Metal-Assembled Cobalt(II) Resorc[4]arene-Based Cage Molecules That Reversibly Capture Organic Molecules from Water and Act as NMR Shift Reagents

O. Danny Fox,[†] **Jenny F.-Y. Leung, Jesse M. Hunter, N. Kent Dalley, and Roger G. Harrison***

Department of Chemistry and Biochemistry, Brigham Young University, Provo, Utah 84602

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The complex $Co_4\mathbf{1}_2^{8-}$ is a tetranuclear cobalt(II) cage compound that assembles in aqueous solutions above pH 4 and is capable of encapsulating a variety of organic guest molecules, for example, benzene, hexane, chlorobutane, butanol, and ethyl acetate. Ligand **1** is a resorc[4]arene-based molecule with iminodiacetate moieties appended to its upper rim. ^1H NMR studies of $Co_4\mathbf{1}_2^{8-}\cdot$guest complexes demonstrate inclusion of nonpolar hydrocarbons, substituted phenyls, alcohols, halogen-containing hydrocarbons, and polar organic molecules. The complex $Co_4\mathbf{1}_2^{8-}$ acts as an NMR shift reagent and causes substantial upfield isotropic hydrogen shifts (−30 to −40 ppm) in the guest molecule and separation of the guest hydrogen chemical shifts by typically 12 ppm. The complex $Co_4\mathbf{1}_2^{8-}$ will encapsulate molecules with fewer than eight atoms in a linear chain, mono- and disubstituted benzenes, and polar molecules with greater than two carbon atoms. The solid-state structure of $Ba_4[Co_4\mathbf{1}_2\cdot C_6H_5C_2H_5]$ shows a disordered guest molecule encapsulated within the cavity of $Co_4\mathbf{1}_2^{8-}$. The cavity dimensions, bond lengths, and bond angles of $Ba_4[Co_4\mathbf{1}_2\cdot C_6H_5C_2H_5]$ are very similar to those determined in $Ba_4[Co_4\mathbf{1}_2\cdot 6H_2O]$.

Introduction

Cardboard boxes and metal cages are used extensively in our every day lives for storage, protection, and transportation. Chemists have sought to form boxes and cages at a molecular level. Research in this area has developed our understanding of the self-assembly process, the dynamics of a single molecule within a cage, and the mechanism of physical entrapment of a single molecule. Pioneers in the area of molecular cages have been successful in constructing carcerands and hemicarcerands.[1] The formation of these molecules relies on the covalent linking of two cup-shaped resorcinarene molecules. These cages trap molecules permanently in the case of the carcerands and nonpermanently in the case of hemicarcerands.

One goal of this area of host−guest chemistry has been the design of molecules that will trap and release guest molecules.[2] As this field of research has progressed, cage molecules that are linked by hydrogen bonds have been synthesized.[3] The hydrogen-bonded cages have the unique ability to be opened and closed without destroying the components of the cage. Their ability to encapsulate guest molecules has also been explored, and the cages have proven to be selective in what they encapsulate. Hemicarcerands can be caused to release guests upon heating, while the hydrogen-bonded cages can be opened or closed by adjusting the solvent or the guest. Other methods of guest release, including photo-, pH-, and redox-induced chemistry, will be employed as these molecules are applied to the areas of sensors and separations.

Another area of chemistry that has been exploding in research activity is formation of metal-assembled structures.[4] Most notable are metal-assembled grids, ladders, rings, interlocking grids, and two- and three-dimensional lattices.[5] Our understanding is advancing on how to make ordered one-, two-, and three-dimensional materials that are based on metal ions and might serve as molecular magnets, separations materials, or ion sensors. Some of these grids and structures have units that are shaped like boxes and might prove to be able to encapsulate guest molecules.

The research in our group has focused on a union between molecular cages and metal-assembled grids, resulting in the formation of metal-assembled cage molecules. There has recently been a flurry of interest in forming metal-assembled cage molecules.[6] Ligand structure, ligand chelation properties,

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* To whom correspondence should be addressed. Phone: (801) 378-8096. Fax: (801) 378-5474. E-mail: roger_harrison@byu.edu.

[†] Current address: Inorganic Chemistry Laboratory, South Parks Road, Oxford, Oxon, OX1 3QR, U.K.

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and metal coordination geometry are important in the formation of the cages. We have shown that metal-assisted assembly of two cup-shaped resorcinarene molecules results in the formation of carcerand type molecules.[7] The cage formation is in contrast to the many examples of metal coordination by other resorcinarenes and calixarenes where metal ions coordinate to one calixarene or do not form an encapsulated cavity.[8] The metal-assembled cage molecules are formed in water, and the metal–ligand bonds make them stable at neutral pH. However, at low pH, the ligands become protonated, the metal ions no longer coordinate to the resorcinarene molecules, and the cage falls apart. This is very unlike the hydrogen-bonded cage complexes that are destroyed in protic solvents and the covalently linked complexes that are unaffected by pH if they are soluble in protic solvents at all.

Because of the unique aspects of assembling cage complexes with metal ions and the pH dependence of the assembly process, we have explored the ability of the cage molecules to encapsulate organic guests and shift their NMR signals. Our goals are to give insight into the feasibility of trapping organic molecules from aqueous solution, into how these metal-assembled cages can be used as NMR shift reagents, and into how pH can be used to induce cage formation or destruction. Through NMR spectroscopy and X-ray crystallography, our results show that a variety of organic guests are encapsulated by the cage molecules. The encapsulation of organic molecules from water is noteworthy because of the application these molecules might have for the removal of organic contaminants from water. The metal-assembled containers also act as NMR shift reagents, causing the NMR signals of encapsulated guests to shift 25–40 ppm. However, the guest does not need to contain a heteroatom that coordinates to the paramagnetic metal to have its proton resonances shifted, as is the case with other NMR shift reagents. These metal–resorcinarene based molecules act as true cage molecules because they encapsulate guest molecules that are not solvent molecules and not counterions but are molecules that have been introduced into the solution. This is important because it shows that these metal-assembled cages prefer to encapsulate guest molecules instead of solvent and thus have potential as selective hosts.

Experimental Section

General Procedures. All commercial reagents and solvents were used as supplied unless noted. IR spectra were recorded using a Perkin-Elmer instrument. ^{1}H NMR spectra were obtained on Varian spectrometers operating at 500, 300, or 200 MHz and referenced to TMS = 0 ppm or HDO = 4.80 ppm. FAB mass spectra were obtained on a Joel JMS-SX102A operating with Xe ionization. MHW laboratories, AZ, performed elemental analyses. Elemental analyses for these compounds are included. However, because of the large molecular weights of these complexes and the presence of numerous solvent molecules within the crystal lattice, this method is not accurate enough to be used for determining whether guest inclusion has occurred.

Synthesis of 1,21,23,25-Tetramethyl-2,20:3,19-dimetheno-1*H*,21*H*,23*H*,25*H*-bis[1,3]dioxocino[5,4-*i*:5′,4′-*i*′]benzo[1,2-*d*:5,4-*d*′]bis[1,3]-benzodioxocin-7,11,15,28-tetramethylene Ethyl Iminodiacetate, 1a. To a solution of tetra(bromomethyl)cavitand[9] (1.0 g, 1.0 mmol) and diethyl iminodiacetate (1.6 g, 8.3 mmol) in freshly distilled THF (150 mL) was added potassium carbonate (3.0 g, 22 mmol), and the mixture was heated under reflux (12 h). When the mixture was cooled to room temperature, insoluble impurities and residual potassium carbonate were removed by filtration and the solution evaporated (under reduced pressure) to a viscous yellow oil. The addition of diethyl ether afforded a brown solid, which was removed by filtration through a Celite pad and discarded. Upon standing, white crystals of **1a** were deposited (0.82 g, 56%). Crystals suitable for X-ray diffraction were grown by vapor diffusion of diethyl ether into a solution of **1a** in chloroform, mp 159–162 °C. IR (KBr mull) cm^{-1}: 2977s, (CO) 1742vs, 1468s, 1192s, 979s, 585w. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.20 (s, 4 H, C_6H), 5.80 (d, 4 H, $J = 7.2$, outer OCH_2O), 4.98 (q, 4 H, $J = 7.4$, $CHCH_3$), 4.13 (m, 12 H, inner OCH_2O overlapped with ester CH_2CH_3), 3.71 (s, 8 H, benzyl CH_2), 3.49 (s, 16 H, CH_2CO_2R), 1.73 (d, 12 H, $J = 7.2$, $CHCH_3$), 1.14 (t, 12 H, $J = 7.2$, ester CH_2CH_3). MS (FAB) *m*/*e*: 1396 (M^+, 100%). Anal. Calcd for $C_{72}H_{92}N_4O_{24}\cdot 0.5CHCl_3$: C, 59.70; H, 6.40; N, 3.84. Found: C, 59.70; H, 6.17; N, 3.57.

Synthesis of $Ba_4$1·*x*H_2O. A solution of **1a** (0.40 g, 0.29 mmol) in THF (75 mL) was treated with a suspension of barium hydroxide octahydrate (0.81 g, 2.6 mmol) in water (50 mL). The mixture was heated and stirred (80 °C, 14 h) and cooled to room temperature. The precipitate thus formed was removed by filtration, washed with acetone and ether, and left to dry to yield the barium salt of **1** as a white powder (0.60 g, 96%). IR (KBr mull) cm^{-1}: 3400br, 1578vs, 1408, 974. ^{1}H NMR (500 MHz, D_2O/trifluoroacetic acid): δ 7.71 (s, 4 H, C_6H), 5.83 (d, 4 H, $J = 7.0$, outer OCH_2O), 4.36 (s, 8 H, benzyl CH_2), 4.21 (d, 4 H, $J = 7.0$, inner OCH_2O), 4.04 (s,16 H, CH_2CO_2H), 1.79 (d, 12 H, $J = 7.0$, $CHCH_3$). Anal. Calcd for $C_{56}H_{52}Ba_4N_4O_{24}\cdot 24H_2O$: C, 31.33; H, 4.70; N, 2.61. Found: C, 31.24; H, 4.07; N, 2.37.

Synthesis of $Ba_4$2·*x*H_2O. Compounds **2a** and Ba_4**2** were synthesized in a manner similar to that for **1a** and Ba_4**1** except the tetra(bromomethyl)cavitand with ethyl instead of methyl groups on the lower rim was used.[9] ^{1}H NMR for **2a** (300 MHz, $CDCl_3$): δ 7.07 (s, 4 H, C_6H), 5.80 (d, 4 H, $J = 7.0$, outer OCH_2O), 4.67 (t, 4 H, $J = 7.2$, $CHCH_2CH_3$), 4.11 (m, 20 H, inner OCH_2O overlapped with ester CH_2CH_3), 3.71 (s, 8 H, benzyl CH_2), 3.49 (s, 16 H, CH_2CO_2R), 2.24 (m, 8 H, $CHCH_2CH_3$), 1.12 (t, 24 H, $J = 7.2$, ester CH_2CH_3), 0.97 (t, 12 H, $J = 7.2$, $CHCH_2CH_3$). ^{1}H NMR for Ba_4**2** (300 MHz, D_2O/trifluoroacetic acid): δ 7.34 (s, 4 H, C_6H), 5.67 (d, 4 H, $J = 7.0$, outer OCH_2O), 4.42 (t, 4 H, $J = 7.2$, $CHCH_2CH_3$), 4.20 (s, 4 H, benzyl CH_2), 4.04 (d, 4 H, $J = 7.0$, inner OCH_2O), 3.89 (s, 16 H, CH_2CO_2R), 2.15 (m, 8 H, $CHCH_2CH_3$), 0.75 (t, 12 H, $J = 7.2$, $CHCH_2CH_3$).

Synthesis of $Ba_4[Co_4$1$_2\cdot C_6H_5C_2H_5]\cdot$*x*$H_2O$. Compound Ba_4**1**$\cdot 24H_2O$ (33 mg, 0.016 mmol) was stirred in 1 M hydrochloric acid (1 mL) and water (2 mL) until a clear solution was obtained. Cobalt(II) chloride hexahydrate (9.0 mg, 0.038 mmol) and ethylbenzene (0.25 mL) were added and the resultant pale-pink mixture stirred vigorously for 30 min. Potassium carbonate was then added until the solution became pink (approximately pH 5), at which time it was filtered and layered with isopropyl alcohol. After 2 days, pink prism crystals of $Ba_4[Co_4$**1**$_2\cdot C_6H_5C_2H_5]\cdot 48H_2O$ formed.[10] Anal. Calcd for $C_{112}H_{104}Co_4Ba_4N_8O_{48}\cdot C_6H_5C_2H_5\cdot 48H_2O$: C, 35.27; H, 5.14; N, 2.74. Found: C, 35.27; H, 4.31; N, 2.79.

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Encapsulation Studies. The following technique was used. To a solution of $\mathrm{Ba_4L{\cdot}24H_2O}$ (100 mg) dissolved in 1 M HCl (2.0 mL) and water (7.0 mL) was added $\mathrm{K_2SO_4}$ (50 mg) and $\mathrm{CoCl_2{\cdot}6H_2O}$ (25 mg). The white precipitate of $\mathrm{BaSO_4}$ that formed was removed by filtration. The potassium salt of **1** was used for the NMR studies because of the good solubility of $\mathrm{K_8Co_4}\mathbf{1}_2$ in water and the low solubility of $\mathrm{Ba_4Co_4}\mathbf{1}_2$. After the solution was filtered, to 3 mL of this stock solution was added guest (0.25 mL) and the mixture stirred vigorously (20 min). While the mixture was stirred, $\mathrm{K_2CO_3}$ was added until pH 5 was reached, and the mixture was then placed under vacuum (24 h, 1 mmHg). The dry residue was dissolved in $\mathrm{D_2O}$ and filtered over Celite, and its ^{1}H NMR spectra were recorded over the range 200 to −100 ppm. No significant improvement in reproducibility of chemical shifts values was found by addition of a reference compound, e.g., ethanol, isopropyl alcohol, or DMF. Control experiments were conducted to verify that observation of included guest molecules required the presence of ligand and cobalt(II) at pH 5 or greater. If the resorc[4]arene ligand was substituted for *N*-benzyliminodiacetic acid or iminodiacetic acid, guest inclusion was not observed. These latter experiments were run in duplicate, with benzene or toluene as guest molecules.

Encapsulation of the guest can also be done in solution without isolating solid $\mathrm{Co_4}\mathbf{1}_2^{8-}{\cdot}$guest. To a solution of $\mathrm{Ba_4L{\cdot}24H_2O}$ (100 mg) dissolved in 20 wt % $\mathrm{DCl/D_2O}$ (0.20 mL) and $\mathrm{D_2O}$ (4.0 mL) was added $\mathrm{K_2SO_4}$ (50 mg). The solution was centrifuged and the white precipitate of $\mathrm{BaSO_4}$ removed. $\mathrm{CoCl_2{\cdot}6H_2O}$ (25 mg) was added to the clear supernatant. To an aliquot of this stock solution (1 mL) was added guest (0.10 mL), and the mixture was stirred vigorously for 1 h. $\mathrm{K_2CO_3}$ was added until pH 5 was reached, and then the ^{1}H NMR spectra were recorded over the range 200 to −100 ppm. These experiments, which were prepared directly in $\mathrm{D_2O}$, confirmed that it is not necessary to place the compounds under vacuum to encapsulate guest molecules. Larger, less volatile guests (benzene, toluene, THF), when encapsulated this way, give the same results as they did when encapsulated by the vacuum-drying method. Preparation of $\mathrm{Co_4}\mathbf{1}_2^{8-}{\cdot}$guest in solution was employed for guests that leave the cavity after encapsulation, such as acetonitrile and ethanol.

X-ray Crystallography for Compounds 1a and $\mathbf{Ba_4[Co_4 1_2{\cdot}C_6H_5C_2H_5]}$. Crystallographic and structural refinement data are listed in Table 12. The data for **1a** were collected using a Siemens R3m/V automated diffractometer with graphite monochromated Mo Kα radiation (λ = 0.710 73 Å). Data for $\mathrm{Ba_4[Co_4}\mathbf{1}_2\mathrm{{\cdot}C_6H_5C_2H_5]}$ were collected using a Bruker P4 diffractometer also using Mo radiation. Lattice parameters for these compounds were calculated using a least-squares procedure involving a suitable number of carefully centered reflections. Partial structures were obtained using direct methods, and the structures were completed using Fourier methods. The refinement and display of each structure were carried out using the SHELXTL PC program package.[11] Complex $\mathrm{Ba_4[Co_4}\mathbf{1}_2\mathrm{{\cdot}C_6H_5C_2H_5]}$ contains disordered barium cations in two positions (2:1 ratio), separated by 1.5 Å and coordinated to carboxylate oxygens from the resorcinarene as well as water molecules. The non-hydrogen atoms and most of the water oxygen atoms of $\mathrm{Ba_4[Co_4}\mathbf{1}_2\mathrm{{\cdot}C_6H_5C_2H_5]}$ were refined anisotropically. The positions of the hydrogen atoms bound to carbon atoms in the structures were calculated and allowed to ride on their neighboring carbon atoms during the refinement. For $\mathrm{Ba_4[Co_4}\mathbf{1}_2\mathrm{{\cdot}C_6H_5C_2H_5]}$, the structure also included loosely held solvent water molecules outside of the cavity and disordered electron density within the cavity. The crystals lost solvent rapidly, so they were immersed in the mother liquor and sealed in a capillary tube for data collection.

Table 1. Crystal Data and Structure Refinement for **1a** and $\mathrm{Ba_4[Co_4}\mathbf{1}_2\mathrm{{\cdot}C_6H_5C_2H_5]}$

compound	**1a**	$\mathrm{Ba_4[Co_4}\mathbf{1}_2\mathrm{{\cdot}C_6H_5C_2H_5]}$
empirical formula	$\mathrm{C_{73}H_{93}Cl_3N_4O_{24}}$	$\mathrm{C_{123}H_{160}Ba_4Co_4N_8O_{75}}$
fw (g mol^{-1})	1516.86	3729.68
T (K)	293(2)	293(2)
λ (Å)	0.710 73	0.710 73
crystal system	monoclinic	tetragonal
space group	$P2_1/n$	$I4_1/a$
color of crystal	cream	pink
a (Å)	17.766(11)	20.118(2)
b (Å)	17.159(10)	20.118(2)
c (Å)	25.958(9)	54.35(2)
α (deg)	90	90
β (deg)	106.30(4)	90
γ (deg)	90	90
V (Å^3)	7595(7)	21997(7)
Z	4	4
ρ_{calcd} (g cm^{-3})	1.327	1.126
μ(Mo Kα) (mm^{-1})	0.200	1.068
F(000)	3208	7532
θ range (deg)	2.51−20.06	2.29−19.99
total no. of reflections	7419	5803
no. of unique reflections	7118	5045
no. refined	7089	5014
no. of parameters	932	502
R (int)	0.0742	0.0686
GOF	1.055	1.059
R [$I > 2\sigma(I)$]^a	0.0819	0.0988
wR2^b	0.1872	0.1970

^{a} $R = \sum||F_o - F_c||/\sum|F_o|$. ^{b} $\mathrm{wR2} = \{\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]\}^{1/2}$.

Results

The metal cage complexes we have synthesized rely on two cup-shaped resorcinarenes being brought together. Resorcinarenes are closely related to calixarenes.[12] Synthesis of resorcinarenes involves the joining of four phenyl moieties into a ring, which results in a molecule with a cavity. By the attachment of four metal-coordinating ligands to the upper rim of a resorcinarene, **1a** is formed (Scheme 1). This is accomplished by adding a brominated resorcinarene to iminodiacetate ethyl ester in the presence of base. The crystal structure of **1a** shows (Figure 1) four phenyl moieties in a ring with iminodiacetate groups bonded to them. While it is common to draw functional groups attached to resorcinarenes extending upward, in **1a** they do not increase the depth of the cavity but lie along the side of the cavity. This placement of the iminodiacetate groups away from the cavity is beneficial for guest binding to the cavity because metal coordination can be directed away from the cavity without obstructing it. Hydrolysis of **1a** with barium hydroxide results in the formation of the barium salt of compound **1**, which has iminodiacetate groups on the resorcinarene. The barium salt of **1** is used as the source of **1** in studies with metal ions. Compound **2** is similar to **1** except it has ethyl groups around the lower rim of the resorcinarene instead of methyl groups (Scheme 1). The presence of ethyl groups is helpful in making assignments of the hydrogen NMR resonances of the metal-bound resorcinarenes.

^{1}H NMR Studies of $\mathbf{Co_4 1_2^{8-}}$. When Co^{2+} ions are added to a neutral aqueous solution of **1**, metal coordination occurs.[13]

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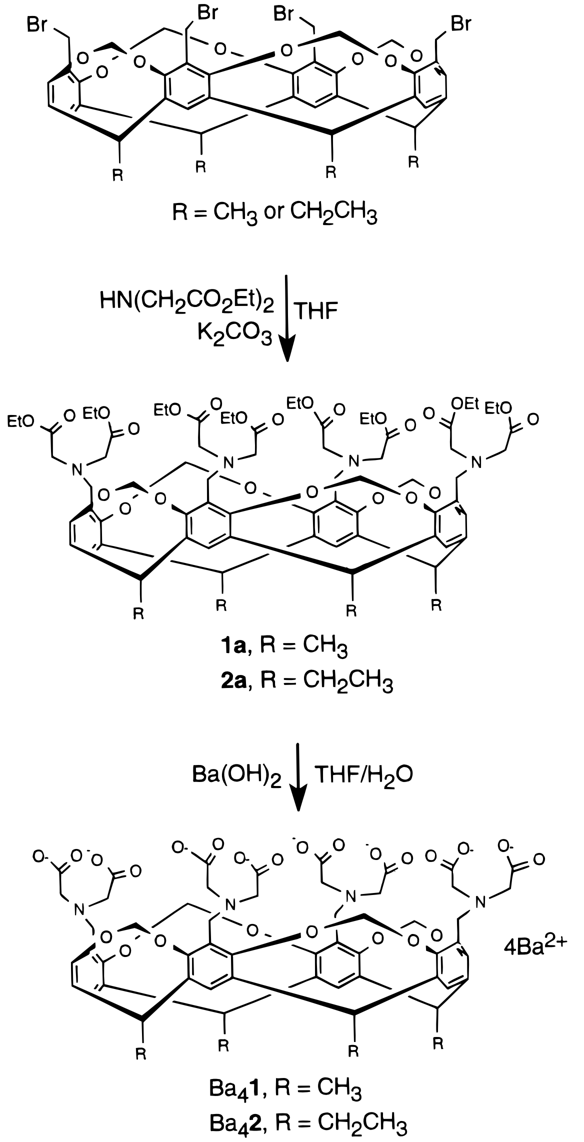
Scheme 1



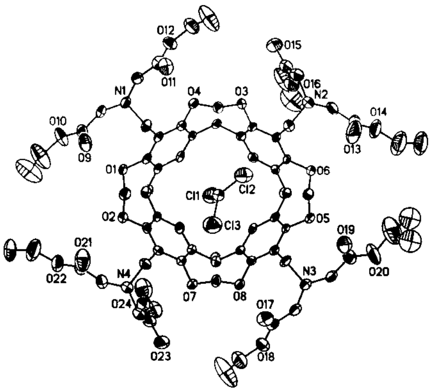
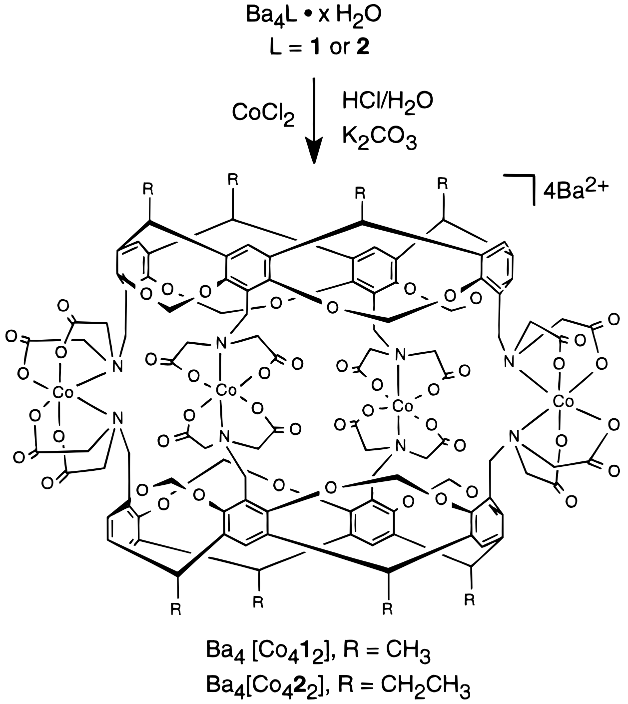


Figure 1. Solid-state structure of **1a** showing the cavity and a chloroform molecule within the cavity. The ellipsoids are 30%, noncarbon atoms are labeled, and hydrogen atoms have been omitted for clarity.

Scheme 2



Instead of the metal ions bonding to only one molecule of **1**, they coordinate to two molecules of **1** and do so in a fashion that creates a cage molecule with a cavity, $Co_4\mathbf{1}_2^{8-}$ (Scheme 2). X-ray crystallography establishes the structure of the tetranuclear cobalt(II)-assembled resorcinarene-based cage molecule. Knowing the solid-state structure of $Co_4\mathbf{1}_2^{8-}$ helps in understanding the ^1H NMR spectra of $Co_4\mathbf{1}_2^{8-}$. Fifteen proton resonances are observed for $Co_4\mathbf{1}_2^{8-}$, eight more than the seven observed for **1**. Not only are there more proton resonances, but they are spread over 200 ppm and are significantly broader than they were before. The resonances come at δ (ppm, DHO = 4.80 ppm, peak integration or description in parentheses) 166 (broad), 132 (broad), 93 (broad), 15.8 (4H), 12.4 (4H), 4.6 (12H), 1.7 (8H), −1.4 (12H), −7.6 (4H), −9 (broad), −11.7 (4H), −21 (broad), −28.4 (4H), −32.5 (4H), −68 (broad). The fifteen resonances can be explained by careful consideration of the arrangement of the isomeric forms of the cobalt centers. Each cobalt center can be in a Δ or Λ configuration. The crystal structure shows the cobalt centers in $Ba_4[Co_4\mathbf{1}_2{\cdot}6H_2O]$ to be in an alternating $\Delta\Lambda\Delta\Lambda$ arrangement. With this arrangement of cobalt centers, the cage belongs to the D_{2d} point group and has one principle C_2 axis and two perpendicular C_2 axes that run across the molecule through the cobalt centers.[14] These perpendicular C_2 axes relate the top bowl to the bottom bowl and four of the methyls, methynes, and ether methylenes to each other but do not relate all eight to each other. The cage molecule also has two dihedral planes of symmetry that bisect the methyl, methyne, and etheryl groups. These planes relate the aryl, benzylic, and acetate hydrogens of the different subunits, and thus, the aryl hydrogens are chemically equivalent, the benzylic hydrogens are chemically equivalent, and the acetate hydrogens are chemically equivalent. The planes do not, however, relate the methyl, methyne, and etheryl hydrogens. Thus, two sets of resonances for the hydrogens on the methyl, methyne, and etheryl groups are expected. If the arrangement of cobalt centers that exists in the crystal structure is retained in solution, then 15 proton resonances are expected. Fifteen NMR proton resonances are observed. These 15 resonances can be attributed to 4 acetate protons, 2 benzylic protons, 1 aryl proton, a set of

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(14) For a discussion of predicted hydrogen signals for the different possible isomers, see Supporting Information. See Supporting Information for a table of chemical shifts, peak assignments, and a labeled structural drawing.

2 methyl protons, a set of 2 methyne protons, a set of 2 inner etheryl protons, and a set of 2 outer etheryl protons. If the ΔΔΔΔ or ΛΛΛΛ, ΔΔΔΛ or ΛΛΛΔ, ΔΔΛΛ or ΛΔΔΛ, or fast exchange conformers were to exist, then 11, 44, 26, and 8 resonances would be expected, respectively.

The peak assignments of $\mathrm{Co}_4\mathbf{1}_2^{8-}$ can be made by using the ^{1}H chemical shifts, peak integration, and t_1 values that lengthen with increased hydrogen distance from cobalt[15] and by using the ^{1}H chemical shifts of complex $\mathrm{Co}_4\mathbf{2}_2^{8-}$. The ^{1}H NMR spectrum of complex $\mathrm{Co}_4\mathbf{2}_2^{8-}$ had two new resonances, one at 5.70 and another at −1.60 ppm, and two resonances that decreased in integration and shifted slightly to 4.38 and −0.84 ppm. Many of the ^{1}H absorptions remained unchanged and are attributed to hydrogens that are in the same environment for both $\mathrm{Co}_4\mathbf{1}_2^{8-}$ and $\mathrm{Co}_4\mathbf{2}_2^{8-}$, namely, the acetate, benzylic, aryl, and etheryl. After considering peak chemical shifts, integrations, t_1 values, and positions in $\mathrm{Co}_4\mathbf{2}_2^{8-}$, the peak assignments for $\mathrm{Co}_4\mathbf{1}_2^{8-}$ are δ 166, 93 benzylic; 132, −9, −21, −68 acetate; 15.8, −11.7, −28.4, −32.5 etheric; 12.4, −7.6 methyne; 4.6, −1.4 methyl; 1.7, aryl.[16] We have not assigned inner or outer etheric hydrogens, but we believe the resonances at −28.4 and −32.5 belong to the inner hydrogens. This is based on them having a chemical shift similar to those of encapsulated guest molecules and their movement downfield upon guest encapsulation. As these assignments show, each of the methyl, methyne, and etheric groups give rise to a set of two peaks.

Although water is observed within the cavity of $\mathrm{Co}_4\mathbf{1}_2^{8-}$ in the solid state, it is not easily observed by NMR spectroscopy.[17] Deuteriums from D_2O exchange with hydrogens from the water in the cavity. To observe the encapsulated water, we prepared $\mathrm{Co}_4\mathbf{1}_2^{8-}$ in H_2O/D_2O (4:1) solutions. At room temperature there is not an observed hydrogen peak corresponding to encapsulated water even in this H_2O solution. However, as the temperature is lowered, a resonance grows in and becomes intense at −20 °C.[18] The new resonance (−30 ppm) is observed in the chemical shift region where organic guest molecules are observed, while the host resonances remain in the same relative positions. For more evidence that this peak arises because of encapsulated water, we lowered the temperature of D_2O solutions of $\mathrm{Co}_4\mathbf{1}_2^{8-}$ and 4:1 H_2O/D_2O solutions of $\mathrm{Co}_4\mathbf{1}_2^{8-}$•benzene and $\mathrm{Co}_4\mathbf{1}_2^{8-}$•acetonitrile. New resonances were not observed in any of these experiments, and the benzene and acetonitrile guest resonances remained.

Guest Inclusion Studies. Noticing that $\mathrm{Co}_4\mathbf{1}_2^{8-}$ possessed a cavity with a volume of approximately 300 Å^3 motivated us to attempt to encapsulate guests. The solid-state structure showed that the cavity was lined with phenyl groups and that the anionic metal centers were positioned around the exterior of the cavity. We thus attempted to encapsulate organic molecules even though $\mathrm{Co}_4\mathbf{1}_2^{8-}$ is water-soluble. When $\mathrm{Co}_4\mathbf{1}_2^{8-}$ is formed in the presence of small organic molecules, the ^{1}H NMR signals of $\mathrm{Co}_4\mathbf{1}_2^{8-}$ shift from where they are when $\mathrm{Co}_4\mathbf{1}_2^{8-}$ is assembled without guest present.[19] The new resonances of $\mathrm{Co}_4\mathbf{1}_2^{8-}$ are consistently close to the same chemical shift over a wide range of guest molecules. As an example, when $\mathrm{Co}_4\mathbf{1}_2^{8-}$ is formed in the presence of cyclohexane, the new resonances for $\mathrm{Co}_4\mathbf{1}_2^{8-}$ are δ (ppm, DHO = 4.80 ppm, peak description or integration in parentheses) 159 (broad), 120 (broad), 96 (broad), 12.8 (4 H), 11.8 (4 H), 4.5 (12 H), 2.2 (8 H), −1.0 (12 H), −4 (broad), −6.4 (4 H), −12.4 (4 H), −22 (broad), −23.9 (4 H), −30.2 (4 H), −60 (broad). Most of the resonances with positive ppm values move upfield, while those with negative ppm values move downfield. In other words, the hydrogen resonances move slightly to the diamagnetic region.

Along with changes in the ^{1}H NMR chemical shifts of $\mathrm{Co}_4\mathbf{1}_2^{8-}$, new resonances appear that correlate to the protons on the added guest. In the following paragraphs we discuss the encapsulation results for aromatic molecules, alkanes, haloalkanes, alcohols, and nitrogen- and oxygen-containing molecules. To show the versatility of $\mathrm{Co}_4\mathbf{1}_2^{8-}$ in capturing organic molecules of varying size, shape, and polarity, a wide range of molecules are reported. The NMR chemical shifts for the encapsulated guests are found in Table 2.

Aromatic Molecules. Compound $\mathrm{Co}_4\mathbf{1}_2^{8-}$, although water-soluble, has a cavity lined with aromatic and aliphatic groups. When benzene is present during the formation of $\mathrm{Co}_4\mathbf{1}_2^{8-}$, the host cage ^{1}H NMR signals are shifted from where they come when no benzene is present and a new resonance is observed at −26.8 ppm (Figure 2). An almost identical NMR spectrum is obtained when d_6-benzene is present during cage formation, except for the expected loss of the resonance at −26.8 ppm. However, ^{2}D NMR spectra confirmed the presence of d_6-benzene. When toluene is present during cage formation, four new signals, −20.0, −23.4, −29.2, and −32.2 ppm with integral ratios of 1:3:2:2, are observed. Experiments with d_8-toluene give similar spectra except without the four new resonances. Interestingly, excellent resolution of the ortho, meta, and para protons of the toluene guest is observed, the separation between the lowest and highest field resonance being 12 ppm. This high degree of spectral resolution is also observed in the spectra of other monosubstituted aromatic host−guest complexes, such as chlorobenzene and bromobenzene (Table 2). As Table 2 shows, complete and facile capture of many aromatic guests is observed, even though most of the aromatic guests studied were imiscible with water. Aromatic molecules of intermediate size, such as 1,2-dichlorobenzene and *o*-xylene, consistently gave spectra indicative of mixtures of $\mathrm{Co}_4\mathbf{1}_2$•guest and $\mathrm{Co}_4\mathbf{1}_2$•6$H_2O$. Larger aromatic molecules such as 2-bromotoluene are not detected to enter $\mathrm{Co}_4\mathbf{1}_2^{8-}$, but instead $\mathrm{Co}_4\mathbf{1}_2$•6$H_2O$ is formed. Notably, with the family of xylenes, only *p*-xylene capture is quantitative, whereas *m*-xylene and *o*-xylene capture is not. This behavior is clearly consistent with the elliptical shape of the cavity within the cage and it being able to house a linear molecule. In all cases, integration of host and guest peaks is consistent with capture of a single guest molecule.

Alkanes. After observing encapsulation of aromatics, we felt aliphatic molecules would also be encapsulated even though

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(15) See Supporting Information for t_1 values.

(16) Because of the short t_1 values for both benzylic and acetate protons and their similar chemical shifts, the peak assignments for these protons are tentative.

(17) We initially placed the encapsulated water molecules outside the cavity, but through symmetry they are found to be within the cavity. Water molecules have previously been found within resorc[4]arene container molecules, both in mass spectrometric and X-ray studies, although this is not a frequently encountered phenomenon. (a) Choi, H.-J.; Buhring, D.; Quan, M. L. C.; Knobler, C. B.; Cram, D. J. *J. Chem. Soc., Chem. Commun.* **1992**, 1733. (b) Robbins, T. A.; Knobler, C. B.; Bellew, D. R.; Cram, D. J. *J. Am. Chem. Soc.* **1994**, *116*, 111.

(18) Peaks attributed to $\mathrm{Co}_4\mathbf{1}_2^{8-}$ remain constant in intensity and constant in position relative to each other. However, their chemical shifts change because of magnetic field changes with temperature. A temperature of −20 °C is obtained, since the solution contains $K_8[\mathrm{Co}_4\mathbf{1}_2]$ and $NCCD_3$. We did not observe a new deuterium resonance when deuterium NMR was performed on a D_2O solution of $\mathrm{Co}_4\mathbf{1}_2^{8-}$ in a manner similar to the that in low-temperature hydrogen NMR experiments.

(19) The resorc[4]arene ligand is needed for the ^{1}H NMR chemical shift changes. When *N*-benzyliminodiacetic acid or iminodiacetic acid is added to an aqueous solution of $CoCl_2$ and organic molecules in a manner similar to that for the resorc[4]arene ligand, no change in proton resonances is observed and no new signals for organic molecules are observed.

Table 2. ^{1}H NMR Chemical Shifts[a] and Percent Occupancy for Encapsulated Guest Molecules

guest	^{1}H chemical shift (integration)[b]					% occupied[c]
aromatic compounds						
benzene	−26.8					100
toluene	−20.0 (1)	−23.4 (3)	−29.2 (2)	−32.2 (2)		100
fluorobenzene	−24.0					100
chlorobenzene	−19.26 (1)	−28.3 (2)	−31.8 (2)			100
bromobenzene	−18.4 (1)	−26.7 (2)	−32.4 (2)			100
phenol	−19.2 (1)	−25.8 (2)	−30.8 (2)			100
o-xylene	−26.4 (2)	−29.0 (2)	−32.7 (3)	−33.5(3)		30
m-xylene	−24.4 (6)	−25.2 (3)	−33.1 (1)			35
p-xylene	−22.1 (3)	−32.0 (2)				100
ethylbenzene[d]	−23.4 (2)	−23.9 (5)	−30.7 (2)	−32.5 (2)		100
anisole[d]	−18.7 (1)	−20.7 (3)	−26.7 (2)	−32.1 (2)		100
alkanes and alkenes						
pentane	−26.7 (3)	−33.9 (2)	−37.1 (1)			80
hexane (2 sets, 9:1)[e]	−25.0 (3)	−34.7 (2)	−37.8 (2)			100
heptane	−24.7 (3)	−32.5 (2)	−34.2 (2)	−39.9 (1)	−40.4 (1)	90
2-methylpentane	−26.1 (3)	−32.5(6)	−33.3 (2)	−34.9 (1)	−37.2 (2)	90
2,2-dimethylpentane	−24.8 (2)	−32.0 (1)	−36.1 (6)	−37.1 (3)	−38.6 (2)	40
cyclohexane (2 sets, 9:1)[e]	−27.0 (1)	−34.7 (3)	−37.7(2)			90
alcohols						
ethanol	−30.7 (2)	−32.7 (3)				40
propanol	−26.8 (3)	−32.4 (2)	−32.8 (2)			90
butanol	−27.1 (3)	−32.6 (2)	−35.6 (2)	−36.6 (2)		80
pentanol	−26.2 (3)	−32.7 (4)	−36.1 (2)	−37.2 (2)		65
hexanol (2 sets, 4:1)[e]	−25.1 (3)	−25.4 (2)	−34.7 (2)	−36.4 (2)		95
	−38.0 (2)	−38.4 (2)				
2-propanol	−32.6					60
nonalcohols that contain oxygen or nitrogen						
acetone	−30.1 (1)	−32.6 (1)				50
diethyl ether	−26.9 (3)	−32.5 (2)				95
tetrahydrofuran	−30.3 (1)	−32.2 (1)				90
cyclohexanone	−31.0 (2)	31.4 (2)	−39.9 (1)			90
ethyl acetate	−24.8 (3)	−28.6 (2)	−30.6 (3)			95
acetonitrile	−24.8					100
haloalkanes						
chloroform	−27.3					100
dichloromethane	−22.5					90
ethyl iodide	−25.5 (3)	−31.2 (2)				95
1,2-dichloroethane	−26.0					90
1-bromopropane	−28.0 (2)	−33.6 (5)				100
2-bromopropane	−31.3 (6)	−32.5 (1)				100
1,3-dibromopropane	−29.8 (2)	−36.1 (1)				90
1-chlorobutane	−26.3 (3)	−29.5 (2)	−34.6 (2)	−36.6 (2)		100
2-chlorobutane	−28.0 (3)	−28.5 (3)	−33.6 (1)	−35.9 (1)	−36.2 (1)	100
1-bromobutane	−25.5 (3)	−30.9 (2)	−34.0 (2)	−36.6 (2)		100
1-iodobutane	−25.3 (3)	−33.7 (2)	−33.9 (2)	−36.5 (2)		100

[a] D_2O solutions at ambient temperature, ppm, referenced to DHO = 4.80 ppm. [b] Integral values are relative to other guest resonances and reliable to within 0.25 protons. [c] $[Co_2\mathbf{1}_4^{8-}\cdot\text{guest}/(Co_2\mathbf{1}_4^{8-}\cdot\text{guest} + Co_2\mathbf{1}_4^{8-}\cdot\text{water})] \times 100\%$. The narrow −1.0 and −1.4 ppm peaks were used for this calculation. [d] This guest causes each host peak to split into two signals of equal intensity. [e] Two sets of peaks are observed for the guest. The least intense set are 0.5−2 ppm upfield from the most intense set of peaks. Only the chemical shifts for the most intense set of peaks are given.

they also are quite insoluble in water. Indeed they are encapsulated. When an aqueous solution of **1** and alkane are vigorously stirred with $CoCl_2$ at pH above 5, host ^{1}H NMR resonances are shifted and new peaks correlating to alkane appear (Table 2). Straight-chain alkanes containing five to seven carbon atoms are encapsulated, while the eight-carbon-containing octane is not. Branched alkanes (2-methylpentane and 2,2-dimethylpentane) are also encapsulated. However, there is a limit to the degree of branching that is allowable; 2,4-dimethylpentane and 2,2,4-trimethylpentane are not encapsulated. These studies show that for alkanes to be encapsulated, they must have fewer than eight carbons in a straight chain and branching only at one end of their carbon chain.

Haloalkanes. As with aromatic and aliphatic compounds, when various haloalkanes, including fluorine, chlorine, bromine, and iodine functionalized compounds, are stirred with **1** and $CoCl_2$, host peaks are shifted and new resonances are observed (Table 2). Small multihaloalkanes such as 1,2-dibromoethane and 1,3-dibromopropane, as well as relatively small haloalkanes such as ethyl iodide, chloro-, bromo-, and iodobutane, were all captured quantitatively. The larger compounds, bromohexane and 1,2,3-tribromopropane, were not encapsulated. Guest resonances occur typically between −22 and −38 ppm. Several haloalkanes, notably chloro-, bromo-, and iodobutane, give excellent resolution of all of the hydrogens. Frequently, signals attributed to the methyl groups of guest molecules occur around −25 ppm, whereas methylene groups show larger variations in chemical shifts. The ability of $Co_4\mathbf{1}_2^{8-}$ to bind haloalkanes may be exploited in the sensing and/or removal of halogen-containing organic compounds from water.

Alcohols. The alcohols are polar molecules and miscible in water, unlike the aromatic, aliphatic, and haloalkane molecules. In order for alcohols to be trapped within $Co_4\mathbf{1}_2^{8-}$, their bonding interactions to water have to be overcome. When alcohols are stirred with **1** and $CoCl_2$, again the host cage peaks are shifted and new peaks correlating to alcohol arise (Table 2). However,

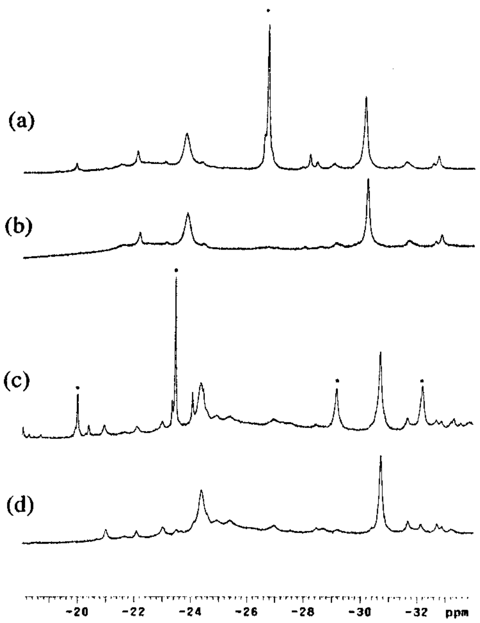

Figure 2. ^{1}H NMR spectra (-18 to -34 ppm, 300 MHz, D_2O) of (a) $\mathrm{Co}_4\mathbf{1}_2^{8-}$·benzene, (b) $\mathrm{Co}_4\mathbf{1}_2^{8-}$·benzene-$d_6$, (c) $\mathrm{Co}_4\mathbf{1}_2^{8-}$·toluene, and (d) $\mathrm{Co}_4\mathbf{1}_2^{8-}$·toluene-$d_6$. An asterisk (*) denotes a guest peak.

smaller alcohols such as methanol and ethanol are encapsulated to a lesser extent than the larger alcohols. This may be attributed to their stronger interaction with water. This shows the competition for the guest between the hydrophobic cavity of $\mathrm{Co}_4\mathbf{1}_2^{8-}$ and the solvent. The larger, more hydrophobic alcohols are quantitatively encapsulated by $\mathrm{Co}_4\mathbf{1}_2^{8-}$. Not only are the smaller alcohols more difficult to trap but they are observed to diffuse out of the cage over a period of a couple of days. The largest alcohol captured is hexanol; both heptanol and octanol are not.

Nonalcohols That Contain Oxygen and Nitrogen Atoms. After observing the encapsulation of alcohols, we attempted encapsulation of other polar molecules. When ethers, ketones, esters, and nitriles are stirred in water with **1** and $CoCl_2$, the host cage ^{1}H NMR peaks are shifted and new peaks are observed. Even though these molecules have shapes ranging from linear (acetonitrile, diethyl ether) to bent (acetone, ethyl acetate) to cyclic (THF, cyclopentanone, cyclohexanone), they are encapsulated. These polar molecules are more soluble in water and form stronger interactions with water than aromatic, aliphatic, and haloalkane molecules, yet this does not limit them from being encapsulated by $\mathrm{Co}_4\mathbf{1}_2^{8-}$. Thus, $\mathrm{Co}_4\mathbf{1}_2^{8-}$ competes favorably with solvent water for these molecules. Of the nonalcohols that contain oxygen listed in Table 2, acetone is the only one not encapsulated in quantities greater than 90%. Encapsulation of the very polar DMF in a manner similar to that of the other polar molecules is not successful. The encapsulation of polar molecules, including alcohols, demonstrates the versatility of $\mathrm{Co}_4\mathbf{1}_2^{8-}$ as a host molecule.

Host−Guest Complex Stability. The encapsulation of the guest molecules is dependent on pH. At pH values below 2, the carboxyl groups and amine nitrogen atoms are protonated and do not coordinate to cobalt(II) ions; thus, only free resorcinarene is detected at low pH. Upon deprotonation of the carboxyl groups at pH 5 by addition of base, the octaanionic, tetranuclear cobalt(II) cage assembles and is detected by ^{1}H NMR. Also, the ^{1}H NMR resonances of the guest are also observed to only shift upfield when the pH is above 5. Between pH 2 and 4, spectra attributed to a mixture of cage and free ligand are observed. This process can be put in a cycle by raising the pH and lowering it again, which promotes the opening and closing of the cage.

Most of the $\mathrm{Co}_4\mathbf{1}_2^{8-}$·guest complexes, especially those with guests of intermediate size such as benzene and hexane, are stable for weeks in D_2O solutions as shown by no decrease in intensity of the ^{1}H NMR signals of encapsulated guest over a period of a month. However, small guests that form bonding interactions with water (ethanol and propanol) are observed to leave the cage within days after encapsulation. Once the guests are encapsulated, they do not exchange with external guest molecules. This was seen by exposing 1 mL of aqueous solution of $\mathrm{Co}_4\mathbf{1}_2^{8-}$·benzene to 0.1 mL of d_6-benzene and toluene for 2 weeks while being stirred. No exchange of encapsulated guest for free guest or for water was observed. The cage is stable to excess cobalt(II) and does not fall apart into two halves because there is enough cobalt ions to occupy all of the ligand sights on **1**. This is shown by not observing a reduction in $\mathrm{Co}_4\mathbf{1}_2^{8-}$ formation when $CoCl_2$ is added in excess (greater than 2:1 ratio of Co^{2+} to **1**) or when $CoCl_2$ is added after $\mathrm{Co}_4\mathbf{1}_2^{8-}$ has been formed. These results indicate that $\mathrm{Co}_4\mathbf{1}_2^{8-}$·guest is in most cases stable in water and that the cage does not readily open and close. Thus, the straightforward way to release the guest is to disassemble the cage by lowering the pH.

Encapsulation Dependence on Guest Concentration. After noting that $\mathrm{Co}_4\mathbf{1}_2^{8-}$ selectively encapsulates small nonpolar molecules, we investigated its ability to capture the guest as a function of guest concentration. We thus added varying amounts of guest (toluene and benzene), 0.0005, 0.001, 0.002, 0.005, 0.01, 0.05, and 0.10 mL, to 1 mL of a 6.32×10^{-3} M $\mathrm{K}_8\mathbf{1}$ solution, vigorously stirred the solution for 20 min, and added $CoCl_2$ to form a cage. This study shows the competition between guest and water for the cage. We found that at low volumes of guest (<0.005 mL for toluene and < 0.01 mL for benzene), water competed for the cage's cavity, while at higher volumes of guest (>0.01 for toluene and 0.05 for benzene),[20] the cavities contained only guest. It is interesting to note that the formation of only the cage−guest complex occurs after the amount of guest added is beyond the solubility of guest in water. The solubility of guest (benzene 2.3×10^{-2} and toluene 6.6×10^{-3} M at 22 °C) is comparable to the concentration of $\mathbf{1}^{8-}$. Guest encapsulation may occur by **1** enhancing the solubility of guest in water or by guest being captured at the water−dispersed guest interface. Also noteworthy is that toluene is encapsulated more easily than benzene even though it is less soluble than benzene, which may indicate that trapping of guest occurs at the water−guest interface. These studies have led us to investigate the rate of cage formation and the selectivity of encapsulation between guests, experiments which will be reported later. Also, the current studies have given us an incentive to find association constants for guests and to develop a mechanism of guest encapsulation. The mechanism of encapsulation involves several steps and is more complicated than a simple guest + host equilibrium with host−guest complex. Some steps in the mechanism are association of guest with **1**, $\mathrm{Co}_4\mathbf{1}$, and/or $\mathrm{Co}_4\mathbf{1}_2^{8-}$ (before it closes), cobalt binding to **1**, and the coming together of two molecules of **1** and/or $\mathrm{Co}_4\mathbf{1}$.

Solid-State Structure of $\mathbf{Ba_4[Co_4}\mathbf{1}_2\mathbf{\cdot C_6H_5C_2H_5]}$. After observing guest encapsulation by NMR spectroscopy, we attempted to obtain solid-state evidence. Single crystals were grown by stirring an acidic aqueous solution of $\mathrm{Ba}_4\mathbf{1}$, $CoCl_2 \cdot 6H_2O$, and ethylbenzene for 30 min, raising the pH to 5 with K_2CO_3, and layering the solution with 2-propanol. The X-ray

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(20) Supporting Information contains a table of guest volume versus percentage of host−guest complex.

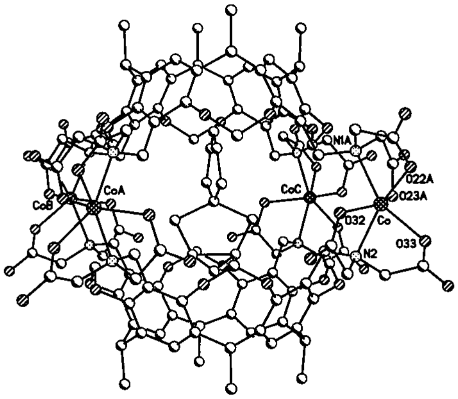

Figure 3. Solid-state structure of $\mathrm{Ba_4[Co_4}\mathbf{1}_2\cdot\mathrm{C_6H_5C_2H_5]}$. The atoms within the cage represent the disordered ethylbenzene. Barium cations, hydrogen atoms, and solvent molecules have been omitted for clarity. Selected bond lengths (Å) and angles (deg) for $\mathrm{Ba_4[Co_4}\mathbf{1}_2\cdot\mathrm{C_6H_5C_2H_5]}$ are the following: Co−N2, 2.228 (14); Co−N1A, 2.206 (14); Co−O32, 2.049 (13); Co−O33, 2.088 (14); Co−O22A, 2.081 (13); Co−O23A, 2.087 (14); N2−Co−N1A, 123.92 (0.47); N2−Co−O22A, 156.17 (0.53); N2−Co−O23A, 87.57 (0.60), O32−Co−O22A, 89.22 (0.58).

structure of $\mathrm{Ba_4[Co_4}\mathbf{1}_2\cdot\mathrm{C_6H_5C_2H_5]}$ indicates that the resorcinarene structure and cobalt(II) coordination are isostructural with $\mathrm{Ba_4[Co_4}\mathbf{1}_2\cdot\mathrm{6H_2O]}$ (Figure 3). The unit cell parameters are almost identical in the two structures, and they both crystallize in the same tetragonal space group. The cage consists of two hemispherical resorcinarene molecules held together by four cobalt(II) ions. The cobalt centers are positioned at the edge of the resorcinarene rim, or more explicitly, around the equator of the complex. Although the molecules appear to possess psuedo-D_{4h} symmetry, detailed examination of the X-ray structure shows a D_{2d} symmetry, without consideration of the guest molecule. Two iminodiacetate moieties coordinate each cobalt(II) ion, yielding an octaanionic complex. The tridentate iminodiacetate moieties bind to the cobalt(II) ions in the *N*,*N*-cis-fac geometry, and the metal center exhibits a significant distortion from octahedral toward trigonal prismatic geometry. Interstitial countercations of barium and cobalt are bound to oxygen atoms of the iminodiacetates and to water molecules. The dimensions of the cavity are 10.9 Å (distance between the lower rim carbons of the resorcinarenes) by 9.7 Å (distance across between benzyl carbons of the same resorcinarene). These distances are within 0.05 Å of those observed when the cavity contained water. Bond distances and angles for $\mathrm{Ba_4[Co_4}\mathbf{1}_2\cdot\mathrm{C_6H_5C_2H_5]}$ are within 0.05 Å and 1° of those determined in $\mathrm{Ba_4[Co_4}\mathbf{1}_2\cdot\mathrm{6H_2O]}$. Thus, the guests in these complexes do not impose structural changes upon the complexes.

X-ray diffraction studies of $\mathrm{Ba_4[Co_4}\mathbf{1}_2\cdot\mathrm{C_6H_5C_2H_5]}$ show the presence of atoms in the $\mathrm{Co_4}\mathbf{1}_2^{8-}$ cavity, indicating the presence of a guest. The high symmetry of the cavity ($\mathrm{Co_4}\mathbf{1}_2^{8-}$ possesses a 4-fold inversion axis of rotation) requires guest within the cavity to be disordered, and this disorder could not be resolved. X-ray crystallographic data indicate the present of electron density within the cavity; however, because the guest is disordered, the identity of the guest cannot be determined. Disorder of the guest and the presence of loosely bound solvent molecules are common for molecules of this type.[21] Although we initially reported that no ordered guest molecules were within the cavity of $\mathrm{Ba_4Co_4}\mathbf{1}_2$ when it is formed without organic guest present,[7] further study of the crystallographic data revealed that an octahedron of water molecules resides within the cavity. This indicates that water can be trapped by $\mathrm{Co_4}\mathbf{1}_2^{8-}$ in the absence of small organic molecules. However, when small organic molecules such as ethylbenzene are present when $\mathrm{Co_4}\mathbf{1}_2^{8-}$ is formed, the organic molecules can be encapsulated within the cavity.

Conclusions

The cobalt cage complex $\mathrm{Co_4}\mathbf{1}_2^{8-}$ is an example of a metal-assembled molecule that can bind and release guest molecules in water as a function of pH. Facile encapsulation of a wide range of both water-miscible and water-imiscible organic molecules demonstrates the encapsulation capabilities and versatility of $\mathrm{Co_4}\mathbf{1}_2^{8-}$. As shown by the failure to encapsulate large and branched molecules, the cavity dimensions impose guest size and shape selectivity. Both NMR and X-ray crystallographic studies are consistent in indicating that the guest resides within the cavity of $\mathrm{Co_4}\mathbf{1}_2^{8-}$. Large upfield shifts in the proton resonances (30−40 ppm) of the guest molecules are observed when the guest is encapsulated by $\mathrm{Co_4}\mathbf{1}_2^{8-}$. Thus, complex $\mathrm{Co_4}\mathbf{1}_2^{8-}$ functions as an NMR shift reagent for the included guest. For example, excellent separation (12 ppm) of the ortho, meta, and para protons of aromatic compounds is observed.

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Supporting Information Available: Cartoon representations and a discussion of predicted hydrogen signals for the different possible isomers of $\mathrm{Co_4}\mathbf{1}_2^{8-}$, t_1 values for $\mathrm{Co_4}\mathbf{1}_2^{8-}$, table of chemical shift assignments, table of the percentage of host−guest complex. Two X-ray crystallographic files in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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[21] See ref 3 and the following. MacGillivray, L. R.; Atwood, J. L. *J. Am. Chem. Soc.* **1997**, *119*, 6931.