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Synthesis and Characterization of New Mono- and Heptazinc Complexes with Unusual Amide Coordination Modes

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Two novel, a mono- and a heptanuclear, zinc complexes have been prepared and characterized by exploiting the flexibility and chelating and bridging ability of a new carboxylate- and amide-rich dinucleating ligand under different reaction conditions.

Zinc ion, which is represented in all classes of enzymes, is the second most abundant transition metal, following iron, in biological systems. The understanding of zinc coordination chemistry, in both biological systems and small complexes, therefore, is vital to the understanding of substrate binding and reaction mechanisms of zinc enzymes. Zinc-containing enzymes range from simple one zinc binding sites with common coordination modes, such as in carbonic anhydrase and carboxypeptidase A, to metalloenzymes with more than one zinc ion and unusual protein coordination modes.[1] The discovery of structural polyzinc nucleic acid polymerases and transcription factors, shown to bind as many as 11 zinc ions and in even more complicated coordination modes, has rekindled interest in the coordination chemistry of zinc.[2] Most of the known mono- and polyzinc enzymes are coordinated to either His, Asp, or Glu amino acid residues and/or are bridged to each other through OH^- and/or H_2O or carboxylate groups in different coordination modes. Similar to the coordination modes observed in biological systems, Krebs and co-workers reported hexa- and trinuclear zinc model complexes derived from some phenol-based dinucleating ligands,[3] while Mikuriya et al. utilized the corresponding amine to isolate an octanuclear zinc complex.[4] Recently, we have reported the synthesis and characterization of a new hexanuclear μ_6-sulfatozinc(II) complex derived from a carboxylate-rich symmetric dinucleating ligand.[5] On the basis of the nature of the bridging ligands, Zn—Zn internuclear distances ranging from 3.0 to 3.5 Å have been reported in the literature.[6–9]

In contrast to the large body of information obtained in the metal carboxylate coordination, practically very little is known about the metal complexes of amide ($-CONH_2$) ligands, although amide-containing amino acid residues, such as Gln or Asn, are key components in the structure of proteins.[10] In order to explore the coordination nature of amides, we synthesized and fully characterized novel mono- and heptanuclear zinc complexes, $[Zn(H_2O)_6][Zn(H_2cadp)(H_2O)_2]_2\cdot 12H_2O$ (**1**) and $[Na_4(ZnCl_3OH)][Zn_7(Hcadp)_2(cahdb)_2(\mu_3\text{-}OH)_2]\cdot 16H_2O\cdot 2CH_3OH$ (**2**), respectively. Reported herein are the unique coordination of zinc with amide-, alkoxo-, and carboxylate-containing symmetrical bridging ligands, *N*,*N*′-bis(2-carboxybenzomethyl)-*N*,*N*′-bis(carbamoylmethyl)-1,3-diaminopropan-2-ol (H_5cadp), and the transformed ligand 2-{[carbamoylmethyl-[2-hydroxy-3-(1-oxo-1,3-dihydroisoindol-2-yl)propyl]amino]methyl}benzoic acid (H_3cahdb; Scheme 1).

The reaction of $Zn(ClO_4)_2\cdot 6H_2O$ with H_5cadp in a 2:1 molar ratio in the presence of mild bases, such as NEt_3 or K_2CO_3, in methanol, at room temperature, for 2 h yielded a water-soluble colorless mononuclear complex **1**.[11] To our surprise, even mixtures of substoichiometric quantities of $Zn(ClO_4)_2\cdot 6H_2O$ and H_5cadp yielded the same mononuclear complex, **1**. However, the reaction of $ZnCl_2$ with H_5cadp in a 2:1 molar ratio in the presence of NaOH in methanol−water (1:1, v/v) produced a water-soluble colorless heptanuclear

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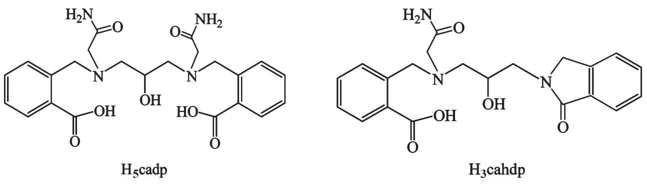
Scheme 1. Ligands H_5cadp and H_3cahdb



complex **2**.[12] The H_5cadp ligand has undergone an intramolecular reaction between the N-alkylated amide and the benzoate functionality at the half-end of the symmetrical ligand to produce a new unsymmetrical ligand, H_3cahdb, with an isoindol moiety. The 1-oxo-1,3-dihydroisoindol ring is most likely achieved via the known mechanism that involves the activation of the tertiary amine and aromatic carboxylate backbone after cleaving the pendant acetamide arm as a hydroxy acetamide group promoted by the zinc ions in the presence of NaOH.[13] Corona et al. have reported the synthesis of a series of novel isoindolone derivatives in good yields by using the aza-Wittig reaction of iminophosphoranes with dialdehydes under different conditions.[14] More recently, we have reported the zinc(II)-mediated cyclization and complexation of an unsymmetrical dicarboxyamine ligand that has undergone an intracyclization reaction between the secondary amine and the benzoate functionality to produce a new ligand with an isoindol moiety.[15] Recently, Dietrich et al. have also reported the complexation behavior of isoindoline pincer ligands with different coordination modes toward zinc(II), cadmium(II), and palladium(II) ions.[16]

The single-crystal X-ray analysis[17] of complex **1** reveals that the complex crystallizes as two $[Zn(H_2cadp)(H_2O)_2]^-$ complex anions, one $[Zn(H_2O)_6]^{2+}$ countercation, and 12 water molecules of crystallization. The crystal structure of the anion complex $[Zn(H_2cadp)(H_2O)_2]^-$ is depicted in Figure 1. The anion complex has a zinc ion, a dinucleating ligand H_2cadp^{3-}, and two water molecules coordinated to the zinc center. The coordination geometry around the zinc ion is best described as a distorted octahedral geometry formed by an alkoxo oxygen, an amide nitorgen, an aromatic carboxylate oxygen, a tertiary amine nitrogen, and two oxygen atoms from the two water molecules. The hexaaquozinc cation is sitting on a crystallographic center of symmetry. The crystal structure of complex **1** reveals one interesting feature that, although the alkoxide part of the ligand acts as a bridging-cum-spacer group, only one zinc ion is coordinated to the dinucleating ligand. The other potential metal binding site remains uncoordinated. Instead, there is a network of strong hydrogen bonding among the free amide, benzoate, bridging alkoxide, and $[Zn(H_2O)_6]^{2+}$ groups. Each unit cell contains 12 water molecules of crystallization that form hydrogen bonds among each other, with the carboxylate oxygen atoms and amide nitrogen atoms of the ligand as well as with the hexaaquozinc cation (Figure 1; see also Figure S1 in the Supporting Information). This network of hydrogen bonding, systematically distributed through the lattice, adds to the structural stabilization of the lattice. The $Zn-O_{carboxylate}$ and $Zn-N_{amine}$ bond distances for complex **1** are consistent with values reported in the literature.[18] The $Zn-N_{amide}$ bond distances are in the expected ranges.[19]

The crystal structure of the dianion heptanuclear zinc cluster, **2**, is depicted in Figure 2. The structural analysis[20] of **2** indicates that, in strong alkaline media and in the presence of zinc ions, one arm of the ligand H_5cadp undergoes transformation to produce colorless heptazinc cluster **2**. Single-crystal X-ray structure analysis reveals that cluster **2** consists of seven zinc ions, two $Hcadp^{4-}$ ligands, two transformed $cahdb^{3-}$ ligands, two μ_3-OH groups, and four Na^+ and one $ZnCl_3OH^{2-}$ ions as counterions. A total of 16 water molecules and two methanol molecules cocrystallized with the complex. The central Zn4 center exhibits a distorted tetrahedral geometry provided by two bridging μ_3-OH groups and two nitrogen atoms of the two bridging amido groups (η^2-μ_2-NHC(μ-O)CH_2−) of the $Hcadp^{4-}$ ligand. The average bond lengths around Zn4 are somewhat shorter than those of other zinc centers in the complex. This observation is consistent with the fact that bond lengths in a tetrahedral geometry are generally shorter than those in other geometries possessed by the other zinc centers in the complex. The bond angles around the tetrahedral zinc ion vary between 98.54(14)° and 135.96(14)°. The $Zn-O_{hydroxo}$ bond distances [1.975(3)−2.063(3) Å] are in the range of those previously reported in the literature.[21] Zn3 and Zn7 atoms adopt a distorted trigonal-bipyramidal geometry. A bridging alkoxo oxygen, a monodentate carboxylate oxygen, a tertiary amine nitrogen, a monodentate amide nitrogen of the $Hcadp^{4-}$ ligand, and one bridging μ_3-OH group make up the coordination environment. However, Zn1 and Zn5 exhibit a dis-

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(11) Synthesis of **1**: A methanolic solution (10 mL) of $Zn(ClO_4)_2 \cdot 6H_2O$ (0.780 g, 2.094 mmol) was slowly added into a stirring 15 mL methanol solution of H_5cadp (0.494 g, 1.047 mmol) and K_2CO_3 (0.868 g, 6.282 mmol). The reaction mixture was then stirred for 2 h at room temperature. The off-white precipitate formed was filtered and washed with methanol−water (1:1, v/v) followed by Et_2O and hexane. The product was dried in vacuo over anhydrous calcium sulfate. The X-ray-quality single crystals were grown by slow ether diffusion into the H_2O−MeOH solution of the complex. Yield: 0.680 g (85%). Anal. Calcd for $C_{46}H_{70}N_8O_{24}Zn_3$: C, 42.04; H, 5.36; N, 8.52. Found: C, 42.62; H, 5.15; N, 8.76.

(12) Synthesis of **2**: An aqueous solution (10 mL) of $ZnCl_2$ (0.288 g, 2.113 mmol) was slowly added to a solution of ligand H_5cadp (0.500 g, 1.059 mmol) and NaOH (0.254 g, 6.350 mmol) in 15 mL of methanol. The reaction mixture was stirred at room temperature for 2 h. It was then filtered. The clear filtrate was rotary evaporated and isolated as an off-white solid. The X-ray-quality single crystals were obtained by slow ether diffusion into the H_2O−MeOH solution of the complex. Yield: 1.130 g (75%). Anal. Calcd for $C_{88}H_{87}Cl_{3-}$ $N_{14}O_{27}Na_4Zn_8$: C, 42.38; H, 3.51; N, 7.86. Found: C, 42.57; H, 4.04; N, 7.63.

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(17) Crystallographic data: **1**, $C_{46}H_{94}N_8O_{36}Zn_3$, M_r = 1531.40, triclinic, space group $P\bar{1}$, α = 10.361(2) Å, b = 12.638(2) Å, c = 14.161(2) Å, α = 76.263(4)°, β = 71.423(5)°, γ = 65.824(5)°, V = 1591.2(5) $Å^3$, Z = 1, μ = 1.225 mm^{-1}, ρ_{calcd} = 1.598 mg/m^3, 21 220 reflections collected, 11 284 unique (R_{int} = 0.0305), R = 0.0569 [$I > 2\sigma(I)$], R_w = 0.1628 (all data).

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(20) Crystallographic data: **2**, $C_{90}H_{127}N_{14}O_{45}C_{l3}Na_4Zn_8$, M_r = 2846.33, monoclinic, space group $P2_1/c$, a = 18.482(2) Å, b = 37.887(5) Å, c = 17.466(2) Å, β = 113.341(5)°, V = 11229(2) $Å^3$, Z = 4, μ = 1.860 mm^{-1}, ρ_{calcd} = 1.684 mg/m^3, 95 986 reflections collected, 19 757 unique (R_{int} = 0.0254), R = 0.0563 [$I > 2\sigma(I)$], R_w = 0.1614 (all data).

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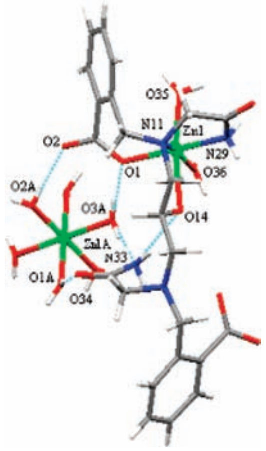

Figure 1. Labeled stick representation of the molecular structure of the anion portion of complex **1**, depicting hydrogen bonding.

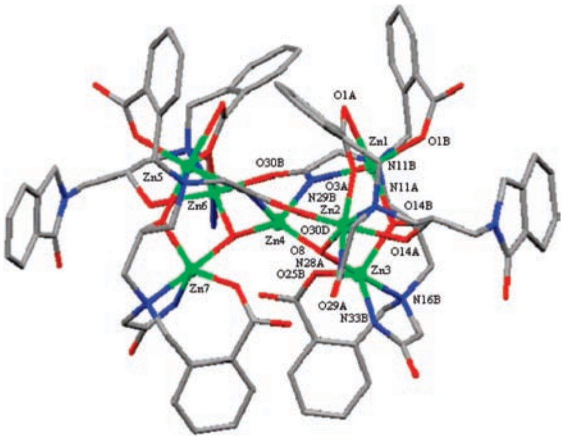

Figure 2. Labeled stick representation of the molecular structure of the dianion portion of complex **2**.

torted octahedral geometry, each center with one bridging alkoxo oxygen, one monodentate carboxylate oxygen, one tertiary amine nitrogen, one bridging amide nitrogen from the Hcadp^{4-} ligand, and one bridging oxygen and one monodentate oxygen of a carboxylate group from the cahdb^{3-} ligand. The coordination geometry around Zn2 and Zn6 is best described by the distorted octahedral geometry, each surrounded by one bridging carboxylate oxygen from one Hcadp^{4-}, one bridging amide oxygen from the other Hcadp^{4-}, one monodentate alkoxo oxygen, one tertiary amine nitrogen and one monodentate amide nitrogen of cahdb^{3-}, and one bridging μ_3-OH group.

One acetamide group ($-CONH_2$, pK_a = 15.1)[22] in one arm of the H$_5$cadp ligand becomes deprotonated in a strongly alkaline medium and bridges between Zn1 and Zn4 through μ_2-NH bonding and Zn6 through μ-O bonding. To the best of our knowledge, complex **2** is the first crystallographically characterized solid-state structure where a singly deprotonated amide group shows a unique bridging mode (η^2-μ_2-NHC(μ-O)CH$_2-$). Voss et al. reported the synthesis, structure, and bonding of a butterfly-like MnRu$_3$ cluster where an acetamidato ligand shows η^2-μ_3-NC(μ-O)CH$_3$ bridging coordination.[23] In the transformed ligand H$_3$cahdb, the one arm is the isoindol moiety and it remains uncoordinated to any of the zinc centers. At the half-side of the transformed ligand, the carboxylate group exhibits a η^2-μ_2-OOC-bridging coordination mode where the single oxygen atom (O3A) bridges between Zn1 and Zn2 ions in a μ-syn,syn fashion. The Zn$-$O$_{\text{bridging alkoxo}}$ and Zn$-$O$_{\text{bridging carboxylate}}$ distances indicate that Zn$-$O alkoxo bridges are close to symmetric [Zn1$-$O14B, 2.052(3); Zn3$-$O14B, 2.009(3) Å] and Zn$-$O carboxylate bridges deviate from symmetry [Zn1$-$O3A, 2.032(3); Zn2$-$O3A, 2.107(3) Å]. At a Zn1$-$O1A distance of 2.406(4) Å, O1A of the bridging carboxylate group of the cahdb^{3-} ligand is weakly interacting with Zn1 and is not involved in any bridging.[24] As shown in Figure 3, the zinc centers that acquire either a distorted tetrahedral trigonal-bipyramidal or a distorted octahedral geometry make up the core structure of the complex.

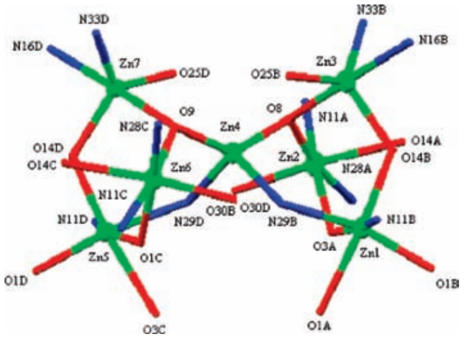

Figure 3. Labeled stick representation of the core structure of complex **2**.

The ^{1}H NMR spectrum of complex **1** shows broad multiplets in the range 2.35$-$4.21 ppm corresponding to the propylenic, ethylenic, and benzylic protons. Complex **2** also shows broad multiplets in the range 2.43$-$4.17 ppm corresponding to the same sets of protons.

In conclusion, we have synthesized and fully characterized novel mononuclear (**1**) and heptanuclear (**2**) zinc complexes. Even in substoichiometric ratios, the new symmetrical dinucleating ligand, H$_5$cadp, forms a unique mononuclear zinc complex, **1**, in weakly alkaline media. However, the heptanuclear zinc complex, **2**, was synthesized in strongly alkaline media via the transformation of one arm of 50% of the symmetrical ligand H$_5$cadp to a new unsymmetrical ligand H$_3$cahdb. The heptazinc complex displays several versatile coordination modes and a unique bridging mode (η^2-μ_2-NHC(μ-O)CH$_2-$) of the amide groups of the Hcadp^{4-} ligand. These unique coordination and transformation abilities of the ligand will positively contribute to the field of coordination and supramolecular chemistry.

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Supporting Information Available: Experimental details, ORTEPs, table of bond lengths and bond angles, synthetic scheme of H$_3$cadp, NMR spectra, and X-ray crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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