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Preparation and Characterization of Chiral Copper 12-Metallacrown-4 Complexes, Inorganic Analogues of Tetraphenylporphyrinatocopper(II)

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Transition metal complexes of chiral ligands have been applied with great success to the enantioselective synthesis of organic compounds, and also show promise for chiral recognition of organic compounds in solution.[1] While discrete mononuclear complexes of chiral ligands are often readily prepared, the controlled synthesis of chiral, polynuclear clusters poses considerable challenges.[2] Metallacrowns, inorganic analogues of organic crown ethers,[3] offer one solution to this problem, as we recently reported the facile preparation of chiral, face-differentiated 15-metallacrown-5 complexes derived from optically pure α-aminohydroxamic acids.[4] We have now extended this strategy to the preparation of chiral 12-metallacrown-4 complexes through the use of enantiomerically pure *β*-aminohydroxamic acids. Herein, we describe structural and spectroscopic properties of these compounds, which confirm the solution stability of the chiral clusters and reveal that these 12-metallacrown-4 complexes adopt structures reminiscent of complexes of the versatile *meso*-tetraphenylporphyrinato ligand.

Achiral 3-aminopropionohydroxamic acid (*β*-alaninehydroxamic acid) generates the copper 12-metallacrown-4 complex $Cu^{II}[12\text{-}MC_{Cu^{II}N(\beta-aha)}\text{-}4](ClO_4)_2$ in aqueous solution.[5] We have now demonstrated that chiral *β*-aminohydroxamic acids may also be used to prepare metallacrowns under similar conditions. The synthesis of such ligands relies on the isolation of multigram quantities of optically pure *β*-amino acids or their esters. Our approach to the synthesis of *S*-3-amino-3-phenylpropionohydroxamic acid (*S*-*β*-phenylalaninehydroxamic acid) is shown in Supporting Information as Scheme S1, and relies on precedented methods for the synthesis, esterification, and resolution of *β*-amino acids.[6,7] This strategy allows access to both antipodes of *β*-phenylalaninehydroxamic acid (*R*- and *S*-H_2-*β*-pheha) in multigram quantities (in about 10% overall yield) using readily available, inexpensive starting materials, and also allows for the introduction of functional groups into the ligands through the use of appropriately substituted benzaldehydes.[8]

Chiral pentacopper 12-metallacrown-4 complexes were obtained by the reaction of one antipode of the chiral hydroxamic acids with an appropriate copper(II) source in the presence of a weak base (Figure 1).[6] Thus, $Cu^{II}SO_4[12\text{-}MC_{Cu^{II}N(S-\beta-pheha)}\text{-}4]$ (*S*,*S*,*S*,*S*-**1**) was prepared by admixture of $CuSO_4{\cdot}5H_2O$, *S*-H_2-*β*-pheha, and NaOAc in water, and was isolated as a green crystalline solid by filtration in 89% yield. Similarly, stirring $Cu(OAc)_2{\cdot}H_2O$, *S*-H_2-*β*-pheha, and NaOAc in methanol yielded $Cu^{II}(OAc)_2[12\text{-}MC_{Cu^{II}N(S-\beta-pheha)}\text{-}4]$ (*S*,*S*,*S*,*S*-**2**) and $Cu^{II}Cl[12\text{-}MC_{Cu^{II}N(S-\beta-pheha)}\text{-}4]Cu^{II}(OAc)_3$ (*S*,*S*,*S*,*S*-**2′**), which cocrystallized in 79% overall yield [based on Cu^{II}]. The source of the chloride anion in *S*,*S*,*S*,*S*-**2′** is ascribed to substoichiometric amounts of HCl present in bulk samples of *S*-H_2-*β*-pheha.[6] These metallacrowns are soluble and stable in polar protic media, and were subjected to comprehensive physicochemical characterization. The FAB-MS of crystalline *S*,*S*,*S*,*S*-**1** is dominated by a molecular ion (M^+) envelope corresponding to $\{Cu^{II}SO_4[12\text{-}MC_{Cu^{II}N(S-\beta-pheha)}\text{-}4] + H\}^+$, whereas that of *S*,*S*,*S*,*S*-**2** contains an M^+ peak corresponding to $\{Cu^{II}OAc[12\text{-}MC_{Cu^{II}N(S-\beta-pheha)}\text{-}4]\}^+$. Examination of methanol solutions of *S*,*S*,*S*,*S*-**1** and *S*,*S*,*S*,*S*-**2**/*S*,*S*,*S*,*S*-**2′** by electrospray ionization mass spectrometry (ESI-MS) revealed intact M^+ envelopes which are entirely consistent with those obtained for solid samples. The visible spectra of methanol solutions of *S*,*S*,*S*,*S*-**2**/*S*,*S*,*S*,*S*-**2′** and *R*,*R*,*R*,*R*-**2**/*R*,*R*,*R*,*R*-**2′** (prepared identically, substituting *R*-H_2-*β*-pheha)[9] exhibited a d−d band at 602 nm ($\epsilon = 435\ M^{-1}\ cm^{-1}$), and the CD spectra over the same range revealed equal but opposite extinction of polarized visible light by the two enantiomeric complexes (Figure S1), behavior which has been observed previously in chiral, face-differentiated 15-metallacrown-5 complexes prepared from α-aminohydroxamic acids.[4] Thus, these copper(II) metallacrowns retain their structure and their chirality in polar, protic media.

Single crystals of cocrystallized *S*,*S*,*S*,*S*-**2**/*S*,*S*,*S*,*S*-**2′** proved amenable to X-ray structural analysis, which revealed the presence of two crystallographically independent metallacrowns in the asymmetric unit of the triclinic (*P*1) unit cell.[10] The 12-metallacrown-4 motif is present in both complexes, with square planar or square pyramidal Cu(II) in both the ring and central

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(8) We have prepared functionalized chiral 12-metallacrown-4 complexes from para-substituted *β*-phenylalaninehydroxamic acids by the methodology shown in Scheme S1 utilizing para-substituted benzaldehydes: Bodwin, J. J.; Pecoraro, V. L., unpublished results.

(9) Obtained by resolution of *rac*-methyl-3-amino-3-phenylproprionate with D-tartaric acid followed by condensation of the *R*-methyl ester with hydroxylamine as shown in Scheme S1.[9b] (b) Hanessian, S.; Sanceau, J.-Y. *Can. J. Chem.* **1996**, *74*, 621−624.

(10) X-ray data for *S*,*S*,*S*,*S*-**2**/*S*,*S*,*S*,*S*-**2′**: $C_{85}H_{100}Cl_1Cu_{11}N_{16}O_{42}$, MW = 2752.20, green prismatic crystal, triclinic space group *P*1 (No. 1) with $a = 12.5406(3)$ Å, $b = 13.8416(3)$ Å, $c = 16.6932(4)$ Å, $\alpha = 88.737(1)°$, $\beta = 76.001(1)°$, $\gamma = 71.135(1)°$, $V = 2655.57(11)$ Å^3 at 158(2) K, $Z = 1$, $\rho_{calcd} = 1.721$ g cm^{-3}, $2\theta_{max}$ (Mo Kα) = 58.76°. Data were collected on a Siemens SMART system, and the structure was solved by direct methods. Full-matrix least-squares refinement on F^2 converged to current residuals $R1 = 0.0376$, $wR2 = 0.0849$, and $S = 1.041$ for 21 543 independent reflections with $I > 2(\sigma)\ I$, 1397 parameters, and 9 restraints on the single uncoordinated acetate counterion.

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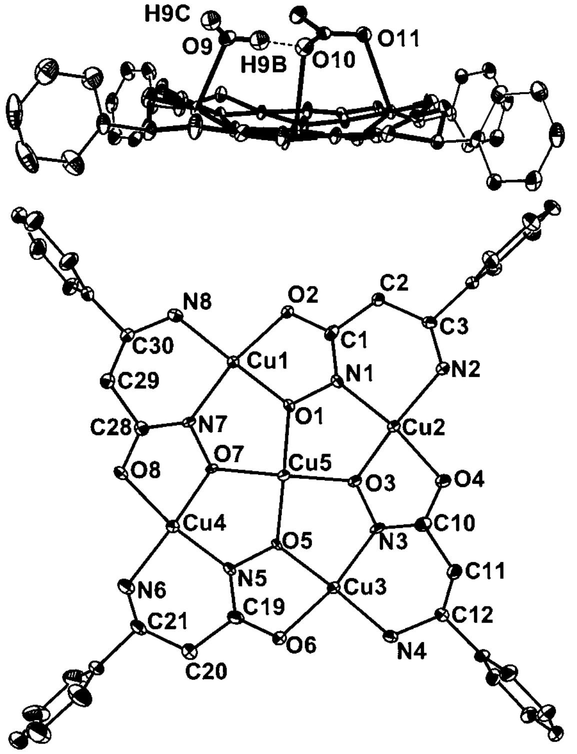

Figure 1. (Top) Side view thermal ellipsoid representation (50% probability) of the X-ray crystal structure of S,S,S,S-**2** including bound acetate and water; all nonwater hydrogen atoms are omitted for clarity. (Bottom) Top view thermal ellipsoid representation of *S*,*S*,*S*,*S*-**2** with bound acetate, bound water and hydrogen atoms omitted for clarity. Selected interatomic distances (Å) and angles (deg): Cu5−O1, 1.877(3); Cu5−O5, 1.881(3); Cu5−O3, 1.906(3); Cu5−O7, 1.921(3); $[\mathrm{Cu(ring)-Cu5}]_{\mathrm{avg}} = 3.27(5)$; *cis*-$[\mathrm{Cu(ring)-Cu(ring)}]_{\mathrm{avg}} = 4.59(4)$; O1−Cu5−O5, 176.2(2); O1−Cu5−O3, 90.71(14); O5−Cu5−O3, 90.33(13); O1−Cu5−O7, 88.74(13); O5−Cu5−O7, 89.78(13); O3−Cu5−O7, 173.11(14).

positions (shown for *S*,*S*,*S*,*S*-**2** in Figure 1 and in the Supporting Information for *S*,*S*,*S*,*S*-**2′**). In *S*,*S*,*S*,*S*-**2**, an acetate counterion bridges the central Cu(II) [Cu5] and a ring Cu(II) [Cu2] in a symmetric syn-syn fashion. A hydrogen bond between the bridging acetate [O10] and a bound water [O9] is responsible for the tilted orientation of the bridging acetate unit (Figure 1). The structure of *S*,*S*,*S*,*S*-**2′** is similar, excepting that a chloride ion is found to bridge the central Cu(II) [Cu15] and a ring Cu(II) [Cu12] in this cluster, and an additional equivalent of $\mathrm{Cu(O_2CCH_3)_3 \cdot H_2O}$ [Cu16], external to the 12-metallacrown-4 unit, is found to coordinate to a peripheral carbonyl oxygen [O13] and a ring Cu(II) [Cu11]. Crystallographic analysis of *S*,*S*,*S*,*S*-**1** was complicated by rotational twinning of the sample, but preliminary analysis has revealed the presence of two crystallographically independent metallacrowns which are topologically similar to *S*,*S*,*S*,*S*-**2**, but which differ in the nature of their coordinated anions ($\mathrm{SO_4^{2-}}$ in *S*,*S*,*S*,*S*-**1** vs $\mathrm{OAc^-}$ in *S*,*S*,*S*,*S*-**2**). Overall, these structures illustrate that despite the change in bridging anion, the basic shape of the molecule is maintained.

Significant structural differences exist between the chiral 12-metallacrown-4 complexes presented herein and the related chiral 15-metallacrown-5 species reported previously.[4] In the latter class of complexes, ligand chirality and planar five-membered chelate rings results in clear differentiation of the two faces of the metallacrown. In contrast, the expansion of this ring to 6 atoms in the chiral 12-metallacrown-4 complexes renders the chelate rings more flexible. In fact, all of the six-membered chelate rings present in these complexes approximate boat conformations, with the phenyl substituents borne on the chiral carbons occupying equatorial positions. This low energy conformation imparts a distinct bowl shape (mean displacements of each atom from the least-squares plane of the four hydroximate oxygens are given in Supporting Information) onto the 12-metallacrown-4 core similar to domed porphyrin structures, with the phenyl groups directed away from the center of the metallacrown. This significant deviation from planarity represents a new structural phenomenon in 12-metallacrown-4 complexes and is a direct consequence of the flexibility of the aliphatic β-aminohydroximate ligands compared to the previously described, aromatic salicylhydroximate ($\mathrm{shi^{3-}}$) ligands.[11] Moreover, the disposition of these phenyl groups in the chiral 12-metallacrown-4 complexes results in structures which are highly reminiscent of *meso*-tetraphenylporphyrinatocopper(II), **3**.[12] The symmetrically disposed phenyl groups in *S*,*S*,*S*,*S*-**2** and the pseudo-C_4 symmetry of the molecule mimics the analogous features found in **3**. Additionally, *S*,*S*,*S*,*S*-**2** is only ∼35% larger than **3**, resulting in a substantially higher metal ion density per unit surface area for the metallacrowns compared to the structurally related porphyrin complex. While sharing a similar structure, significant differences between these two classes of molecules exist including charge (+2 for the metallacrowns, neutral for **3**), electronic structures, and most importantly, the chirality of the metallacrowns compared to achiral **3**. Furthermore, a simple synthetic alteration to the precursor chiral β-phenylalaninehydroxamic acids can lead to functionally modified metallacrowns, providing access to planar molecules that otherwise would be synthetically challenging using a porphyrinic platform.

In summary, chiral 12-metallacrown-4 complexes, like their 15-metallacrown-5 congeners, are readily isolated in high yield from one-step syntheses in polar, protic media. Spectroscopic measurements indicate that the chiral metallacrowns retain their integrity in solution, while crystallographic studies have revealed that these clusters bear a striking structural resemblance to complexes of the familiar *meso*-tetraphenylporphyrinato ligand. The ease of synthesis of these complexes, which contain five metal ions and four chiral centers, invites the use of more highly derivatized β-aminohydroxamic acids to prepare additional chiral metallacrowns with specific physical, spectroscopic, or chiral recognition properties. Such molecules may serve as a replacement for porphyrins in applications where molecular shape and high metal density is of paramount importance.

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Supporting Information Available: Synthetic details and characterization data for new compounds and details of the X-ray crystallographic analysis of *S*,*S*,*S*,*S*-**2**/*S*,*S*,*S*,*S*-**2′** including thermal ellipsoid representations and atomic displacements from the mean plane of the 4 hydroximate oxygen atoms for both *S*,*S*,*S*,*S*-**2** and *S*,*S*,*S*,*S*-**2′** (23 pages). X-ray crystallographic files, in CIF format, are available on the Internet only. Ordering and access information is given on any current masthead page.

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