Capsule formation in novel cadmium cluster metallocavitands†

Peter D. Frischmann and Mark J. MacLachlan*

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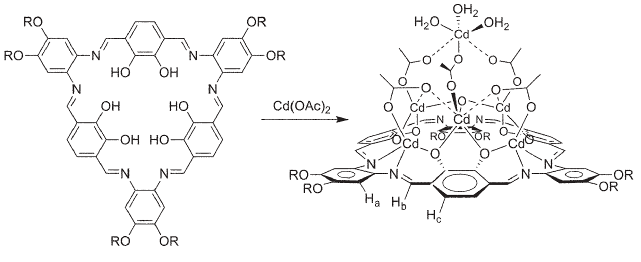
We report the synthesis and characterization of a new heptanuclear cadmium cluster complex formed within a Schiff base macrocycle and study its surprising dimerization in the solid-state and solution to form capsules.

The self-assembly of cavitands is an important concept within supramolecular chemistry.[1] Capsules formed by bowl-shaped organic macrocycles, such as calixarenes and resorcinarenes, are attractive as nano-reaction chambers, where they can facilitate reactions that occur by a different pathway than in the bulk.[2] The geometry and chemistry of the cavity is important for directing the size- and shape-selective processes. Homodimerization of cavitands into capsules is most often facilitated by H-bonding[3] or metal coordination, where the transition metals act as coordinative fasteners, covalently sealing two cavitands.[4] The quintessential bowl-like structure of the latter cavitands results from the organic macrocycle and not the presence of transition metals. Metallocavitands in which metals are intrinsic structural elements of the cavity are rare due to often unpredictable coordination geometry but should exhibit rich host–guest chemistry much like their organic analogues.[5] The design of self-assembling inorganic cavitands with multiple metal sites accessible to encapsulated guests promises to wed the selectivity and recognition of organic supramolecular chemistry with the catalytic, magnetic, and optical properties of metals, producing functional materials.[6]

We recently reported that the reaction of macrocycle **1a** with zinc acetate forms a heptanuclear zinc cluster complex, **3a**.[7] In this structure, the metallomacrocycle adopts a bowl shape, accommodating a basic zinc acetate cluster at its apex. Herein, we report on the formation of a novel cadmium acetate cluster complex of macrocycle **1**, with an even deeper bowl shape. Although the cadmium cluster also has seven metal centers, it is structurally distinct from the zinc cluster complex. Moreover, we demonstrate for the first time that these metallocavitands form interlocking capsules in the solid state and reversibly dimerize in aromatic solvents and DMF. This self-assembly process appears to be *entropy-driven*, reminiscent of Cram's velcrands.[8]

Reacting macrocycles **1a** and **1b**[9] with $Cd(OAc)_2$ afforded red microcrystalline solids **2a** and **2b** (Scheme 1). Compound **2a** is only soluble in DMF, while **2b** is soluble in various organic solvents. ^1H NMR spectroscopy of the products (hot DMF-d_7 for **2a**, $CDCl_3$ for **2b**) showed that they retained the three-fold symmetry of the starting macrocycle and contained acetate ligands. The OCH_2 resonance displayed an ABX_2 coupling pattern arising from diastereotopic protons, indicative of C_{3v} symmetry. Cadmium satellites with $^3J_{Cd–H}$ = 34.2 Hz were observed for the imine resonances, confirming that the N_2O_2 pockets of the macrocycle were occupied by cadmium.[10] In order to determine the structure of the cadmium complexes, we undertook a single-crystal X-ray diffraction study of **2a**.‡ Crystals of **2a** were grown from DMF, and its solid-state molecular structure is illustrated in Fig. 1.



1a R = C_2H_5
1b R = C_8H_{17}

2a R = C_2H_5
2b R = C_8H_{17}

Scheme 1 Reaction of macrocycles **1a–b** with seven equivalents of $Cd(OAc)_2$ in EtOH affords metallocavitands **2a–b** (**a** R = C_2H_5, **b** R = C_8H_{17}). The seventh Cd ion and sixth acetate ligand are obscured by the depiction of the cluster.

While zinc carboxylate clusters are well known (*e.g.*, basic zinc acetate $[Zn_4O(OAc)_6]$), cadmium carboxylate cluster complexes are less common, but are of interest as fluorescent materials[11] and molecular building blocks for metal–organic frameworks.[12] In **2a**, the macrocycle coordinates three Cd^{2+} ions in the N_2O_2 salphen-like pockets, a rare binding motif for cadmium. Similar to previous reports,[11*b*,13] the Cd–N and Cd–O bond lengths are 2.307(9) and 2.240(6) Å, respectively. This sterically strained coordination distorts the near-planar macrocycle into a bowl shape that further coordinates a $[Cd_3O(OAc)_6Cd(H_2O)_3]$ cluster. Above the macrocycle, each of the catechol moieties is coordinated to a Cd^{2+} ion, and these three cadmium ions are bridged by a central oxo ligand. Interestingly, this trigonal pyramidal oxo ligand is coordinated to only three Cd^{2+} ions, whereas in the zinc complexes, the oxo ligand is tetrahedral. Bridging acetate ligands hold the capping octahedral $Cd(OH_2)_3{}^{2+}$ species in place. The solid-state structure is consistent with the solution NMR spectroscopic data. Remarkably, complex **2a** is stable in boiling water for hours despite the known hydrolytic instability of Schiff bases and the lability of Cd–OAc bonds.

The first evidence for dimerization of **2a** came from its solid-state structure – in the crystal structure, the molecule is packed into perfect capsules with crystallographically-imposed D_{3d} symmetry (Fig. 1(c) and (d)). The complementary monomers organize in a face-to-face interlocking fashion with a 60° rotation between them. The capsule is stabilized by 12 weak CH···π interactions (3.00 Å) as illustrated in Fig. 1(e). A single DMF molecule appears to be

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Department of Chemistry, University of British Columbia, 2036 Main Mall, Vancouver, BC, V6T 1Z1, Canada.
E-mail: mmaclach@chem.ubc.ca; Fax: 604-822-2847; Tel: 604-822-3070

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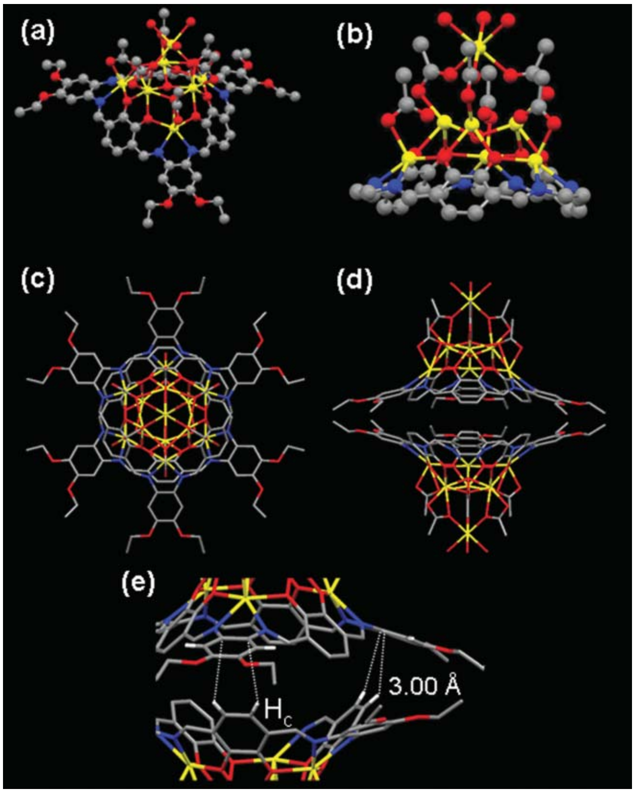

Fig. 1 Solid-state depictions of **2a** as determined by single-crystal X-ray diffraction (crystallized from DMF, $R\bar{3}m$ space group). (a) Side view of the metallocavitand. (b) Expanded view of the capping cadmium cluster (periphery omitted). (c) Top view of the dimeric capsule. (d) Side view of the capsule. (e) Expanded view of the intermolecular CH···π interactions between H_c protons (Scheme 1) and the π cloud of the complementary monomer moiety (contacts between H7 and C5 are depicted; see CCDC 643623). Hydrogen atoms are omitted for clarity in (a) through (d). Most H atoms and some C, O, and N atoms are omitted for clarity in (e) (grey = C, blue = N, red = O, yellow = Cd).

encapsulated in the interior of the complex, but its position could not be accurately determined due to disorder.

To probe the dimerization of compound **2a** in solution, we carried out variable temperature, variable concentration (VTVC) ^{1}H NMR experiments. At room temperature, the resonances of **2a** in DMF-d_7 are broad but they sharpen upon heating. When a sample of **2a** in DMF-d_7 was cooled to 265 K the resonances characteristic of the complex split into two sets of peaks (Fig. 2(a)). As the intensity of the peaks showed concentration dependence, we were able to assign one set of resonances to the monomer, and the other to the dimer. Significantly, in the dimer, the aromatic resonances assigned to the protons on the catechol ring (H_c from Scheme 1) were observed at 5.8 ppm, more than 0.8 ppm upfield from the same resonance assigned to the monomeric complex. This additional shielding is consistent with formation of a face-to-face dimer, as the protons on the catechol ring are directly over the π-cloud of the diimine rings of the complementary complex as shown in Fig. 1(e).[14]

Fig. 2(b) displays the van't Hoff plot constructed to establish the thermodynamics of dimerization of metallocavitand **2a** in DMF-d_7. Association constants at 238, 247, 256 and 265 K were obtained from integration of the monomer and dimer resonances (aromatic

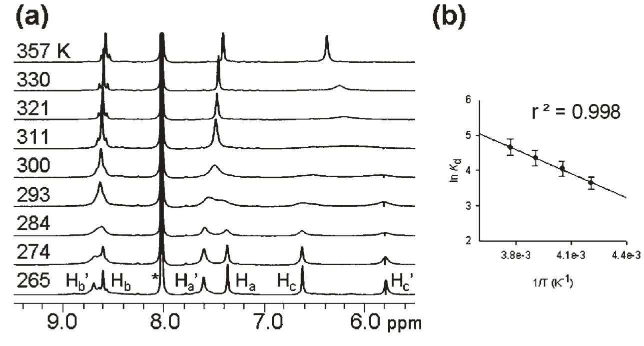

Fig. 2 (a) Variable-temperature 400 MHz ^{1}H NMR spectra of **2a** in DMF-d_7 ([**2a**] = 5 mmol L^{-1}). Protons are labeled according to Scheme 1 with the primes referring to dimeric species and an asterisk indicating solvent. (b) Van't Hoff plot of **2a** in DMF-d_7 ([**2a**] = 2.6 mmol L^{-1}) from integration of resonances assigned to protons H_a and H_c (Scheme 1) in the ^{1}H NMR spectra at 238, 247, 256 and 265 K.

protons H_a and H_c in the ^{1}H NMR spectrum). An enthalpy of 19 ± 1 kJ mol^{-1} and entropy of 110 ± 2 J mol^{-1} K^{-1} for dimerization was calculated from the van't Hoff plot. Unexpectedly, these thermodynamic parameters indicate that dimerization in DMF is an *entropy-driven* process.

In an effort to expand our thermodynamic study to other solvents, our focus shifted to metallocavitand **2b**. Significant broadening of the imine, aromatic and OCH_2 resonances was observed by ^{1}H NMR spectroscopy in benzene-d_6, toluene-d_8 and *p*-xylene-d_{10} (but not $CDCl_3$). This preliminary evidence for dimerization prompted us to undertake VTVC ^{1}H NMR experiments. In these solvents, it was not possible to resolve distinct monomer and dimer resonances, and guests could not be observed directly due to rapid exchange. However, the variation of the imine chemical shift as a function of concentration was fit to a dimerization model, enabling us to extract the association constants at each temperature.[15] Thermodynamic parameters for self-association were then determined from van't Hoff plots. The experimental association constants, enthalpies, and entropies of dimerization for compound **2b** are shown in Table 1.

The association constants for dimerization (K_{dim}) of **2b** in the three aromatic solvents are similar in magnitude. Surprisingly, in π-bonding solvents dimerization of these cluster-capped macrocycles appears to be an *entropy-driven* process. Most self-association processes are *enthalpy-driven* and *entropy-opposed* since order is generally being imparted on the system and the dimers are held together by strong intermolecular interactions.

Much like Cram's velcrands and Rebek's molecular capsules,[16] we attribute the entropy-driven process to the expulsion of solvent molecules from monomers upon dimerization. Although entropy-driven aggregation is common in aqueous media where it is important in biological systems (hydrophobic effect), it is rarely observed in non-polar organic solvents. In the case of **2a** and **2b**, aromatic solvents can form strong π–π interactions with the interior of the bowl of the monomeric metallocavitand. When dimerization of the metallocavitand occurs, solvent is expelled from the bowl, increasing the net entropy in the system.

While the entropy changes upon dimerization are consistently positive, there are no clear trends for the enthalpy changes. The balance between solvent–solvent, macrocycle–solvent, and

Table 1 Thermodynamic parameters for dimerization of **2b** and **3b** (R = C_8H_{17}) in different solvents compared to **2a** (R = C_2H_5) in DMF-d_7

Complex	Solvent[a]	K_{dim} (25 °C)[b]/L mol^{-1}	ΔH/kJ mol^{-1}	ΔS/J mol^{-1} K^{-1}
2a	DMF-d_7	270 ± 10	19 ± 1	110 ± 2
2b	Benzene-d_6	800 ± 100	−7 ± 5	32 ± 14
	Toluene-d_8	1500 ± 400	1 ± 4	64 ± 14
	p-Xylene-d_{10}	1000 ± 300	11 ± 8	94 ± 24
3b	Benzene-d_6	10 ± 3	24 ± 12	100 ± 34

[a] Solubility and the melting/boiling point of the solvents limited the temperature ranges over which the experiments could be performed. [b] Association constants at 25 °C are calculated from van't Hoff plots.

macrocycle–macrocycle interactions leads to near cancellation of the enthalpy changes that occur upon dimerization.

Compared with the macrocyclic bowls of the zinc cluster complexes, the bowls of **2a** and **2b** are deeper and greater in volume. This is a consequence of accommodating the larger cadmium cluster inside the macrocycle, requiring the ring to open wider. To determine whether the bowl dimensions influence the dimerization of the complexes, we synthesized zinc complex **3b** and measured its dimerization constants in benzene-d_6 using VTVC ^{1}H NMR spectroscopy. Remarkably, at 298 K the association constant for the zinc bowl complex **3b** is only 10 ± 3 mol L^{-1}, substantially smaller than that of cadmium complex **2b**. The zinc cluster complex also exhibits *entropy-driven* dimerization. Unlike organic capsule-forming molecules, which often require several steps to modify, our results illustrate a simple method to modify the bowl shape of the metallocavitands, and thus significantly alter the monomer–dimer equilibrium.

In summary, we have discovered a new stable heptanuclear cadmium cluster complex that is formed within a Schiff base macrocycle. A single-crystal X-ray diffraction experiment revealed that these molecules organize into face-to-face capsules in the solid state. We have demonstrated the first reversible dimerization of these metallocavitands, a process that appears to be *entropy-driven*. Moreover, we have illustrated the ability to use coordination chemistry to change the curvature of the bowl, and to modify the thermodynamics of capsule formation. These tunable metallocavitand capsules with accessible metal sites on their interiors are alluring candidates for host–guest catalysis and molecular recognition. We are now expanding the dimerization and guest inclusion studies of the metallocavitands.

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Notes and references

‡ *Crystal data* for **2a**: $C_{87}H_{121}Cd_7N_{13}O_{35}$, M_r = 2695.77, red plate (0.25 × 0.25 × 0.10 mm), rhombohedral, space group $R\bar{3}m$, $a = b$ = 28.712(3), c = 26.128(3) Å, V = 18654(4) Å^3, Z = 6, D_c = 1.440 g cm^{-3}, λ = 0.710 69 Å, T = 173(2) K, , 46300 reflections collected, 2884 unique (R_{int} = 0.1841). Final GoF = 1.005, $R1$ = 0.0665, $wR2$ = 0.1847, R indices based on 1816 reflections with $I > 2\sigma(I)$. CCDC 643623. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b710809e

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