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Highly Selective Supramolecular Catalyzed Allylic Alcohol Isomerization

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Enzymatic catalysis often relies upon the highly constrained environment of substrates within the active site cavity to govern selectivity and reactivity. Recent examples in organometallic chemistry mimic this approach by using host−guest interactions.[1] A supramolecular M_4L_6 tetrahedral assembly developed by Raymond and co-workers[2] provides a host that mediates a variety of organic and organometallic transformations.[3] We have previously demonstrated the efficient encapsulation of Ir(III) guests by this M_4L_6 assembly that are capable of stoichiometric C−H bond activation with high size and shape selectivity.[3a,c] We envisioned that a similar *catalytic* encapsulated metal complex system could also be achieved. Herein we report a remarkable and selective supramolecular encapsulation of discrete organometallic catalysts that display catalytic activity controlled by the size and shape of the host cavity.

The $M_4L_6^{12-}$ host is formed from the self-assembly of four octahedral metal centers ($M = Ga^{III}$) that comprise the vertices and six bis-catecholamide naphthalene ligands (L^{4-}) that span the edges of a tetrahedron (Figure 1). The host has been found to encapsulate monocationic guests ranging from ammonium cations to cationic organometallic species.[2,3]

Due to the large number of known monocationic rhodium catalysts, we decided to pursue the encapsulation of these species as potentially reactive guests. Small bis-phosphine rhodium complexes of the general formula [(P−P)Rh(diene)][BF_4] (P−P = 2 PR_3 or 1,2-bis(dimethylphosphino)ethane (dmpe), diene = 1,5-cyclooctadiene (COD) or norbornadiene (NBD)) were prepared, and their suitability as guests was investigated (Table 1). Upon addition of the rhodium complexes to an aqueous solution of the $Na_{12}[Ga_4L_6]$ host assembly, encapsulation was observed, yielding discrete host−guest assemblies of the general form $Na_{11}[L_nRh \subset Ga_4L_6]$. There is a sharp cutoff in the size allowed for the encapsulated guest. Rhodium complexes that are too sterically demanding such as $[(PEt_3)_2Rh(COD)]^+$ were not encapsulated.

The equilibrium constants of encapsulation for these guests were determined by ^{1}H NMR spectroscopy. The binding affinities are 1 to 2 orders of magnitude lower than those of the iridium complexes studied previously.[3c] We attribute this to the poorer shape complementarity of the square planar geometry compared to the more compact half-sandwich structure with the host cavity. This shape selectivity may explain the difference in binding affinity between different rhodium complexes: the COD-substituted complexes bind more favorably than the NBD-substituted ones, while the similarly shaped PMe_3 and dmpe complexes have comparable binding affinities.

The NMR resonances for the guest are shifted upfield by 2−3 ppm due to shielding by the naphthalene walls of the host, which is diagnostic of encapsulation. Additionally, the chirality of the host cavity breaks the symmetry of the guest. Since the tetrahedral host has *T* symmetry, no mirror planes exist within the cavity; however, C_2 axes remain intact. This is exemplified by the NMR spectra of the encapsulated guests $[(PMe_3)_2Rh(COD)]^+$ (**1**) and [(dmpe)Rh(COD)]$^+$ (**2**). In the ^{1}H NMR spectrum of [**1** ⊂ Ga_4L_6], the PMe_3 ligands remain equivalent due to the retention of C_2 symmetry (Figure 2a). In the ^{1}H NMR spectrum of [**2** ⊂ Ga_4L_6], the dmpe methyl groups are split into two resonances; while there is a lack of mirror symmetry relating the methyl groups, C_2 symmetry still relates two of the four methyl groups (Figure 2b). This loss of symmetry is consistent with free rotation of the encapsulated guest within the chiral host cavity; restricted rotation would result in a further loss of symmetry.

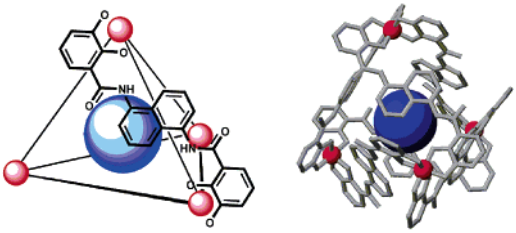


Figure 1. (Left) Schematic of M_4L_6 assembly with one of the edge-spanning ligands displayed containing a cartoon guest. (Right) Crystal structure of Fe_4L_6 assembly with a cartoon guest.

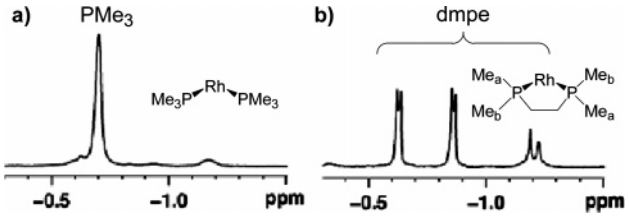


Figure 2. (a) ^{1}H NMR spectrum of Na_{11}[**1** ⊂ Ga_4L_6] displaying upfield but equivalent PMe_3 peaks. (b) ^{1}H NMR spectrum of Na_{11}[**2** ⊂ Ga_4L_6] displaying upfield but nonequivalent dmpe methyl and methylene peaks.

Table 1. Encapsulation Affinities for Rhodium Complexes in D_2O as Determined by ^{1}H NMR Spectroscopy

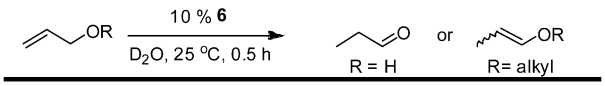
Guest	Encapsulation Guest Affinity (M^{-1})
(**1**) $(PMe_3)_2Rh(COD)^+$	5.2×10^2
(**2**) $(dmpe)Rh(COD)^+$	5.7×10^2
(**3**) $(PMe_3)_2Rh(NBD)^+$	1.2×10^2
(**4**) $(dmpe)Rh(NBD)^+$	1.2×10^2
(**5**) $(PEt_3)_2Rh(COD)^+$	not encapsulated

Cationic rhodium complexes catalyze a wide variety of chemical transformations[4] including the isomerization of allylic alcohols.[5] This reaction serves as an ideal model reaction for the host−guest assembly since it involves a single substrate reacting with the encapsulated catalyst. In addition, many allylic alcohols are water soluble, which should ensure homogeneous reactivity.

While rhodium complexes bearing large phosphine groups have been used in these isomerizations,[5] little work has been done on complexes bearing small phosphine groups such as PMe_3. Therefore, the scope of the reaction of unencapsulated **1** with allylic alcohols was first examined (Table 2). In order to generate the active catalyst $(PMe_3)_2Rh(OD_2)_2^+$ (**6**),[6] 1 atm of H_2 was added to hydrogenate

10.1021/ja068688o CCC: $37.00

Table 2. Isomerization of Allylic Substrates by **6**



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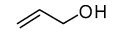
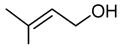
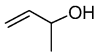
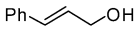
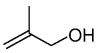
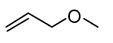
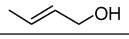
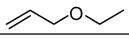
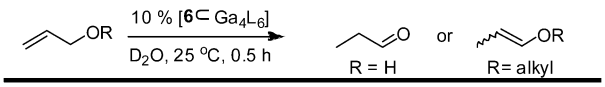
1		95 %	5		n. r.
2		95 %	6		n. r.
3		95 %	7		95 %[b]
4		n. r.	8		95 %[b]

[a] Determined by ^{1}H NMR spectroscopy. [b] 1:1 *E*:*Z* enol ether was obtained.

Table 3. Isomerization of Allylic Substrates by [**6** ⊂ Ga_4L_6]



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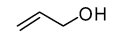
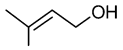
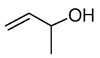
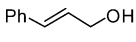
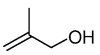
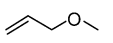
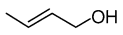
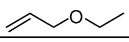
1		95 %	5		n. r.
2		n. r.	6		n. r.
3		n. r.	7		95 %[b]
4		n. r.	8		n. r.

[a] Determined by ^{1}H NMR spectroscopy. [b] 1:1 *E*:*Z* enol ether was obtained.

the COD ligand. Upon addition of the allylic alcohol, complete conversion to the corresponding isomerized product was observed within 0.5 h at 25 °C (Table 1, entry 1). Isomerization of allylic ethers to the corresponding enol ethers was also observed (Table 1, entries 7 and 8). The reaction does not tolerate terminal substitution; no isomerization of crotyl alcohol was observed (Table 1, entry 4). Significantly, when both allyl alcohol and crotyl alcohol were added to the active catalyst, no isomerization of either substrate was observed, indicating that crotyl alcohol inhibits the catalyst.

Having established the catalytic behavior of **6**, the encapsulated catalyst was generated by addition of 1 atm H_2 to an aqueous solution of [**1** ⊂ Ga_4L_6]. Under these conditions, a new species was observable by NMR spectroscopy after several hours at room temperature, which was identified as [**6** ⊂ Ga_4L_6]. However, after 12 h at room temperature, the guest was no longer encapsulated by the host, indicating that the equilibrium favors the unencapsulated rhodium complex. This is not surprising, considering that **6** is highly solvated. This result suggests that **6** is kinetically formed within the host cavity and slowly dissociates irreversibly into the bulk solution. Indeed, when **6** was independently prepared and added to an aqueous solution of $Na_{12}[Ga_4L_6]$, no encapsulation was observed. Thus, any reactivity with [**6** ⊂ Ga_4L_6], including substrate entrance and product release, must be rapid enough to occur prior to guest dissociation.

In sharp contrast to the results with unencapsulated **6**, selective isomerization of specific allylic alcohols was observed when substrates were added to [**6** ⊂ Ga_4L_6] (Table 3). Only alcohols of the correct size and shape are able to enter the host cavity and react with the metal catalyst. For example, the small allyl alcohol is isomerized within 0.5 h at room temperature (Table 3, entry 1), whereas larger substrates are not isomerized. Substrates with methyl branching do not react at all, in contrast to the results with **6** (Table 3, entries 2 and 3). We infer that branching inhibits the ability of the substrate to enter the host cavity through the channels in the ligand walls, preventing it from interacting with the active catalyst. This is an example of the high shape selectivity of the supramolecular catalyst: the isosteric linear allyl methyl ether is isomerized quantitatively (Table 3, entry 7).

When both allyl alcohol and crotyl alcohol were added to [**6** ⊂ Ga_4L_6], selective isomerization of allyl alcohol to propionaldehyde was observed. This suggests that, while the supramolecular host prevents crotyl alcohol from entering the cavity and deactivating the catalyst, allyl alcohol has ready access to the encapsulated catalyst. In combination with the slow rate of catalyst dissociation, these selectivity results indicate that the highly specific substrate selectivities are enforced by encapsulation within the well-defined cavity of the host.

In conclusion, a supramolecular Ga_4L_6 host has been shown to encapsulate a variety of cationic rhodium catalysts. This is a remarkable example of the supramolecular encapsulation of discrete organometallic catalysts, in this case resulting in supramolecular control over the catalytic isomerization of allylic alcohols to give highly specific size and shape substrate selectivities. In contrast to the behavior of the free rhodium catalyst, in situ selectivity between allyl alcohol and crotyl alcohol resulted in no inhibition by crotyl alcohol and complete isomerization of allyl alcohol. These results demonstrate that a synthetic supramolecular outer-sphere environment can direct control of catalytic reactivity at a metal center—much like enzymes do in nature.

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Supporting Information Available: Experimental details and characterization of key intermediates. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Ito, H.; Kusukawa, T.; Fujita, M. *Chem. Lett.* **2000**, 598−599. (b) Slagt, V. F.; Kramer, P. C. J.; van Leeuwen, P. W. N. M.; Reek, J. N. H. *J Am. Chem. Soc.* **2004**, *126*, 1526−1536. (c) Kuil, M.; Soltner, T.; van Leeuwen, P. W. N. M.; Reek, J. N. H. *J. Am. Chem. Soc.* **2006**, *128*, 11344−11345. (d) Kleij, A. W.; Lutz, M.; Spek, A. L.; van Leeuwen, P. W. N. M.; Reek, J. N. H. *Chem. Commun.* **2005**, *29*, 3661−3663. (e) Morris, G. A.; Nguyen, S. T.; Hupp, J. T. *J. Mol. Catal. A: Chem.* **2001**, *174*, 15−20. (f) Lee, S. J.; Hu, A.; Lin, W. *J. Am. Chem. Soc.* **2002**, *124*, 12948−12949. (g) Gianneschi, N. C.; Masar, M. S., III; Mirkin, C. A. *Acc. Chem. Res.* **2005**, *38*, 825−837. (h) For a recent review, see: Kleij, A. W.; Reek, J. N. H. *Chem. Eur. J.* **2006**, *12*, 4218−4227 and references therein.

(2) (a) Caulder, D. L.; Powers, R. E.; Parac, T. N.; Raymond, K. N. *Angew. Chem., Int. Ed.* **1998**, *37*, 1840−1843. (b) Caulder, D. L.; Bruckner, C.; Powers, R. E.; Konig, S.; Parac, T. N.; Leary, J. A.; Raymond, K. N. *J. Am. Chem. Soc.* **2001**, *123*, 8923−8938.

(3) (a) Fiedler, D.; Leung, D. H.; Bergman, R. G.; Raymond, K. N. *Acc. Chem. Res.* **2005**, *38*, 351−360. (b) Fiedler, D.; van Halbeek, H.; Bergman, R. G.; Raymond, K. N. *J. Am. Chem. Soc.* **2006**, *128*, 10240−10252. (c) Leung, D. H.; Bergman, R. G.; Raymond, K. N. *J. Am. Chem. Soc.* **2006**, *128*, 9781−9797.

(4) Evans, P. A., Ed. *Modern Rhodium-Catalyzed Organic Reactions*; Wiley-VCH: Weinheim, 2005.

(5) (a) Tani, K. *Pure Appl. Chem.* **1985**, *57*, 1845−1854. (b) Uma, R.; Crévisy, C.; Grée, R. *Chem. Rev.* **2003**, *103*, 27−52.

(6) Rhodium bis-phosphine solvento species have been implicated in the isomerization of allylic substrates. See: Bergens, S. H.; Bosnich, B. *J. Am. Chem. Soc.* **1991**, *113*, 958−967. We thank a referee for the suggestion that in this case a rhodium hydride species may also be the active catalytic species for this transformation. The NMR resonance for the hydride may be masked by H−D exchange with the bulk solvent. Since **6** is highly reactive, we were unable to isolate and fully characterize it to definitively distinguish these two possibilities.

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