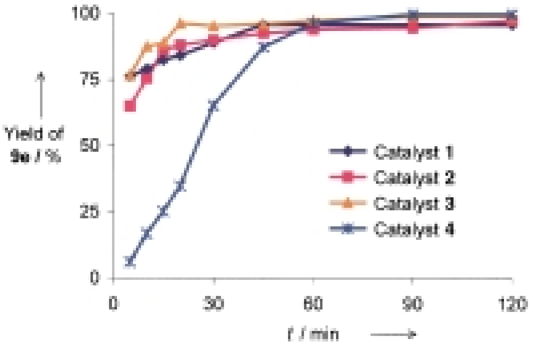

Figure 3. Kinetics of the RCM reaction of **8e** catalyzed by the Ru complexes **1**–**4**.

(ethylene or propylene) plays a pivotal role.[10] These findings add a new dimension to the evolving area of high-throughput catalyst or reagent screening based on IR-thermography.[2–4] Moreover, this study shows that IR-thermography constitutes a simple way to assess the relative rate of initiation of RCM events by different precatalysts as well as the inherent reactivity of variously substituted diene substrates towards the reaction. Therefore the method will greatly facilitate further investigations in this timely field of research.[6]

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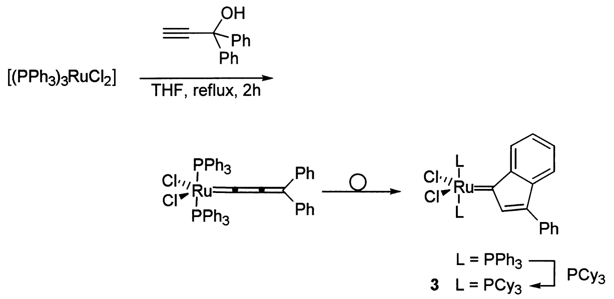

[8] To prevent uncontrolled evaporation of solvent, screening was performed in a closed fume hood without ventilation.

[9] We thank Dr. P. Schwab and Dr. G. Kautz (BASF AG, Ludwigshafen) for this calculation.

[10] Strictly speaking one also has to consider various other enthalpies (i.e. enthalpy of mixing, enthalpy of solvation) which contribute to the effects seen in the thermographic images.

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[12] For the substrate/catalyst activity screening the substrates were placed in the wells of a 96-well polypropylene microtiter plate (100 μL substrate per well). The temperature was calibrated in the range of 25–35 °C. The reaction was initiated by the simultaneous addition of 100 μL of the four different precatalyst solutions (**1**–**4**) in toluene (0.01 M corresponding to 0.26 mol% precatalyst) at 30 °C to each substrate using a multiple pipette (the addition of the precatalyst solutions was completed within 90 s). As before, the temperature changes were detected periodically, shaking being interrupted. The detection time was 5 s, resulting in 250 recordings which were averaged.

Host within a Host: Encapsulation of Alkali Ion–Crown Ether Complexes into a [Ga$_4$L$_6$]$^{12-}$ Supramolecular Cluster[**]

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Kenneth N. Raymond*

We have constructed structures based on supramolecular clusters found in nature and shown that they encapsulate molecular cations.[1] The origins of supramolecular chemistry

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can be traced to the synthesis of hosts for simple ionic species. Examples include amongst others crown ethers, acyclic podands, calixarenes, macropolycyclic cryptands, and spherands.[2] Here we report the combination of these two types of host–guest interactions: alkali cations are incorporated into the large anionic host as a crown ether complex.

Examples in which supramolecular metal clusters act as host molecules include being hosts for small inorganic ions such as Li^+, Na^+, Cl^-, NH_4^+, or BF_4^-,[3] while Fujita et al. have shown that larger guests can induce organization of three-dimensional cagelike complexes.[4] An example of designed self-assembled metal clusters[4] is $K_5(Et_4N)_7[M_4L_6]$ ($M = Ga^{III}$, Fe^{III}, L = 1,5-bis(2,3-dihydroxybenzamido)naphthalene; Figure 1). Both solution and solid-state studies reveal that one of the Et_4N^+ counterions is located inside the tetrahedral cluster cavity.[5] The driving force for the reaction is the gain in entropy associated with solvent release.[6] The positive enthalpy of this host–guest complexation results from desolvation of the guest and the cluster interior, hence cations with small solvation enthalpies are preferentially encapsulated by the $[Ga_4L_6]^{12-}$ host. Increasing the charge of a cation of constant size from +1 to +2 increases the solvation enthalpy approximately fourfold. Hence, singly charged guests are encapsulated into $[Ga_4L_6]^{12-}$ while more highly charged guests are not,[6] and highly solvated, singly charged cations (namely, K^+, Na^+, or Li^+), are very poor guests. This has been confirmed by studies involving ^{39}K NMR spectroscopy, which indicate that the cavity of $[Ga_4L_6]^{12-}$ does not incorporate K^+ ions; the solvated K^+ ions remain exclusively outside the cavity.[6]

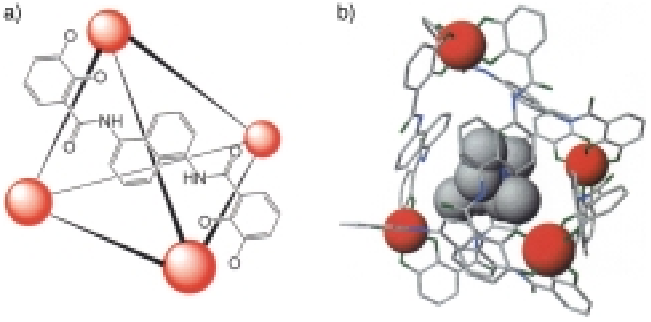

Figure 1. a) A schematic drawing of the tetrahedral $[Ga_4L_6]^{12-}$ host as determined from the crystal structure of the $K_5(Et_4N)_7[FeL_6]$ salt (the rods represent the ligands and the spheres represent the metal ions). b) A view of the crystal structure of $[Ga_4L_6]^{12-}$ showing the encapsulated Et_4N^+ ion (the other counterions are omitted for clarity).

Crown ethers are well known as effective hosts for small supramolecular cationic guests.[7] The high enthalpies of cation desolvation are compensated by strong intermolecular interactions between the cation and the crown ether such that the overall enthalpies are negative.[8] Therefore small cations complexed by crown ethers should be suitable guests for encapsulation into the cavity of $M_{12}[Ga_4L_6]$, since the desolvation enthalpy cost has been paid. Herein we, indeed, demonstrate the inclusion of cation complexes of [12]crown-4, [15]crown-5, and [18]crown-6 ethers into $[Ga_4L_6]^{12-}$.

The three salts of $M_{12}[Ga_4L_6]$ ($M = Li^+$, Na^+, or K^+) were synthesized by the procedure reported earlier;[6] their ^1H NMR spectra in D_2O and D_3COD are identical. The fact that the spectra show no dependence on the cation is consistent with our previous finding that the cations are located outside the cavity.[6] Electrospray ionization (ESI) mass spectra studies on a similar cluster reveal that the metal cations are located outside the cluster and interact with the oxygen atoms at the corners of the tetrahedral cluster.[9]

The addition of $M_{12}[Ga_4L_6]$ ($M = Li^+$, Na^+, or K^+) to [12]crown-4, [15]crown-5, or [18]crown-6 results in a decrease in the intensities of the ^1H NMR signals of the crown ethers and the appearance of new peaks at higher fields.[10] The new, high-field ^1H NMR resonances are a clear indication of encapsulation: the magnetically shielded cluster cavity, surrounded by naphthalene and phenyl groups of the ligand, shifts the proton resonances of the encapsulated guest to much higher field.[11] Additional evidence for the formation of the host–guest complex is provided by the 2D NOESY NMR spectra, which show cross-peaks between the naphthalene resonances of the cluster and the new, high-field peaks, which implies close proximity of these protons (Figure 2).

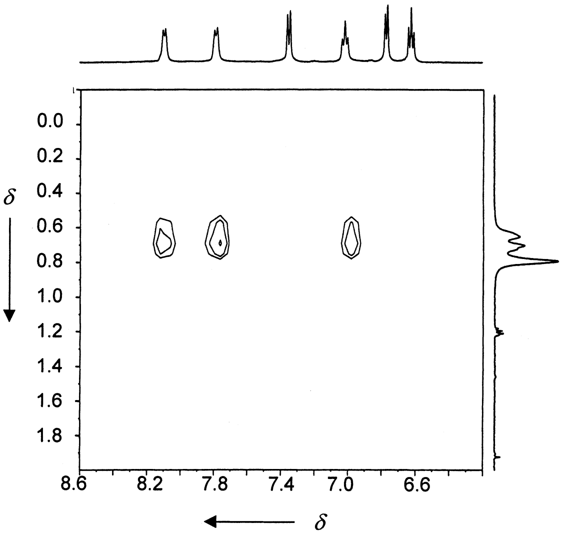

Figure 2. A 2D NOESY spectrum of a mixture containing $K_{12}[Ga_4L_6]$ and [12]crown-4 in D_3COD. The horizontal scale represents proton resonances of the naphthalene ligand in the metal cluster, and the vertical scale represents proton resonances of the encapsulated crown ether.

Significantly, the crown ethers are incoporated into the cavity in each of the $M_{12}[Ga_4L_6]$ salts even though no extra M^+ is added to the solution. Since only positively charged molecules are incorporated into the cluster,[5, 6] the crown ether must have complexed one of the twelve cations from $M_{12}[Ga_4L_6]$, to form a positively charged guest which enters the cluster. Specific evidence for the formation of the cation–crown ether complex is provided by the ^7Li NMR spectrum of the Li^+–crown ether complex: in the absence of the cluster only one peak is seen for the solvated Li^+ ion, since the exchange between the complexed and solvated Li^+ ions in D_2O and D_3COD is fast on the NMR scale. In contrast, the ^7Li NMR spectra of [12]crown-4 and [15]crown-5 solutions upon

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addition of $Li_{12}[Ga_4L_6]$ (Figure 3) show a strong peak for the solvated Li^+ ions (referenced at 0.0 ppm) and one new peak at $\delta = -3.20$ or -4.05. The appearance of new ^7Li resonances at higher field is consistent with complexation of the Li^+ ion by the crown ether.[12] Incorporation of the Li^+–crown ether complex into the cluster cavity slows exchange between the crown-complexed Li^+ ion and aqueous Li^+ ions in solution, so that both species are seen in the ^7Li NMR spectrum.

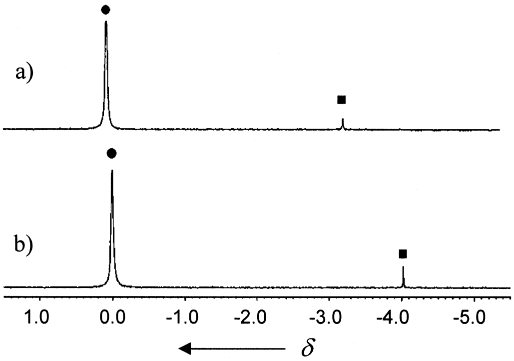
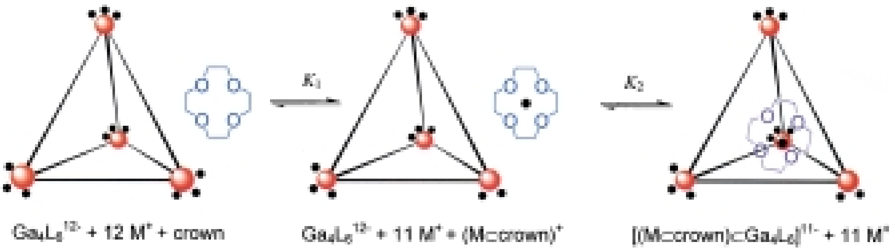


Figure 3. ^7Li NMR spectra of a) $Li_{11}[(Li^+ \subset [12]crown\text{-}4) \subset Ga_4L_6]$ and b) $Li_{11}[(Li^+ \subset [15]crown\text{-}5) \subset Ga_4L_6]$. The filled circle represents fully solvated Li^+ ions located outside the cluster, and the filled squares represent Li^+ ions complexed to the crown ether and encapsulated inside the cluster cavity.

Equilibrium constants for the encapsulation of crown ethers into the host were determined on the basis of the reaction sequence shown in Scheme 1. The first step is coordination of the aqueous cation by the crown ether to form the metal–crown ether complex $M^+ \subset$ crown ($M^+ = K^+$, Na^+, Li^+), for which the equilibrium constant is designated K_1 [Eq. (1)]. (We have used the literature values for K_1.[13] Although interaction between M^+ and the catecholate oxygen atoms has been observed in the ESI-mass spectra, this binding does not affect all 12 of the counterions and in any case is much smaller than the formation constants of the macrocyclic ether. We have therefore assumed no significant reduction in the concentration of M^+ by ion-pair formation in these calculations.) The next step is the inclusion of $M^+ \subset$ crown into the tetrahdral host cluster (Ga_4L_6) to form $[(M^+ \subset \text{crown}) \subset Ga_4L_6]^{11-}$ for which the equilibrium constant is K_2 [Eq. (2)].



Scheme 1. The encapsulation of an alkali metal cation from $M_{12}[Ga_4L_6]$, ($M = Li^+$, Na^+, or K^+) by a crown ether (equilibrium constant K_1) is followed by encapsulation of the crown ether complex into the cluster cavity (K_2).

$$K_1 = \frac{[M^+ \subset \text{crown}]}{[\text{crown}]\,[M^+]} \qquad (1)$$

$$K_2 = \frac{[(M^+ \subset \text{crown}) \subset Ga_4L_6]}{[Ga_4L_6]\,[M^+ \subset \text{crown}]} \qquad (2)$$

The concentration of all the species included in the equation are determined from the ^1H NMR spectra and the values of K_2 are calculated.[14] The results in Table 1 show that K_2 decreases as the size of the crown ether increases. This trend is similar to that previously observed in the encapsulation of amines, in which equilibrium constants decrease in the order $Et_4N^+ > Pr_4N^+$ (while Bu_4N^+ was not encapsulated at all). The weaker binding of the larger crown complex guests is attributed to their inability to fit into the host cavity.[5]

Table 1. The equilibrium constants [$mol^{-1}\,dm^3$] for the inclusion of various M^+–crown ether complexes ($M = Na^+$ or K^+) into $[Ga_4L_6]^{12-}$ in D_3COD at 298 K. For the definition of K_1 and K_2 see Scheme 1.

Guest	K_1[a]		K_2	
	Na^+	K^+	Na^+	K^+
[12]crown-4	29	38	3400	2700
[15]crown-5	1400	3900	21	18
[18]crown-6	2300	1.4×10^6	< 0.1	< 0.1

[a] The K_1 values are taken from ref. [13]. Values for Li^+ are not included because the differences in literature values are too large to consider these values reliable.

The conformational freedom of crown ethers in solution results in a single, dynamically averaged proton resonance in the NMR spectra of both the free ligands and cation complexes of [12]crown-4, [15]crown-5, and [18]crown-6. However, inclusion of the cation–crown ether complex into the $[Ga_4L_6]^{12-}$ cavity results in a splitting of this single resonance into multiple peaks, which implies that there is a conformational constraint of the encapsulated cation–crown ether complex. This splitting of the NMR resonances occurs regardless of the particular cation ($M^+ = Li^+$, Na^+, or K^+). The limited volume of the cluster interior evidently locks the M^+-crown ether complex in a fixed conformation. The variable temperature studies shown in Figure 4 show a general trend: the constrained conformation of encapsulated [12]crown-4 completely relaxes at 353 K (as indicated by the coalescence of multiple resonances into a singlet), while the encapsulated [15]crown-5 remains in a constrained conformation even at 363 K. The larger volume of [15]crown-5 apparently makes it more constrained inside the host cavity.

The coordination of solvated cations by crown ethers requires complete or partial desolvation of the cation. It has been found that cation complexation by small crown ethers such as [12]crown-4 and [15]crown-5 does not completely remove the solvation shell of the cation.[15] Thus, the inclusion reactions were performed in different solvents to test whether solvent molecules are part of the encapsulated cation–crown

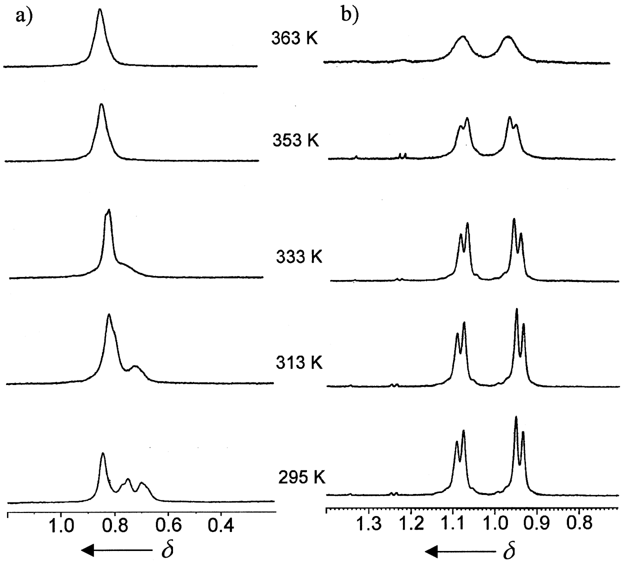


Figure 4. Variable-temperature ^1H NMR spectra of a) $Li_{11}[(Li^+ \subset [12]crown\text{-}4) \subset Ga_4L_6]$ and b) $L_{11}[(Li^+ \subset [15]crown\text{-}5) \subset Ga_4L_6]$ in D_2O. Only the NMR resonances of the encapsulated crown ether are shown.

ether complex. Figure 5 shows that the ^1H NMR resonances of the encapsulated crown ethers differ significantly depending on the solvent. While a set of sharp doublets and doublets of doublets is seen for the encapsulated crown ether of $M_{11}[(M^+ \subset [15]crown\text{-}5) \subset Ga_4L_6]$ in D_2O, only one sharp doublet and a broad peak for the encapsulated ether are observed in D_3COD. The proton NMR spectrum of $M_{11}[(M^+ \subset [12]crown\text{-}4) \subset Ga_4L_6]$ shows a similar trend. In each case examined the solvent affects both the chemical shift and the conformation of the included crown ethers, which implies that the encapsulated metal–crown ether complex is interacting with the solvent. We interpret this as showing that the solvent molecule is incorporated in the inner coordination sphere of the alkali ion–crown complex. The volume of the cluster cavity, estimated as 350 Å^3,[6] should be able to accommodate one [12]crown-4 or [15]crown-5 moiety along with one or two solvent molecules. The ability of the naphthalene bridging groups of the host to bend outward apparently allows accommodation of guests even as large as $[\{C_5(CH_3)_5\}_2Co]^+$.[16]

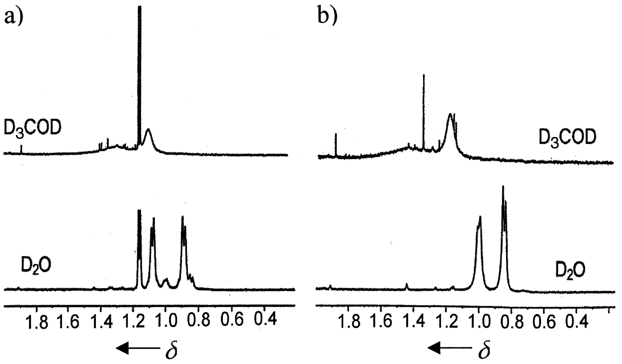


Figure 5. ^1H NMR spectra of a) $Li_{11}[(Li^+ \subset [12]crown\text{-}4) \subset Ga_4L_6]$ and b) $Na_{11}[(Na^+ \subset [15]crown\text{-}5) \subset Ga_4L_6]$ in D_2O and D_3COD. Only the NMR resonances of the encapsulated crown ether are shown.

The host–guest chemistry presented in this study involves multiple recognition events: the cations from the metal cluster complex are first encapsulated by the crown ether host, and subsequently the cation–crown ether host–guest complex is encapsulated into the metal cluster. While the first type of recognition has been well known and thoroughly studied, this is the first example of selective cation incorporation into a metal cluster host by a cation–crown ether: a host within a host.

Experimental Section

The ligand L and the supramolecular cluster $M_{12}[Ga_4L_6]$ ($M = Li^+, Na^+$, or K^+) were synthesized according to previously reported procedures.[5, 6] The crown ethers were purchased and used as such. All NMR measurements were done on a Bruker DRX 500 MHz instrument. For the determination of the equilibrium rate constants, 1×10^{-6} mol of $M_{12}[Ga_4L_6]$ was dissolved in 200 µL of D_3COD, and an equimolar amount of crown ether (10 µL of 100 mM solution in D_3COD) was added to this solution. The total volume was adjusted to 600 µL by addition of D_3COD. For 2D NOESY measurements the sample was prepared in a similar way, except that the crown ether was present in twofold excess with respect to the cluster. 2D NOESY spectra were obtained at 300 K using standard NOESY sequences, with $d_1 = 2$ sec and $d_8 = 100$ msec.

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