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Supramolecular Catalysis

Catalytic Hydrogenation of Norbornadiene by a Rhodium Complex in a Self-Folding Cavitand**

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Reactions mediated by supramolecularly encapsulated transition metal complexes are rare,[1–3] as cavities large enough to encapsulate the transition structure are required. Natural proteins,[4,5] and hydrogen-bonded,[6,7] metal-mediated,[8,9] or hydrophobically driven[10,11] synthetic multimolecular assemblies provide such spaces. For example, Raymond, Bergman et al. used M_4L_6 assemblies as vessels for cationic metal sandwich complexes[12] and controlled the reactivity of the corresponding half-sandwich.[3,13] Herein we show that deep cavitands can also perform chemistry in this regard and present their unprecedented behavior in a catalytic hydrogenation mediated by a rhodium(I) complex.

Cavitands are synthetic unimolecular receptors derived from resorcin[4]arene that contain an aromatic-lined cavity and are open at one end.[14] Some of us[15,16] recently showed that deep-cavity cavitands, synthesized originally by Rebek et al. for the inclusion of neutral molecules[17] and ferrocene derivatives,[18] form inclusion aggregates with several cationic organometallic complexes. We prepared an inclusion complex of the organometallic $[Rh(nbd)_2]BF_4$ (**1**-BF_4; nbd = norbornadiene) and Rebek's self-folding octaamide cavitand **2**. Compound **1**-BF_4 is extensively used as a precursor for coordinatively unsaturated rhodium cationic species having interesting catalytic properties, such as the hydrogenation of unsaturated organic substrates.[19] Substitution of one of the norbornadiene units by mono- or bidentate ligands gives heteroleptic complexes prior to hydrogen exposure. However, inclusion of **1**-BF_4 in **2** provides an alternative to the ligand exchange.

Cobaltocenium cation $\mathbf{3}^+$ forms a stable inclusion complex with **2**.[16] The included metallocene $\mathbf{3}^+$ spins and tumbles freely within **2** even at low temperatures. In contrast, the bisnorbornadiene rhodium(I) cation $\mathbf{1}^+$ is elongated along the axis that goes through the two methylene bridge carbon atoms and the rhodium atom (Figure 1), and thus its inclusion in **2** should show orientation preferences.

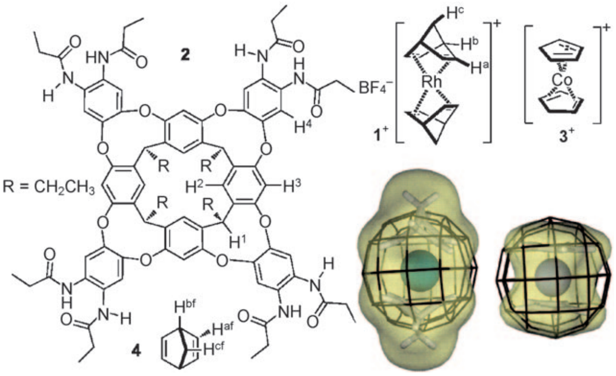

Figure 1. Chemical structures of self-folding cavitand **2**, norbornadiene **4**, and organometallic cationic complexes $\mathbf{1}^+$ and $\mathbf{3}^+$. CAChe minimized structures of $\mathbf{1}^+$ and $\mathbf{3}^+$ shown with their van der Waals surface embedded into a sphere with a radius of 3.5 Å centered on the metal atom.

The ^1H NMR spectrum of **2** in CD_2Cl_2 shows that the signals of the amides (NH) and the aromatic protons (H^4) of the diamidobenzene ring are very broad, which is due to the chemical exchange between cycloenantiomers occurring in this solvent at a rate that is similar to the ^1H NMR timescale.[17,20] The signal of the methine proton (H^1) is sharp and well-resolved; it appears at $\delta = 5.80$ ppm, indicating that **2** is in a vase-like conformation. The addition of 0.4 equiv of the cation **1**-BF_4 to a 5 mM solution of **2** in CD_2Cl_2 produces a new set of proton signals for the bound host. The amide NH groups and the protons of the diamidobenzene (H^4) in bound **2** are sharp singlets at $\delta = 9.63$ ppm and $\delta = 7.61$ ppm, respectively. The inclusion of cation $\mathbf{1}^+$ in **2** induces the fast interconversion of the cycloenantiomers of the octaamide.

The signals of included $\mathbf{1}^+$ appear in two different regions of the ^1H NMR spectrum: two singlets are in the upfield region and are assigned to the protons $H^{b''}$ ($\delta = 0.46$ ppm) and $H^{c''}$ ($\delta = -2.91$ ppm) of the norbornadiene unit deep in the aromatic cavity of **2**; two other singlets are assigned to the protons $H^{a'}$ ($\delta = 4.13$ ppm) and $H^{b'}$ ($\delta = 3.60$ ppm) of the "upper" norbornadiene unit that is not included in the aromatic cavity (Supporting Information, Figure S2). A remaining singlet at $\delta = 2.85$ ppm corresponds to the proton

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$H^{a''}$ of the deeply bound norbornadiene. The observation of separated proton signals for the two norbornadiene units of included $\mathbf{1}^+$ supports axial inclusion geometry for the $\mathbf{1}^+\subset\mathbf{2}$ complex. An EXSY experiment revealed the existence of weak cross-peaks between the proton signals of the two norbornadiene units of bound $\mathbf{1}^+$ ($H^{a'}H^{a''}$, $H^{b'}H^{b''}$ and $H^{c'}H^{c''}$), a result indicative of a slow tumbling motion on the ^{1}H NMR timescale ($k_{\text{exch}} = 0.4\ \text{s}^{-1}$, $\Delta G = 18\ \text{kcal mol}^{-1}$).

Further analysis of the EXSY experiment revealed the presence of other two minor species involved in chemical exchange processes with the $\mathbf{1}^+\subset\mathbf{2}$ complex. One is free norbornadiene **4** and its presence indicates that $\mathbf{1}^+$ is partially dissociated. The dissociation process should afford the cationic species $[\text{Rh(nbd)}(\text{S}_n)]^+$ (where $n = 2$ or 3 and S = H_2O or CH_2Cl_2).[21] Broad signals, which can be assigned to the protons of $[\text{Rh(nbd)}(\text{S}_n)]^+$ included in **2**, are observed at $\delta = -0.04$ ppm and -3.24 ppm in the EXSY experiment. The integral ratios of the H^{af} proton pertaining to the free **4**, to protons $H^{b'''}$ and $H^{c'''}$ of $[\text{Rh(nbd)}(\text{S}_n)]^+\subset\mathbf{2}$ are in agreement with this hypothesis (Figure 2). Figure 3 depicts the minimized structures of the two cationic inclusion complexes formed from $\mathbf{1}^+$ and octaamide **2**.

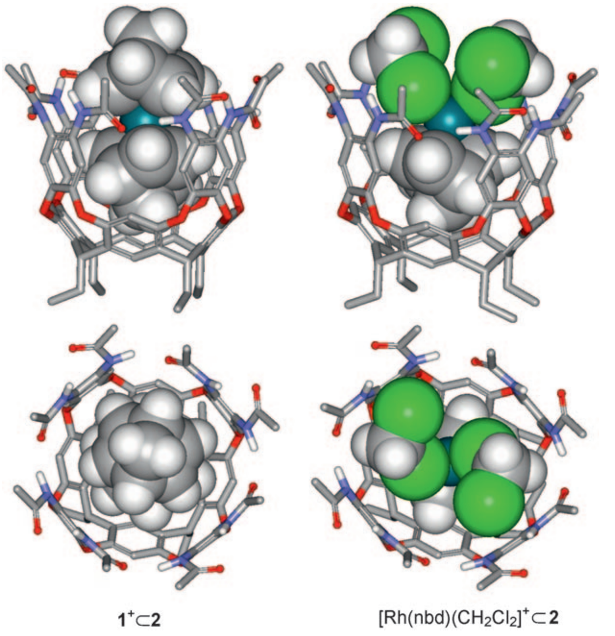


Figure 3. CACHe minimized structures of the cationic inclusion complexes $\mathbf{1}^+\subset\mathbf{2}$ and $[\text{Rh(nbd)}(CH_2Cl_2)_2]^+\subset\mathbf{2}$.

The addition of incremental amounts of **1**-BF_4 produced the expected increase in the intensities of the signals corresponding to the $\mathbf{1}^+\subset\mathbf{2}$ complex at the expense of those of free **2** and a significant increase of the proton signals of **4** and $[\text{Rh(nbd)}(\text{S}_n)]^+\subset\mathbf{2}$. Significant broadening and chemical shift changes were also observed in the signals of the complexes during the titration experiment. Concomitantly, two new signals resonating at $\delta = 3.70$ ppm and $\delta = 3.51$ ppm appeared (Figure 2, top; Supporting Information, Figure S3). We surmise that a binuclear metallo complex is formed, in accord with proposals of Chen and Feder,[22] with three norbornadiene ligands. The structure of this putative complex is unknown, but our subsequent experiments used an excess of host **2** with respect to **1**-BF_4 to suppress such high-order complexes.

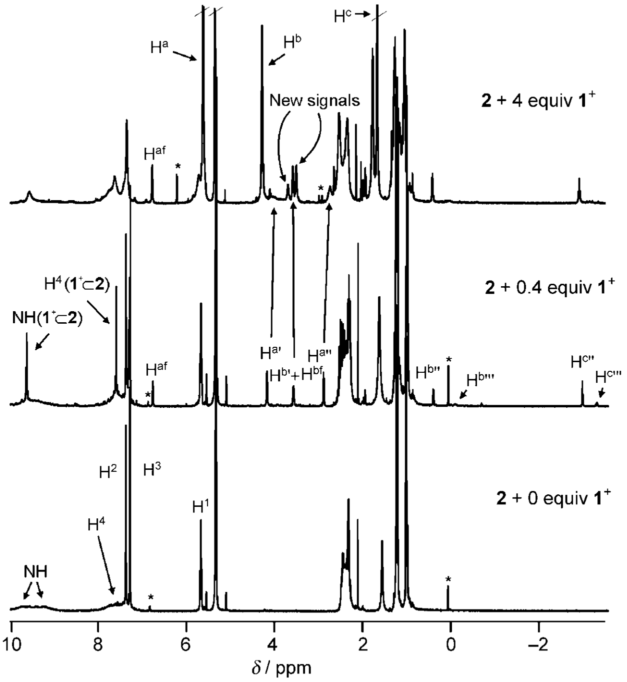


Figure 2. Changes in the ^{1}H NMR spectra (400 MHz, CD_2Cl_2) acquired at 298 K during the titration of **2** with **1**-BF_4 ([**2**] = 5.0 mM). Primed and second primed letters correspond to the protons in the $\mathbf{1}^+\subset\mathbf{2}$ complex and triple-primed letters to the $[\text{Rh(nbd)}(\text{S}_n)]^+\subset\mathbf{2}$ complex. ⋆ = impurities.

Next, the effect on hydrogenation reactions of the two cationic complexes inside of **2** was assessed. We divided a 3 mM solution of **1**-BF_4 in CD_2Cl_2 in two aliquots of equal volume. One was directly shaken under 1 bar of H_2. After two to five minutes, depending on the intensity of the shaking, a black precipitate of rhodium metal was formed and the solution completely lost its original red color. Analysis of the solution showed the total absence of $\mathbf{1}^+$.

The spectrum contained several proton signals with complex multiplicities, suggesting the formation of a mixture of compounds from the H_2 treatment. When the solution was analyzed by GC-MS, an intense peak corresponding to a mass of 188 Da was observed. This compound is most likely formed by the hydrogenation of the partially reduced dimer **6** (MW 186) that Schrock and Osborn described to be the major product of the catalytic hydrogenation of **4** in acetone promoted by $\mathbf{1}^+$.[23] The structure of dimer **6** was elucidated by Roth and Katz.[24] In our case, the production of stoichiometric amounts of rhodium(0) with respect to the partially reduced dimer **6** during the hydrogenation of $\mathbf{1}^+$ may be responsible for the effective overreduction to **7**.[25]

In striking contrast with these findings, the exposure of the second aliquot of the CD_2Cl_2 solution of **1**-BF_4 to which 1.2 equiv of octaamide **2** was added to 1 bar of hydrogen did not produce the formation of detectable amounts of black rhodium(0) to the naked eye. Instead, a change in the color of the solution from orange to pale yellow occurred under the H_2

atmosphere. The ^{1}H NMR spectrum (Figure 4) showed that the signals of the protons of **2** were much broader than in the precursor solution, and we could not observe separate proton signals for free and bound **2**, and only one single set of signals, that of the norbornadiene unit buried inside the aromatic cavity of **2**, was detected. These signals do not coincide with any of the signals previously assigned to the included norbornadiene units of $\mathbf{1}^+\subset\mathbf{2}$ and $[\mathrm{Rh(nbd)(S}_n)]^+\subset\mathbf{2}$.

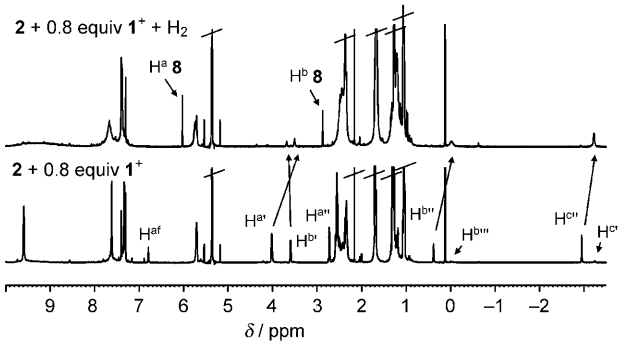
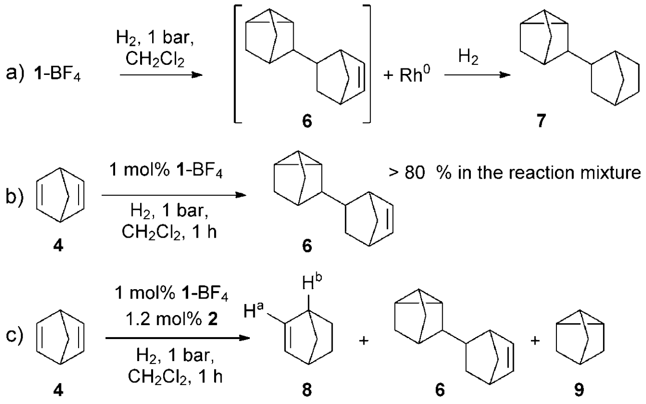


Figure 4. Observed changes in the proton signals of a CD_2Cl_2 solution of **2** ([**2**] = 3.0 mM) with of **1**-BF_4 (0.8 equiv) after hydrogen treatment.

In short, the cavitation slows down the hydrogenation reaction of the included norbornadiene ligand and thus stabilizes the rhodium cationic species towards reduction to rhodium(0). Furthermore, we detected the signals for the norbornadiene ligand that is near the top of the cavity, indicating that **2** also prevents the fast reduction of the "upper" norbornadiene molecule. An EXSY experiment acquired on the mixture under 1 bar of hydrogen showed the existence of another set of proton signals for included norbornadiene (Supporting Information, Figure S8). This new set is not detected in the 1D ^{1}H NMR spectrum but it can be inferred from the cross peaks owing to chemical exchange involving the protons of the external norbornadiene unit and the sharper set of protons of included norbornadiene. We also noticed that the integration value of the sharper proton signals of included norbornadiene is greater than for the external norbornadiene protons. Taken together, these data indicate that when the mixture of inclusion complexes $\mathbf{1}^+\subset\mathbf{2}$ and $[\mathrm{Rh(nbd)(S}_n)]^+\subset\mathbf{2}$ is treated with H_2, neither their norbornadiene ligands nor the rhodium metal centers are readily reduced as occurred in the case of free $\mathbf{1}^+$. Whatever the structures of these complexes are, they must be highly kinetically stable to prevent the formation of rhodium(0) in solution. Their dissociation would produce exposed cationic rhodium species that are readily reduced to rhodium(0) under H_2 atmosphere.

The ^{1}H NMR spectrum of the mixture under 1 bar of hydrogen showed that the proton signals of free norbornadiene (present before H_2 treatment) disappeared and were replaced by signals of norbornene **8**. Presumably, this reduction occurs through the intermediacy of putative dihydrido rhodium inclusion complex.[26] After the free norbornadiene is reduced, the system appears to be stable for hours under 1 bar of hydrogen at room temperature. The coordination of an additional norbornadiene molecule is required to reduce the activation energy of the rate limiting step of the hydrogenation catalytic cycle.[27] Accordingly, we added 10 equiv of norbornadiene to the NMR tube containing the mixture under 1 bar of hydrogen and connected the NMR tube to an H_2 reservoir. The immediate change in color from yellow to orange indicated the formation of the complexes $\mathbf{1}^+\subset\mathbf{2}$ and $[\mathrm{Rh(nbd)(S}_n)]^+\subset\mathbf{2}$. A significant increase of **8** and the disappearance of **4** were also observed by NMR. New signals for dimer **6** also became evident, with the ratio of **8**:**6** as 80:20 with 10% mol of the supramolecular catalyst. Apparently, small quantities of $\mathbf{1}^+$ are released to the solution from the dissociation of $\mathbf{1}^+\subset\mathbf{2}$ and catalyze the dimerization of norbornadiene to **6**.

In a laboratory-scale experiment, we exposed a 3 mM CH_2Cl_2 solution of **1**-BF_4 (1.0 mol%) and octaamide **2** (1.2 mol%) to 1 bar of H_2 for several minutes, then added neat norbornadiene (100 equiv) in one portion. The resulting mixture was stirred for 1 h under H_2 and subsequently analyzed by GC. The resulting mixture contained 58% of **8**, 39% of dimer **6**, and 3% of **9**.[28] The fact that norbornene **8** is the major product testifies to the catalytic activity of the supramolecular, encapsulated transition metal complex. The included metal complex mainly catalyzes the hydrogenation of **4** to norbornene **8**, while non-included metal complex converts **4** to dimer **6** (Scheme 1). The hydrogenation of **4** to norbornene **8** involves included catalytic metal centers, but the transition state of the dimerization process is not attainable in the constrained environment of **2**.



Scheme 1. a) Behavior of **1**-BF_4 under a hydrogen atmosphere (1 bar) in dichloromethane solution. Rhodium-catalyzed hydrogenation of norbornadiene **4** in absence (b) or in presence (c) of the cavitand **2**.

In summary, we have demonstrated the formation of two inclusion complexes, $\mathbf{1}^+\subset\mathbf{2}$ and $[\mathrm{Rh(nbd)(S}_n)]^+\subset\mathbf{2}$ from $\mathbf{1}^+$ and cavitand **2**. Under hydrogen and an excess of norbornadiene, the complexes are catalytically active and produce norbornene **8** as the major reaction product. Although the structure of the catalysts is unknown, its behavior is very different from that of free $\mathbf{1}^+$, which converts norbornadiene into dimer **6**. This work is an example of an organic transformation catalyzed by supramolecularly encapsulated metal complex in which host **2** acts as a second-sphere ligand that modifies the stability, selectivity, and reactivity of organometallic complex **1**$^+$ relative to the free form in solution. We are exploring its potential application as catalyst for other organic transformations.

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[28] An increase in concentration (15–17 mM) and percentage of the supramolecular system, **1**-BF_4 (20.0 mol %) and receptor **2** (24.0 mol %), converts norbornadiene into dimer **6** in just 4 %.