

Chiral 15-Metallacrown-5 Complexes Differentially Bind Carboxylate Anions

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The development of selective metal-based receptors for small molecules and ions is a well studied field of inquiry.^{1,2} Of recent interest are polymetallic species that function as cation or anion recognition agents.^{3–5} We^{6,7} and others⁸ have shown that one group of metallamacrocycles, known as metallacrowns, can function as selective cation recognition agents. For example, Mn(III)-containing 12-metallacrown-4 (Mn(III)-12-MC-4) complexes exhibit a higher affinity for Li⁺ than Na⁺ or K⁺, reminiscent of the cation selectivity of 12-crown-4.⁹ Similarly, planar, achiral 15-metallacrown-5 complexes are selective for complexing the UO₂⁺ cation in the presence of lanthanides.^{10,11} The Mn(III)-12-MC-4 also differentially bind anions with Cl[−] being favored over Br[−], CF₃CO₂[−], F[−], and I^{3−}.⁹ A 15-MC-5 dimer made from tyrosine hydroxamic acid forms a rigid cavity that can distinguish nitrate from chloride.¹² Herein, we present the synthesis, characterization, and solution dynamics of face-differentiated, chiral 15-metallacrown-5 complexes that adopt novel dimeric structures in the solid state. These Ln(NO₃)₃[15-MC_{Cu(II)N(L-pheha)}-5] complexes show selective binding of carboxylate anions in a hydrophobic pocket formed by five phenyl rings.

We have shown that α-amino hydroxamic acids support formation of chiral, face differentiated 15-metallacrown-5 complexes in the presence of Cu(II), a base, and a Ln(III) ion.¹³ Structural characterization of the metallacrown derived from L-alaninehydroxamic acid, Cu(II) and Nd(III) revealed that the five ligand methyl groups extended from only one face of the planar metallamacrocycle.¹³ We felt that chiral ligands with bulkier side-chains would provide 15-metallacrown-5 complexes with enhanced amphiphilic character. When L-phenylalaninehydroxamic acid [L-pheha, 2 mmol], Cu(O₂CCH₃)₂ [2 mmol] and Ln(NO₃)₃·6H₂O (0.4 mmol; Ln = La, Gd) were combined in water, blue solutions were produced that provided crystalline La(NO₃)₃[15-

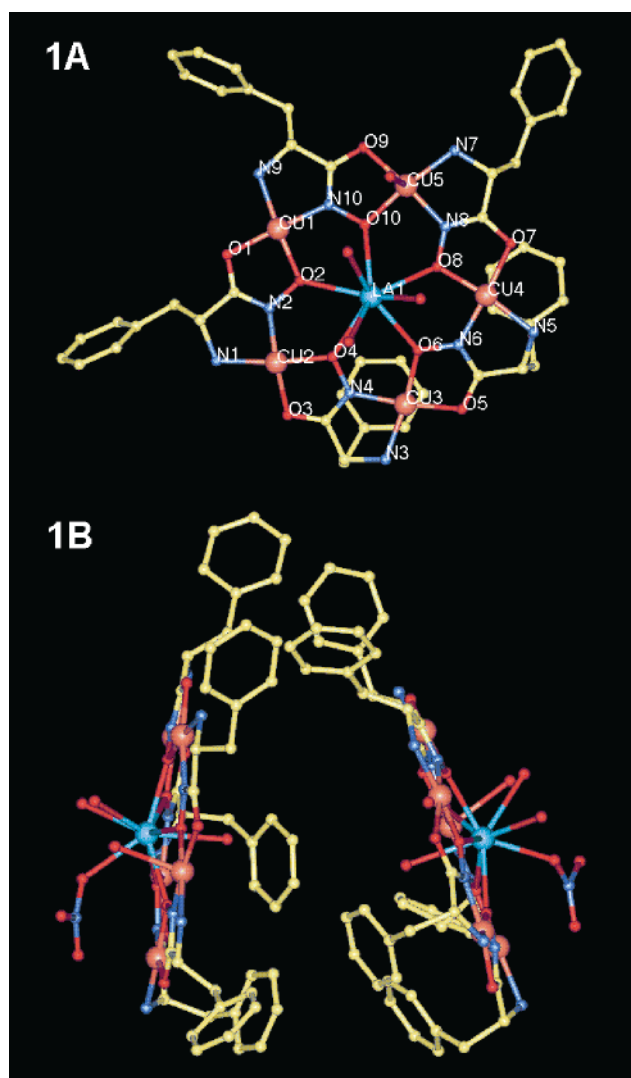


Figure 1. WebLab ViewerPro illustration of **1**. (A) View of the metallacrown looking down the pseudo-five-fold axis. (B) The metallacrown is shown as a solid-state dimer interacting through the hydrophobic interface created by the phenyl rings.

MC_{Cu(II)N(L-pheha)}-5] (**1**) or Gd(NO₃)₃[15-MC_{Cu(II)N(L-pheha)}-5] (**2**) upon evaporation of solvent in ca. 70% yield (Figure 1).¹⁴

Pseudo-five-fold symmetry is displayed by **1** with a La(III) ion bound to five metallacrown ring oxygens. Five Cu(II) ions form the metallacrown ring through Cu–N–O linkages of the hydroximate oxime group. Because all five ligands are resolved, the metallacrown is amphiphilic with aromatic residues adorning one face. In the solid, two metallacrowns are oriented such that the phenyl rings generate a hydrophobic cavity. The radius of the hydrophobic cylinder is 6.8 Å, and the La–La distance is 11.5 Å. X-ray crystallography confirmed that **2** retained the basic symmetrical structure of **1**.

The solution dynamics of the 15-metallacrown-5 complexes were examined using ¹H NMR and MS techniques. In CD₃OD, **1** exhibits a single set of paramagnetically shifted resonances that were assigned on the basis of analogy to other paramagnetic, α-amino hydroxamate-derived 15-MC-5 complexes and are cor-

(14) Crystallographic Data for **1**: C₄₅H_{66.5}N_{12.5}O₂₆Cu₅La, *M* = 1655.22, *T* = 158 K, orthorhombic space group *P*3₂21, *a* = 15.2671(2) Å, *b* = 15.26710(10) Å, *c* = 48.4117(6) Å, *V* = 9772.24(19) Å³, *Z* = 6, *μ* = 2.333 mm^{−1}, 121641 reflections (*R*_{int} = 0.0411), 17062 independent reflections, for observed data *R*₁ = 0.0541, *wR*₂ = 0.1228, for all data *R*₁ = 0.0559, *wR*₂ = 0.1239.

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robored by selective deuteration of the complex. The FAB-MS of **1** dissolved in CH₃OH contains mass envelopes corresponding to {La(NO₃)₂[15-MC_{Cu(II)N(L-pheha)}-5]}⁺, {La(NO₃)₃[15-MC_{Cu(II)N(L-pheha)}-5]}⁺, and {La(OCH₃)[15-MC_{Cu(II)N(L-pheha)}-5]}⁺, observations which further attest to the stability of the 15-metallacrown-5 unit. Addition of an excess of D₅-L-pheha (perdeuterated at the ring positions) to **1** in CH₃OH did not lead to ligand exchange, as revealed by FAB-MS analysis of the resultant solid product. When a CH₃OH solution containing a 1:1 mixture of pure **1** and La(NO₃)₃[15-MC_{Cu(II)N(D₅-L-pheha)}-5] (**1-d₂₅**) was analyzed by FAB-MS, only the parent ions for the two isotopomers were observed, while intermediate mass envelopes were not present. The synthesis of **1** using a mixture of H₅-*d*-pheHA and D₅-L-pheHA results in a mixture of metallacrowns exhibiting a statistical distribution of mass peaks. This demonstrates that assembling the metallacrown does not cause ligand resolution. These experiments indicate that after formation of the Ln(NO₃)₃[15-MC_{Cu(II)N(L-pheha)}-5], the complexes retain their five-fold symmetric structure and are stable in polar, protic media. Furthermore, the 15-MC-5 complexes are inert toward intermolecular ligand exchange reactions with other metallacrowns.

The strongly amphiphilic character of **1** suggested that guests might interact differently with the two faces of the metallacrown. To address this question we examined the binding of carboxylate ions in aqueous solution. Addition of sodium or lithium salts of various aliphatic carboxylic acids (RCO₂H; R = CH₃⁻, CH₃CH₂⁻, (CH₃)₂C⁻, CF₃⁻) to a solution of Ln(NO₃)₃[15-MC_{Cu(II)N(L-pheha)}-5] in CH₃OH resulted in the formation of soluble 1:1 carboxylate:metallacrown adducts in high yield as judged by ¹H NMR and FAB-MS analysis of isolated solid products. In contrast, when salts of aromatic carboxylates were used (RCO₂H; R = C₆H₅⁻, *p*-Cl-C₆H₄⁻, *p*-CH₃-C₆H₄⁻, C₆H₅CH=CH⁻) in the same reaction conditions, highly insoluble 2:1 adducts were isolated. We surmised that aliphatic carboxylates coordinated to the hydrophilic face of the metallacrown, leaving the hydrophobic interactions of the phenyl groups undisturbed. In contrast, we hypothesized that aromatic carboxylates, in addition to binding on the hydrophilic face, were being admitted into the hydrophobic pocket. This forced the hydrophobic faces of the metallacrowns apart, exposing the phenyl groups to the solvent (water) causing the material to be insoluble. These conclusions were confirmed by crystallographic analyses of the trifluoroacetate and the *p*-chlorobenzoate adducts. These observations, coupled with the differences in the solubility of the 1:1 versus the 2:1 adducts, suggested that separation of an aromatic carboxylate in the presence of aliphatic carboxylates might be possible. This was confirmed when a solution of **2** in H₂O was treated with a solution containing equimolar amounts of NaO₂CC₆H₅, NaO₂CCH₃, and NaO₂CCF₃. Solid Gd(O₂CC₆H₅)₂(NO₃)[15-MC_{Cu(II)N(L-pheha)}-5] was the sole product.

We next explored the affinity of dicarboxylates for the cavity, in particular comparing anions that might be able to link metallacrowns across the hydrophobic faces. Adducts of **1** with adipate (**1a**)¹⁵ and **2** with terephthalate (**2a**)¹⁶ have been isolated and show dramatically different behavior (Figure 2).

(15) Crystallographic Data for **1a**: C₉₆H₁₆₃N₂₀O₇₉Cu₁₀La₂, *M* = 3774.68, *T* = 158 K, monoclinic space group *P*2₁, *a* = 14.6821(2) Å, *b* = 38.1937(7) Å, *c* = 15.6385(2) Å, β = 117.862(10)°, *V* = 7752.9(2) Å³, *Z* = 2, μ = 1.98 mm⁻¹, 72009 reflections (*R*_{int} = 0.0379), 31312 independent reflections, for observed data *R*₁ = 0.1090, *wR*₂ = 0.2968, for all data *R*₁ = 0.1150, *wR*₂ = 0.3009.

(16) Crystallographic Data for **2a**: C₁₀₇H₁₂₈N₂₀O₄₅Cu₁₀Gd₂, *M* = 3332.17, *T* = 158 K, monoclinic space group *P*2₁, *a* = 15.098(3) Å, *b* = 28.257(6) Å, *c* = 16.887(3) Å, β = 102.185(3)°, *V* = 7042(2) Å³, *Z* = 2, μ = 2.48 mm⁻¹, 60507 reflections (*R*_{int} = 0.0572), 23826 independent reflections, for observed data *R*₁ = 0.0610, *wR*₂ = 0.1566, for all data *R*₁ = 0.0820, *wR*₂ = 0.1660.

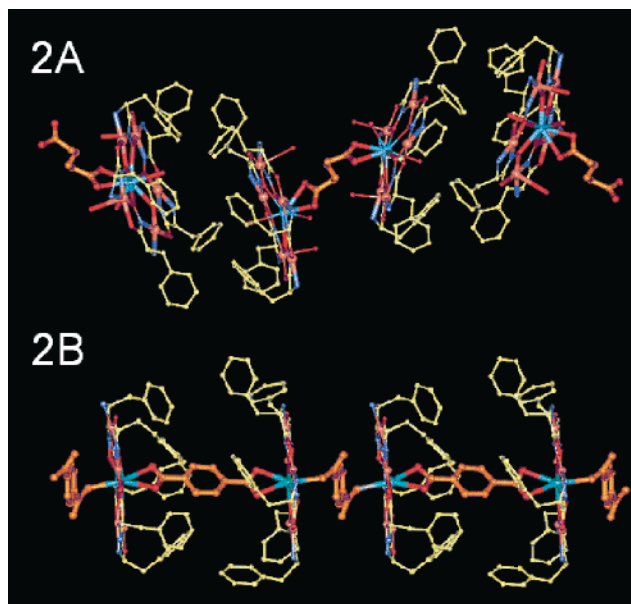


Figure 2. WebLab ViewerPro illustrations of (A) {La(adipate)_{0.5}[15-MC_{Cu(II)N(L-pheha)}-5]}₂ (**1a**) showing metallacrown dimers linked by adipate across the hydrophilic faces, and (B) {Gd(terephthalate)[15-MC_{Cu(II)N(L-pheha)}-5]}₂ (**2a**) showing metallacrown dimers linked by terephthalate across the hydrophobic and hydrophilic faces.

In **1a**, two unique metallacrowns form a dimer similar to the one formed by **1**. The flexible, aliphatic adipate anion, does not enter the cavity. This six-carbon dicarboxylate binds bidentate to the hydrophilic faces of two metallacrowns from adjacent dimers to make a continuous chain of “dimers of dimers” (Figure 2a). The La(III) lies out of the plane of the metallacrown, toward the hydrophilic face, providing less access for coordination to the hydrophobic face; however, identical behavior is also seen when Gd(III), which lies in the plane, is the central metal. Thus, adipate is excluded from the hydrophobic cavity whether coordination to the central metal is possible. The five-carbon dicarboxylate, glutarate, binds to the metallacrown in the same coordination mode.

In contrast, the aromatic terephthalate anion enters the cavity of the dimer (Figure 2b). Inside the cavity the carboxylate groups bind bidentate to the Gd(III) of both metallacrowns. The dimers are also bridged by terephthalate to form a continuous chain, with the anions bound monodentate to the Gd(III) on the hydrophilic faces of metallacrowns of adjacent dimers. The same binding mode is seen for terephthalate when La(III) is the cavity metal. Now, the La(III) is pulled slightly into the hydrophobic cavity, allowing coordination to both faces, despite the fact that it would ordinarily lie out of the plane toward the hydrophilic face. It appears that while aliphatic guests are excluded from the hydrophobic cavity, aromatic guests may enter and bind to the cavity metal of the metallacrown. Thus, the two faces of the metallacrown are not only differentiated structurally (by the presence or absence of hydrophobic benzyl groups), but also in their affinity for guests. We are now exploring whether these face differentiated 15-metallacrown-5 complexes may be used to sequester chiral carboxylates in aqueous solution.

Supporting Information Available: X-ray crystallographic files (CIF) for **1a**, and **2a**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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