (Figure 4). The starting material $[\mathbf{1}\subset Ga_4L_6]^{11-}$ clearly shows two sets of signals for the two diastereomeric host–guest complexes. Upon addition of CO, the formation of the new product $[\mathbf{2}\subset Ga_4L_6]^{11-}$, as well as the disappearance of the starting material, is observed after 1 day; after 5 days, the transformation is complete. Comparison of this product with the independently prepared $[\mathbf{2}\subset Ga_4L_6]^{11-}$ shows that the host–guest complexes are identical.

The corresponding Cp* complexes showed very similar reactivity patterns (see Scheme 1). The cationic octatriene complex [Cp*Ru(*cis*-1,3,7-octatriene)]BF_4 (**3**-BF_4) was formed through halide abstraction from [Cp*RuCl(cod)] with $AgBF_4$. Similar to the Cp complex, **3**-BF_4 completely decomposed in CD_2Cl_2 within 30 hours and in the presence of water within minutes. However, the host–guest complex $[\mathbf{3}\subset Ga_4L_6]^{11-}$, generated through the reaction of [Cp*RuCl(cod)] with $[Ga_4L_6]^{12-}$, was stable in aqueous solution for more than two weeks. Again, the host–guest complex $[\mathbf{3}\subset Ga_4L_6]^{11-}$ was treated with CO, quantitatively yielding the carbonyl complex $[\mathrm{Cp^*Ru(cod)(CO)}\subset\mathrm{Ga_4L_6}]^{11-}$ ($[\mathbf{4}\subset\mathrm{Ga_4L_6}]^{11-}$). As monitored by ^{1}H NMR spectroscopy (see the Supporting Information), the disappearance of the two diastereomeric complexes of $[\mathbf{3}\subset\mathrm{Ga_4L_6}]^{11-}$ is accompanied by the formation of the carbonyl complex $[\mathbf{4}\subset\mathrm{Ga_4L_6}]^{11-}$.

At this point, we are not entirely able to distinguish whether the addition of CO proceeds inside the cavity or if **1** and **3** dissociate from the metal–ligand assembly, undergo reaction in the bulk solution, and then re-enter the cavity. Due to the lack of decomposition of the reactive ruthenium complexes over extended periods of time though (no leaching is observed over several weeks), we can conclude that **1** and **3** reside only transiently, if at all, in the bulk solution. In addition, recent studies on related systems showed that dissociation of the sterically demanding guest molecules $[\mathrm{Cp^*Ir(PMe_3)(C_2H_4)}]^+$ and $[\mathrm{Cp_2^*Co}]^+$ from the host cavity is slow ($t_{1/2}$ = hours to weeks).[13,26] We therefore propose that reactivity takes place within the protective cavity.

In summary, two reactive organometallic intermediates have been stabilized in the inner phase of a chiral metal–ligand assembly. Although these complexes decompose within hours in organic solution and within minutes in water, the corresponding host–guest complexes are stable in aqueous solution for weeks. Encapsulation by the size- and shape-complementary host provides enough binding energy for the guests to prevent their decomposition. Despite their stabilization, the guest molecules are still able to react stoichiometrically with CO. These findings illustrate that supramolecular container molecules may soon find additional use in organometallic chemistry.[27] Not only can encapsulation by a supramolecular host stabilize certain intermediates, but stabilization may also be exploited to alter the chemical reactivity and selectivity of the bound guest molecules. Ideally, novel modes of selectivity or new reactivity can be anticipated by changing the relative stabilities of intermediates along a catalytic cycle, and thus shifting the energy surface of the reaction. In this particular case, we have isolated reactive organometallic species which are intermediates in the catalytic dimerization and oligomerization of substituted butadienes. We are now investigating the catalytic reactivity of these novel host–guest complexes.

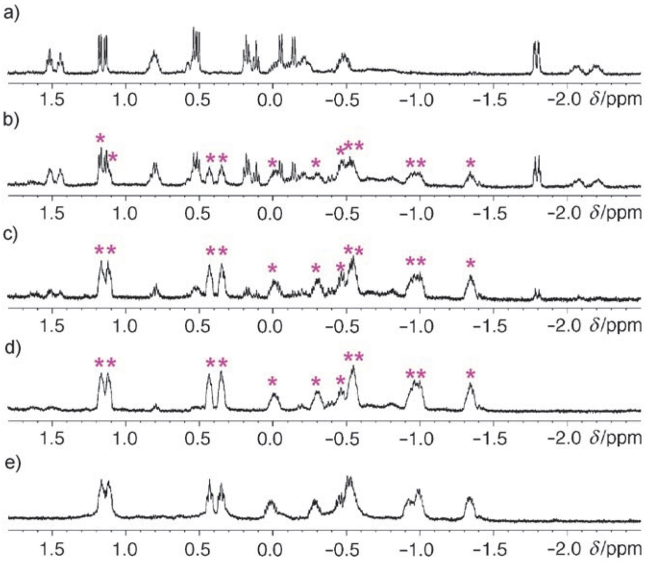
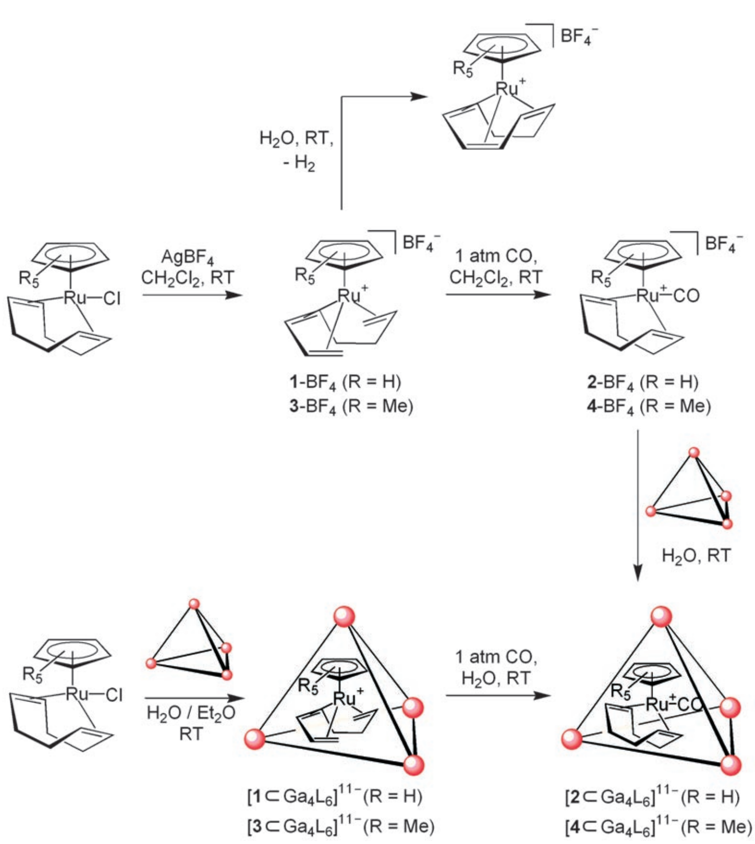


Figure 4. Reaction of $[\mathrm{CpRu}(cis\text{-}1,3,7\text{-octatriene})\subset\mathrm{Ga_4L_6}]^{11-}$ ($[\mathbf{1}\subset\mathrm{Ga_4L_6}]^{11-}$) with CO monitored by ^{1}H NMR spectroscopy. Conversion into the carbonyl complex $[\mathrm{CpRu(cod)(CO)}\subset\mathrm{Ga_4L_6}]^{11-}$ ($[\mathbf{2}\subset\mathrm{Ga_4L_6}]^{11-}$, *) is complete after 5 days. a) $[\mathbf{1}\subset\mathrm{Ga_4L_6}]^{11-}$; b) $[\mathbf{1}\subset\mathrm{Ga_4L_6}]^{11-}$ + CO, 1 day; c) $[\mathbf{1}\subset\mathrm{Ga_4L_6}]^{11-}$ + CO, 2 days; d) $[\mathbf{1}\subset\mathrm{Ga_4L_6}]^{11-}$ + CO, 5 days; e) $[\mathbf{2}\subset\mathrm{Ga_4L_6}]^{11-}$, prepared independently.



Scheme 1. Summary of host–guest reactivity. The reactive intermediates **1** and **3** are stabilized by the presence of the supramolecular host.

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[20] Regarding the proposed mechanism for the formation of **1** based on variable-temperature NMR studies: at −80 °C an intermediate with C_s symmetry is observed, presumably [CpRu(cod)]F–BF_3] (with one of the four fluorine atoms coordinated to the Ru center). This complex is stable up to 0 °C. At this point, formation of **1** starts, along with decomposition to the cyclooctatriene complex, and a weak hydride signal at $\delta = -12.3$ ppm is also observed. A possible mechanism for the formation of **1** starts with insertion of the metal into a methylene C–H bond; hydride migration gives rise to 9-ruthenal(IV)bicyclo[4.2.1]-2-nonene and reductive decyclization leads to the product (also, see the Supporting Information).

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