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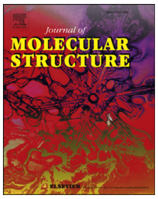

New cyclic tetranuclear copper(II) complexes containing quadrilateral cores: Synthesis, structure, spectroscopy and their interactions with DNA in aqueous solution

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ABSTRACT

Three new cyclic tetranuclear copper(II) complexes, Tetrakis{3-[(2-pyridylmethyl)-amino]-propionato}(tetrachloro)tetracopper(II)methanolhydrate (**1**·CH_3OH·H_2O), Tetrakis{3-[(2-pyridylmethyl)-amino]-propionato}(tetrathiocyanato)tetracopper(II) (**2**) and Tetrakis{3-[(2-pyridylmethyl)-amino]-propionato}(tetraazido)tetracopper(II) (**3**) have been synthesized by exploiting the chelating ability and bridging potential of a carboxyamine functionalized tridentate ligand, HL (HL = 3-[(2-Pyridylmethyl)-amino]-propionic acid). Complexes **1**, **2** and **3** have been synthesized by carrying out reaction of the ligand HL with stoichiometric amounts of $CuCl_2\cdot 2H_2O$, $CuCl_2\cdot 2H_2O/NH_4SCN$, and $CuCl_2\cdot 2H_2O/NaN_3$, respectively, in the presence of NMe_4OH at ambient temperature. Various analytical techniques have been employed to characterize the complexes, including single crystal X-ray diffraction study of **1**. Structures of complexes **2** and **3** have been optimized by DFT calculation at B3LYP/6-311G level. Analysis of X-ray crystal structure reveals that the metallic core of complex **1** contains four distorted square pyramidal Cu(II) ions. The Cu(II) ions in each complex are arranged at the corners of a quadrilateral showing a $\mu_2{:}\eta^1{:}\eta^1$ *syn-anti* bidentate bridging mode of four carboxylate groups of L^- ligands with each bridging between two Cu(II) ions. These complexes represent a new family of 16-MC^{II}_{Cu}-4 metallocoronates with repeating -[Cu^{II}–O–C–O]- units. In aqueous solution (pH~7.5), the interactions of complexes with DNA have been investigated by UV–Vis and fluorescence titration spectroscopy, and viscosity measurements.

1. Introduction

In the past decades, extensive research has been devoted to the construction of polynuclear metal complexes with structural diversity and topological beauty. They have potential applications in gas storage, separation, catalysis, magnetism, sensing, and bioinorganic modeling [1–6]. Among various polynuclear metal complexes, oxo/hydroxo/carboxylate-bridged tetranuclear copper complexes exhibit fascinating plasticity because small structural changes can lead to significantly different magnetic properties [7–11]. A wide variety of polynuclear metal complexes can be synthesized ranging from discrete entities to three-dimensional systems through the bridging of a carboxylate group [12,13]. These complexes display different bridging modes of the carboxylate groups; the most important being *syn-syn*, *syn-anti* and *anti-anti* (Chart 1) [14]. In these polynuclear complexes, the magnetic properties are closely associated with the bridging modes assumed by the carboxylate groups. In general, for copper complexes, the *syn-syn* bridging mode mediates strong antiferromagnetic interactions [15], *syn-anti* bridging mode mediates weak antiferromagnetic interactions [16], and *anti-anti* bridging mode exhibits medium or weak antiferromagnetic or ferromagnetic interactions [14c,17].

Plentiful polynuclear copper complexes have been created by nature and they conveniently carry out the catalytic transformations in biological systems [18,19]. In this context, a number

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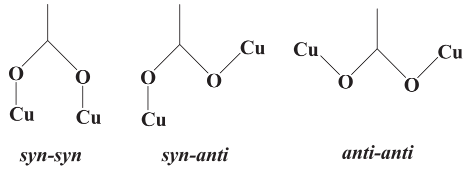


Chart 1. Bridging modes adopted by the carboxylate groups.

of copper complexes are synthesized from ligands containing analogous side chains of proteins for modeling the multinuclear copper(II) enzymes such as hemocyanin and tyrosinase [20–22]. Generally, the synthetic methods employed for the preparation of these polynuclear copper complexes are based on the reaction of copper(II) salts with polydentate ligands, coordination of mono/dimeric copper complexes with other copper(II) salts through non-covalent interaction, or manifold intermolecular interactions involving the bridging ligands [23,24]. Recently, we have reported water-soluble di- and polynuclear complexes of cobalt, nickel, copper and zinc using carboxylate and amine-based polydentate ligands [25–30]. Details in the literature on mono- and dinuclear copper complexes promoting the interaction and cleavage of biological macromolecules such as DNA and protein have been growing [31–34]. Sorenson and Oberley have explored the anticancer activity of copper complexes in animal models [35]. They showed that the complexes exhibited several health benefits such as inhibiting tumor growth and slow-down of metastasis, survivability of host organism, and induction of morphological differentiation of cancerous cells. Besides, many other copper complexes are known to play a significant role in cancer treatment in both *in vitro* and *in vivo* conditions [36]. Careful scrutiny of the literature reveals that there are few reports on polynuclear copper complexes which can efficiently promote the binding and cleavage of biological macromolecules [37,38]. Recently, highly water-soluble tetranuclear Cu_4 and Cu_2Zn_2 complexes showing binding affinity towards BSA protein, has been synthesized and characterized by our group [10]. Gao and co-workers have synthesized and characterized a tetranuclear copper complex containing 3,5-pyridine dicarboxylic acid and 1,10-phenanthroline which shows the binding-cum-cleavage of HC-DNA (HeLa cells DNA) [39]. Thus, in this paper, we report the synthesis, structure, spectral characterization and DNA binding affinity of water-soluble three new cyclic tetranuclear [Cu_4] complexes consisting of quadrilateral cores.

2. Results and discussion

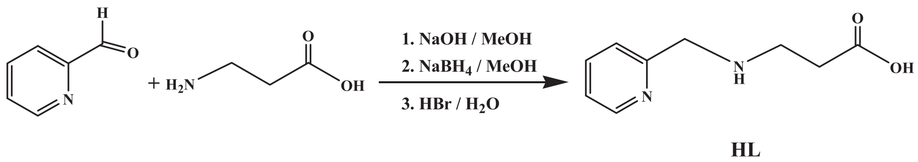
2.1. Synthetic and characterization aspects

The tridentate reduced Schiff base ligand, HL has been synthesized following the published procedure with little modification (Scheme 1) [40]. The ligand is characterized by elemental analysis, FTIR (Fig. S1, Supplementary Information), ^{1}H and ^{13}C NMR (Figs. S2 and S3, Supplementary Information) spectroscopy. This carboxyamine ligand is a very good candidate for the preparation of metal clusters which are found to be highly water-soluble, and this has allowed us to study the DNA binding events in aqueous solution. Previously, copper(II) and nickel(II) ions are known to bind with this ligand to form the mononuclear complexes which have been confirmed by single crystal X-ray crystallography [40,41]. A similar carboxyamine functionalized tridentate *O*,*N*,*O* ligand has been employed by us to afford a bifunctional ligand incorporating the isoindol group which upon reaction with a copper(II) salt produces a dinuclear copper coordination polymer [27,42]. Recently, it has also been reported that similar carboxyamine-based tridentate *N*,*N*,*O* ligands have been utilized to bind with copper(II), cobalt(II) and nickel(II) ions to yield one dimensional coordination polymers [43,44].

In methanol-water, the reaction of HL with $CuCl_2 \cdot 2H_2O$ in 1:1 M ratio in the presence of NMe_4OH, at pH~8 at room temperature produced a green compound, that was crystallized into a tetranuclear cluster, Tetrakis{3-[(2-pyridylmethyl)-amino]-propionato}(-tetrachloro)tetracopper(II)methanolhydrate (**1**$\cdot CH_3OH \cdot H_2O$). Similarly, the reaction of HL with $CuCl_2 \cdot 2H_2O$ in 1:1 M ratio in the presence of NMe_4OH, at pH~8 in methanol-water at room temperature and the use of stoichiometric amounts of NH_4SCN and NaN_3 separately, yielded a blue powder complex, Tetrakis{3-[(2-pyridylmethyl)-amino]-propionato}(tetrathiocyanato)tetracopper(II) (**2**), and a brown powder complex, Tetrakis{3-[(2-pyridylmethyl)-amino]-propionato}(tetraazido)tetracopper(II) (**3**), respectively. The complexes are soluble in H_2O, MeOH, MeCN, DMF and DMSO. All three complexes have been characterized by elemental analysis, FTIR, UV–Vis and room temperature magnetic susceptibility measurements. Additionally, single crystal X-ray structure analysis authenticated the molecular structure of complex **1**. At room temperature, the magnetic moment values of 3.38 μ_B/Cu_4, 3.42 μ_B/Cu_4 and 3.36 μ_B/Cu_4 for **1**, **2** and **3**, respectively, were determined by Guoy method. Therefore, these values per copper center for **1**, **2** and **3** are 1.69, 1.71 and 1.68 μ_B, respectively, indicating the presence of one unpaired electron in each copper center.

2.2. Crystal and molecular structure of complex 1

Complex **1** crystallizes in a tetragonal system and the structure was solved in $P4_2/n$ space group. X-ray crystal data and refinement details for complex **1** are summarized in Table 1. Selected bond distances and angles are given in Table 2. The crystal structure of complex **1** comprises a neutral $[Cu_4(L)_4(Cl)_4]$ species along with one methanol and one water molecule of crystallization. A view of molecular structure of complex **1** is shown in Fig. 1. Four copper(II) ions, four L^- ligands and four Cl^- ions are present in the neutral species of complex **1**. The formation of complex **1** is achieved by self-assembly of four copper(II) ions through exclusive bridging of four carboxylate groups of L^- ligands in a $\mu_2{:}\eta^1{:}\eta^1$ *syn-anti* bidentate fashion. Within the [Cu_4] assembly, each copper center takes similar structural arrangements with respect to the coordination mode of L^- ligand. The bridging carboxylate groups and four copper(II) ions form a 16-membered $(-Cu-O-C-O-)_4$ ring having the metal ions located at the corners of a quadrilateral with the edge of 5.030(2) Å (Fig. 2). Complex **1** can also be viewed as a $16\text{-MC}^{II}_{Cu}\text{-}4$ metallocoronate with repeating -[Cu^{II}–O–C–O]- unit which does not bind any guest cation within the central cavity (Fig. 2). A similar



Scheme 1. Synthesis of the ligand, 3-[(2-Pyridylmethyl)-amino]-propionic acid, HL.