



Ramakrishna Mission Residential College (Autonomous)  
Kolkata 700103, WB, India

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**Collaborative research in functional transition metal complexes**

**Number 45**

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Chemistry**

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**Institute 2: Ramakrishna Mission Residential College (Autonomous)**

**Concerned Faculty: Dr. Prasanta Ghosh, Dept of Chemistry**

**Period of Investigation: 01-10-2019 to 11-12-2020**

**Project: Single Crystal X-ray Measurements**

**Output: Bioactive Transition Metal complexes**

**Publication: One-pot crystallization of 1,4-cyclohexanedicarboxylate based  
two tetranuclear Cu(II) compounds impacts on DNA binding affinities**

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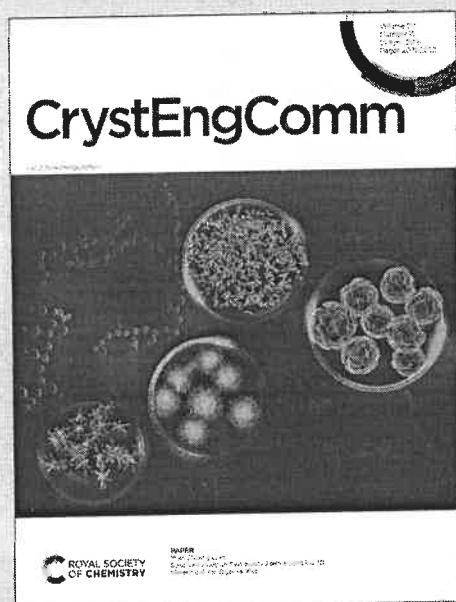
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Journal Name

## ARTICLE

# One-pot crystallization of 1,4-cyclohexanedicarboxylate based two tetranuclear Cu(II) compounds impacts on DNA binding affinities

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Two new tetranuclear compounds  $[\text{Cu}_4(\text{cis-1,4-chdc})_2(2,2'\text{-bpy})_4]\cdot 4(\text{ClO}_4)$  (**1**) and  $[\text{Cu}_4(\text{cis-1,4-chdc})_2(2,2'\text{-bpy})_4(\mu_2\text{-OH})_2]\cdot 2\text{ClO}_4\cdot 2\text{H}_2\text{O}$  (**2**) [ $1,4\text{-H}_2\text{chdc}$  = 1,4-cyclohexanedicarboxylic acid,  $2,2'\text{-bpy}$  = 2,2'-bipyridine] have been prepared by stirring copper(II) perchlorate hexahydrate  $[\text{Cu}(\text{ClO}_4)_2\cdot 6\text{H}_2\text{O}]$  with  $2,2'\text{-bpy}$  and sodium-salt of  $1,4\text{-H}_2\text{chdc}$ . The compounds are formed in one-pot crystallization and visibly distinct in colour with dark blue and sky blue appearances respectively for **1** and **2**. Both compounds have been characterized by elemental analysis as well as single crystal X-ray diffraction (SCXRD) technique. Interestingly, both the compounds show significant DNA binding affinity with ctDNA and these experimental findings are further corroborated by docking study. However, compound **1** with more cationic charge exhibits better DNA binding affinity compared to **2**.

## Introduction

Novel coordination compounds have been widely synthesized for few decades by inorganic synthetic chemists especially in the field of crystal engineering because of their amazing structural motifs and prospective applications in catalysis, molecular adsorption, ion-exchange, magnetism, nonlinear optics, and molecular sensing.<sup>1–14</sup> The structural aspects of the synthesized compounds can potentially be tuned by astute choice of metal containing secondary building units and bridging organic linkers in terms of shape, functionality, flexibility, and symmetry. The impetus is put on the construction of supramolecular architectures with interesting compositions and topologies for fascinating creativity as well as desired applications.<sup>15–23</sup> In view of this, longer dicarboxylates and bidentate pillar linkers are broadly used in the creation of various compounds.<sup>24–26</sup> Of various dicarboxylic acid ligands, usage of 1,4 cyclohexanedicarboxylic acid ( $1,4\text{-H}_2\text{chdc}$ ) seems to be not much explored and could be an interesting choice for the formation of fascinating architectures. Organic nitrogen donor linkers such as pyridine based derivatives  $4,4'\text{-bipyridine}$  ( $4,4'\text{-bpy}$ ),  $4\text{-phenylpyridine}$

( $4\text{-phpy}$ ),  $2,2'\text{-bipyridine}$  ( $2,2'\text{-bpy}$ ) and  $1,10\text{-phenanthroline}$  ( $1,10\text{-phen}$ ) are introduced into the framework of metal–chdc complexes to incorporate special properties in those novel coordination compounds.<sup>27–31</sup>

In another development in the interface of inorganic chemistry and biology, metal-based drugs have become a remarkable success.<sup>32</sup> The choice of metal ion along with its oxidation state and the ligand framework largely influence the design of such metal-based pharmaceuticals.<sup>33–34</sup> In the fields of biotechnology and therapeutic reagents, many transition metal complexes have been explored as effective tools for DNA cleavage activities. The transition metal complexes, known to bind DNA via both covalent and non-covalent interactions, have the ability to induce cleavage of DNA under physiological conditions, which make the way for further research in the development of therapeutic agents.<sup>35–43</sup> Copper (Cu) being a bioessential element demonstrates a key role in biological processes and hence copper complexes are extensively studied for their enormous biological significance in living system.<sup>44–47</sup> A good number of Cu-complexes have been identified for anticancer activity, and some of them are observed to be active both *in vitro* and *in vivo*.<sup>42,48</sup> The kinetic analysis of Cu–DNA interaction and its site-specific binding in DNA are well-documented.<sup>49,50</sup>

In 1947, Michaelis advocated that a planar heterocyclic base is a prerequisite for insertion between the bases of DNA. Ligands with characteristics of water solubility, planarity, aromaticity or heteroaromaticity as well as owning structure like a purine or pyrimidine base pair in overall size are potentially right

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† Electronic Supplementary Information (ESI) available: Table S1–S9, Fig. S1–S3 and X-ray crystallographic data in CIF format for compounds **1** and **2**. CCDC numbers 1985886–1985887. For ESI and crystallographic data in CIF or other electronic format See DOI: 10.1039/x0xx00000x



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**Collaborative Research in Analytical Coordination Chemistry**  
**Number 46**

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Road, Kolkata 700009, India**

**Concerned Faculty: Prof. Debasis Das, Department of Chemistry**  
**&**

**Institute 2: Ramakrishna Mission Residential College (Autonomous)**  
**Concerned Scholar: Dr. Suvendu Maity, Dept of Chemistry**

**Period of Investigation: 20-8-2019 to 23-06-2020**

**Project: Spectroscopic Detection of Cations**

**Output:** The result was published in a journal of international repute

**Publication: A Chemodosimetric Approach for Fluorimetric Detection of  $\text{Hg}^{2+}$  Ions by Trinuclear Zn(II)/Cd(II) Schiff Base Complex: First Case of Intermediate Trapping in a Chemodosimetric Approach**  
Abani Sarkar, Aratrika Chakraborty, Tonmoy Chakraborty, Suranjana Purkait,  
Debabrata Samanta, Suvendu Maity and Debasis Das  
*Inorg. Chem.* 2020, 59, 13, 9014–9028. DOI: 10.1021/acs.inorgchem.0c00857

**Prof. Debasis Das**

**Dr. Suvendu Maity**



# A Chemodosimetric Approach for Fluorimetric Detection of $\text{Hg}^{2+}$ Ions by Trinuclear $\text{Zn}(\text{II})/\text{Cd}(\text{II})$ Schiff Base Complex: First Case of Intermediate Trapping in a Chemodosimetric Approach

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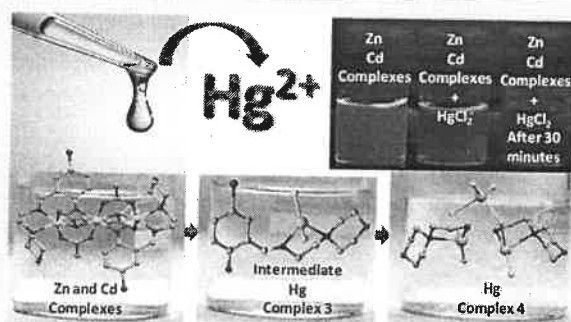


Article Recommendations



Supporting Information

**ABSTRACT:** The present work discloses the application of two fluorescent zinc and cadmium complexes (1 and 2) for sensing of  $\text{Hg}(\text{II})$  ions through a chemodosimetric approach. The ligand under consideration in this work is a  $\text{N}_2\text{O}$  donor Schiff base ligand (*E*)-4-bromo-2-(((2-morpholinoethyl)imino)methyl)phenol (HL), which has been harnessed to generate complexes  $[\text{Zn}_3\text{L}_2(\text{OAc})_4]$  (1) and  $[\text{Cd}_3\text{L}_2(\text{OAc})_4]$  (2). X-ray single crystal diffraction studies unveil the trinuclear skeleton of complexes 1 and 2. Both complexes have been found to be highly fluorescent in nature. However, the quantum efficiency of  $\text{Zn}(\text{II})$  complex (1) dominates over the  $\text{Cd}(\text{II})$  analogue (2). The absorption and emission spectroscopic properties of the complexes have been investigated by density functional theory. Complexes 1 and 2 can detect  $\text{Hg}^{2+}$  ions selectively by fluorescence quenching, and it is noteworthy to mention that the mechanism of sensing is unique as well as interesting. In the presence of  $\text{Hg}^{2+}$  ions, complexes 1 and 2 are transformed to mononuclear mercuric intermediate complex (3) and finally to a trinuclear mercuric complex (4) by hydrolysis. We have successfully trapped the intermediate complex 3, and we characterized it with the aid of X-ray crystallography. Transformation of complexes 1 and 2 to intermediate complex 3 and finally to 4 has been established by UV–vis spectroscopy, fluorescence spectroscopy, ESI-MS spectroscopy,  $^1\text{H}$  NMR spectroscopy, and X-ray crystallography. The spontaneity of the above conversion is well supported by thermodynamic aspects as reflected from density functional theoretical calculations.



## INTRODUCTION

The extreme toxicity of  $\text{Hg}^{2+}$  toward the environment as well as living organisms is no doubt a significant concern for the scientific community. Therefore, invention of a simple but efficient technology to curb its effect is highly necessary.<sup>1–3</sup> Health and environmental concerns over Hg contamination have instigated many researchers to develop suitable strategies for supervision of Hg levels in the environment.<sup>4–9</sup>

In the last few decades the development of cation chemo sensors has become increasingly important for detection of toxic and carcinogenic metal ions such as  $\text{Cd}^{\text{II}}$ ,  $\text{Hg}^{\text{II}}$ , and  $\text{Pb}^{\text{II}}$ , since these cations cannot be characterized by conventional experimental techniques like magnetic measurements, EPR spectra (since they are diamagnetic) and absorption spectra (they have no d–d band).<sup>10</sup> Currently, the most common methods to detect metal ions include atomic absorption spectrometry<sup>11</sup> and inductively coupled plasma mass spectrometry.<sup>12</sup> However, these instrumentally demanding methods can measure only the total metal ion content, which requires extensive sample preparation. Thus, it is a challenging work for chemists to find an easy and inexpensive method that

can not only detect but also quantify these metal ions. Among the various detection techniques, optical detections techniques (via fluorescence or colorimetric changes) have some definite advantages like high sensitivity, low detection limit, easy operational techniques,<sup>13</sup> and so on, and colorimetric changes have the advantage of naked eye recognition.<sup>14</sup>

During the past decade, great efforts have been devoted to the development of fluorescent and colorimetric sensors that are able to selectively detect metal ions, but currently, there still remains plenty of scope to develop selective and sensitive methods for the detection of metal ions. In this regard, organic ligands play a crucial role because of their structural diversity as well as tunable photophysical properties.<sup>15</sup> The group 12

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metals (Zn, Cd, and Hg) have the  $d^{10}$  configuration and generally exist as divalent ions but not only also as monovalent  $Hg_2^{2+}$  ion via a Hg–Hg bond (2.5 Å). However, most of the mercury complexes exist with +2 metal oxidation state because of the lower reactivity and poor purity of the Hg(I) complexes, and only few  $Hg_2^{2+}$  complexes have been structurally reported to date.<sup>16–19</sup> There are several reports on the photophysical properties and relative binding affinity of some Zn(II) and a few examples of Cd(II) and Hg(II)<sup>20–22</sup> complexes in other type of ligand studies. Rational design of fluorescent chemosensors remains a challenge in terms of selectivity and sensitivity. High selectivity is usually achieved when the receptor has high affinity for the metal ion of interest. To meet such a prerequisite, extensive effort needs to be spent on the design and engineering of receptors with varied chemical structures. In particular, for  $Hg^{2+}$  sensing, design of suitable sensors is a challenging task because of its low binding constant and  $d^{10}$  configuration.  $Hg^{2+}$  loses its visual spectroscopic indication, and its optical detection techniques is achieved only through monitoring  $Hg^{2+}$ -triggered changes in the UV–vis or fluorescence of a variety of fluorophore units like metal nanoparticles,<sup>23</sup> proteins,<sup>24</sup> coumarin,<sup>25</sup> macrocycle,<sup>26</sup> imine,<sup>27</sup> phenol,<sup>28</sup> and so on. In most of the cases these methods bear some imminent limitations such as poor solubility issue of probe, cross-sensitivity of other metal ions and cost effectiveness of the probe synthesis. Furthermore, the selective spectroscopic response to detect  $Hg^{2+}$  largely depends upon elegant designing of the probes.

From the literature survey, we have retrieved plenty of reports where  $Hg^{2+}$  sensing is achieved by efficient organic chemosensors.<sup>25–32</sup> However, there are shortage of reports where metal complexes are projected as efficient chemosensors capable of sensing  $Hg^{2+}$ . Metal-complex-based chemosensors excel over traditional organic-chemosensors in the area of selectivity and sensitivity, and hence, their extensive usage might be a fruitful solution to the sensitivity issue.<sup>33</sup>

In contrast to the conventional route, which is usually realized by direct metal–ligand interaction between the receptor and target cation, sensing via metal–metal displacement approach is an interesting alternative. Metal–metal displacement or rather transmetalation reactions have proved to be extremely valuable when implemented, especially in the field of sensing.<sup>33,34</sup> To date, a handful of literature reports are available for this type of sensing mechanism.<sup>33–38</sup> Moreover, there are also inadequate reports with conclusive evidence on the identity of the central metal ion on the sensing performance via metal–metal displacement reactions. Additionally, these reports do not provide any direct proof for their detection mechanism. In this light, trapping of the intermediate species would be a highly interesting approach to justify the mechanism. It is noteworthy that there is significant lack of evidence of chemosensors where the metal–metal displacement is directly probed by the associated crystal structure characterizations and furthermore there is scarcity of literature reports portraying  $Hg^{2+}$  sensing through  $Zn^{2+}/Hg^{2+}$  displacement reactions or  $Cd^{2+}/Hg^{2+}$  ones. Report by Lee et al. delineates sensing of  $Hg^{2+}$  by displacement of  $Zn^{2+}$  in a NABQ based ligand.<sup>34</sup> Apart from the mentioned work, there are no such reports of  $Hg^{2+}$  sensing occurring via transmetalation involving zinc or cadmium. In order to overcome the challenge to develop sensors adequate to sense metal ions with high precision, we have aimed to provide a conclusive mechanistic

pathway of  $Hg^{2+}$  sensing by a zinc/cadmium based complex with high sensitivity and selectivity.

The present work involves fluorimetric detection of  $Hg^{2+}$  ions by fluorescent zinc and cadmium complexes (1 and 2) containing a  $N_2O$  donor Schiff base ligand (HL). Both complexes 1 and 2 were obtained by the condensation of 4-(2-aminoethyl)morpholine and 5-bromosalicylaldehyde in a methanolic medium borea trinuclear based framework as confirmed by X-ray crystallography (Scheme 1). A zinc complex analogous to 1, with a ligand obtained by the condensation of 4-(2-aminoethyl)morpholine with 5-chlorosalicylaldehyde instead of 5-bromosalicylaldehyde, has been previously reported by our group.<sup>39</sup> The work reported therein consisted of the exploration of biorelevant catalytic property of the zinc complex, but no investigation of the photophysical properties of the complex was conducted. The most interesting aspect and one of the rare findings in the sensing approach of the present work is trapping of intermediate complex 3, which is formed through  $Hg^{2+}$  ion promoted transmetalation of the  $Zn^{2+}/Cd^{2+}$  ions from their complexes followed by subsequent hydrolysis of the imine moiety of the ligand (HL). The chemodosimetric pathway has been justified, probably for the first time, by trapping the intermediate Hg(II) complex 3, which finally transformed into new complex 4. The formation of intermediate complex 3 was confirmed and identified by X-ray crystallography as well as mass spectroscopy and  $^1H$  NMR studies. ESI-MS spectroscopic methods prove the displacement of zinc(II) and cadmium(II) metal centers from the trinuclear framework by mercury(II) ions during the course of sensing. For a better understanding of the chemodosimetric mechanism of detection of  $Hg^{2+}$  ions by complexes 1 and 2, DFT calculations have been performed.

## EXPERIMENTAL SECTION

**Materials and Physical Methods.** High-purity 5-bromosalicylaldehyde and 4-(2-aminoethyl)morpholine were purchased from Sigma-Aldrich and used without further purification. Solvents were dried according to standard procedures. All other chemicals used are of AR grade. A PerkinElmer 240C analyzer was used to perform the elemental analyses (C, H and N). Shimadzu FTIR-8400S and PerkinElmer Spectrum Express Version 1.03 were used for recording infrared spectra ( $4000\text{--}400\text{ cm}^{-1}$ ) at  $28\text{ }^\circ\text{C}$  using KBr pellets as medium. Mass spectrometry was carried out in Waters Xevo G2-S Q TOF. Fluorescence emission spectra and excited-state lifetime measurements were carried on in PerkinElmer LS-55 and Horiba JobinYvon Fluorocube-01-NL respectively. UV–vis spectra ( $800\text{--}200\text{ nm}$ ) were obtained at  $27\text{ }^\circ\text{C}$  using a Shimadzu UV-3101 PC. The fluorescence quantum yield ( $\Phi$ ) was evaluated by comparing the corrected emission spectra of the complexes with that of the quinine sulfate measured in  $0.1\text{ M H}_2\text{SO}_4$  ( $\Phi = 0.54$ ) considering the total area under the emission curve. In this calculation,  $\Phi$  is the quantum yield of the compounds,  $A$  is the integrated fluorescence intensity (area under the emission curve), OD is the optical density, and  $n$  is the refractive index of the medium.  $^1H$  NMR spectra ( $400\text{ MHz}$ ) were recorded in  $d_6\text{DMSO}$  on a Bruker ultrashield DPX-400 spectrometer.

### Caution!

Mercury and cadmium salts are toxic and hence extreme caution to be taken while handling these chemicals.

**Synthesis of Complex  $[Zn_3L_2(OAc)_4]$  (1).** 5-Bromosalicylaldehyde (0.402 g, 2 mmol) and 4-(2-aminoethyl)morpholine (0.260 g, 2 mmol) were added to 10 mL of methanol, and the resultant solution was heated in a water bath up to 1 h. As the color of the solution progressed toward dark yellow, a 10 mL methanolic solution of zinc(II) acetate (0.438 g, 2 mmol) was added. After addition of metal salt, the final solution was further heated in water bath for 1 h





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**Institute 2: Ramakrishna Mission Residential College (Autonomous)  
Concerned Scholar: Dr. Suwendu Maity, Dept of Chemistry**

**Period of Investigation: 20-8-2019 to 24-05-2020**

**Project: Transition Metal Schiff Base Complexes and Catecholase Activity**

**Output:** The result was published in a journal of international repute

**Publication: Catalytic promiscuity of a copper(II)-Mannich base complex  
having unprecedented radical pathway in catecholase activity**

Sanchari Dasgupta, Arnab Mandal, Debabrata Samanta, Ennio Zangrando,  
Suwendu Maity and Debasis Das

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**Prof. Debasis Das**

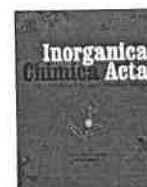
**Dr. Suwendu Maity**





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Research paper

# Catalytic promiscuity of a copper(II)-Mannich base complex having unprecedented radical pathway in catecholase activity

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Phosphatase like activity  
DFT study

## ABSTRACT

A flexible single-side Mannich base ligand namely 4-(*tert*-butyl)-2-((ethyl(2-hydroxyethyl)amino)methyl)phenol ( $H_2L$ ) having O, N, O donor sites has been designed and synthesized using 4-(*tert*-butyl)phenol, formaldehyde and 2-(ethylamino)ethanol as precursors with the view to prepare polynuclear complex(s). In the first attempt a tetranuclear copper (II) complex,  $[Cu_4(L)_2(HL)_2] \cdot (ClO_4)_2 \cdot H_2O$  (**1**) has been synthesized employing  $H_2L$  and copper(II) perchlorate with the aim to explore catalytic promiscuity of the species. Detailed experimental investigations suggest that in solution complex **1** exists as a dinuclear entity. The dinuclear species is a square-planar  $Cu^{II}$  complex as is evident from EPR and UV–Vis spectral studies. It exhibits excellent catalytic activities in catalyzing the oxidation of 3,5-di-*tert*-butyl catechol (3,5-DTBC) to 3,5-di-*tert*-butyl quinone (3,5-DTBQ); oxidation of *o*-aminophenol to phenoxazinone and P–O bond hydrolysis of 4-nitrophenyl phosphate. Amazingly, complex **1** catalyses the aerobic oxidation of 3,5-DTBC not by well established metal centered redox participation, rather via a ligand centered radical pathway, a completely new finding in copper(II) based catechol oxidase modeling as are verified by experiments and seconded by DFT calculations.

## 1. Introduction

‘Catalytic Promiscuity’, a new popular terminology is now widely used by bioinorganic chemists. The term ‘Catalytic Promiscuity’ of an enzyme is defined as its ability to catalyze multiple catalytic transformations which belong to different classes [1]. Another definition of ‘Catalytic Promiscuity’ is the capability of a single active site to catalyze more than one chemical transformation as proposed by Romas J Kazlauskas [2]. Chymotrypsin (that catalyzes hydrolysis of amides, esters, thiol esters, acid chlorides and anhydrides) [3], bovine carbonic anhydrase II (catalyzes phosphotriesterase activity, carbon esterase activity and  $CO_2$  hydrates activity) [4], carbonic anhydrase III (catalyzes hydrolysis of phosphomonoester monocation, carbon ester and hydration of carbon dioxide) [5] are familiar enzymes showing catalytic promiscuity.

In recent times activation of dioxygen by dinuclear transition metal complexes has been studied comprehensively and preparation of biomimetic models of oxidases, oxygenases, dehydrogenases and other metalloenzymes draws the immense attention of the bioinorganic

chemists [6]. Multicopper oxidase belongs to an important class of oxidase enzyme which contains seven kinds of active sites depending on the structural and functional properties of copper centre namely, Type-1, Type-2, Type-3, Type-4,  $Cu_A$ ,  $Cu_B$  and  $Cu_Z$  active sites. Catechol oxidase (CO) and phenoxazinone synthase (PHS) belongs to oxidases group of enzyme [7].

CO, a Type-3 copper protein, contains antiferromagnetically coupled dinuclear copper(II) centers at their active site and catalyzes oxidation of catechol derivative to corresponding quinone [8–14]. This oxidation is worthy for medical diagnosis of the hormonally active catecholamine, adrenaline, noradrenaline and dopa [15,16]. Till date several bio mimicking models of CO have been reported to have an insight about their mechanistic pathways. Generally two kinds of pathways are operative, (i) metal centered redox participation [17–24] and (ii) ligand centered radical pathway [25–32]. The ligand centered radicals till now demonstrated are of three types: (i) imine radical, [25–30] found in Schiff base based models, (ii) arene/benzene anion radical observed in reduced Schiff base complexes [31] and (iii) phenoxo radical for Mannich base complexes [32].

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PHS contains five different copper centers at active site namely type-1, type-2 and type-3 [33]. PHS which is very important in pharmaceutical industries being involved in the last step of biosynthesis of antibiotic actinomycin D by *Streptomyces antibioticus* [34]. The mechanistic pathway of phenoxazinone synthase, involves the formation of organic radical with concomitant reduction of either metal or ligand centre [30,35,36].

On the other hand designing of metal complexes as bio-mimicking models of phosphatase, a class of hydrolysis enzymes became an imperative field to bio-inorganic chemists. These enzymes catalyse the hydrolysis of P–O bond of phosphate monoesters, di-esters, tri-esters, fluorophosphates, fluorophosphonates, phosphoric anhydrides etc. and the hydrolysis reaction plays a significant role in life processes, medical field and agriculture [37–42]. It is well known that bi-valent metal cations play a vital role towards the nucleophilic substitution of naturally occurring phosphate ester bond in most of the cases. It is already well documented in literature that the rate of hydrolysis of phosphate ester bond increases several times in presence of mononuclear model complexes in compare to the uncatalysed reaction and that rate enhance appreciably when dinuclear catalysts are used. Most of the reported models contain zinc(II) as metal centre. However, Sigel et al. and Trogler et al. reported that copper(II) metal ion can also efficiently catalyse the hydrolysis of P–O bond of triphosphates [43,44]. It is already established that  $\text{Cu}^{2+}$  and  $\text{Ni}^{2+}$  metal based models exhibit the highest catalytic activity among the first row transitional metals [44]. Thus in past few decades  $\text{Cu}^{2+}$  has been used as a good alternative to  $\text{Zn}^{2+}$  in model complexes [45–47].

In the present work we report a tridentate Mannich base ligand with O, N, O donor set, which is designed and synthesized for the flexibility of the  $\text{CH}_2\text{-NR}$  moiety (Scheme 1), that may help to produce complexes of different nuclearity [48,49]. In the first attempt, a tetranuclear complex,  $[\text{Cu}_4(\text{L})_2(\text{HL})_2](\text{ClO}_4)_2 \cdot 2\text{H}_2\text{O}$  (1) has been synthesized (Scheme 1) purposefully to explore its catalytic promiscuity in terms of catecholase activity, phenoxazinone synthase activity and phosphatase activity. Complex 1 acts as the catalyst precursor to generate dinuclear active catalyst in solution. Complex 1 appears not only as a highly efficient oxidizing catalyst but also as a potential hydrolytic agent. It catalyses the aerobic oxidation of the model substrate 3,5-DTBC to 3,5-DTBQ in excellent rate. The reaction proceeds not via metal centered redox participation but through ligand centered radical pathway. It is a completely new finding in catecholase activity study in dinuclear copper(II) system as is established by combined experimental and theoretical investigations. The mechanistic pathways of phenoxazinone synthase activity and phosphatase activity of complex 1 have also been extensively studied. All those findings have been vividly portrayed in

this communication.

## 2. Experimental section

### 2.1. Physical methods and materials

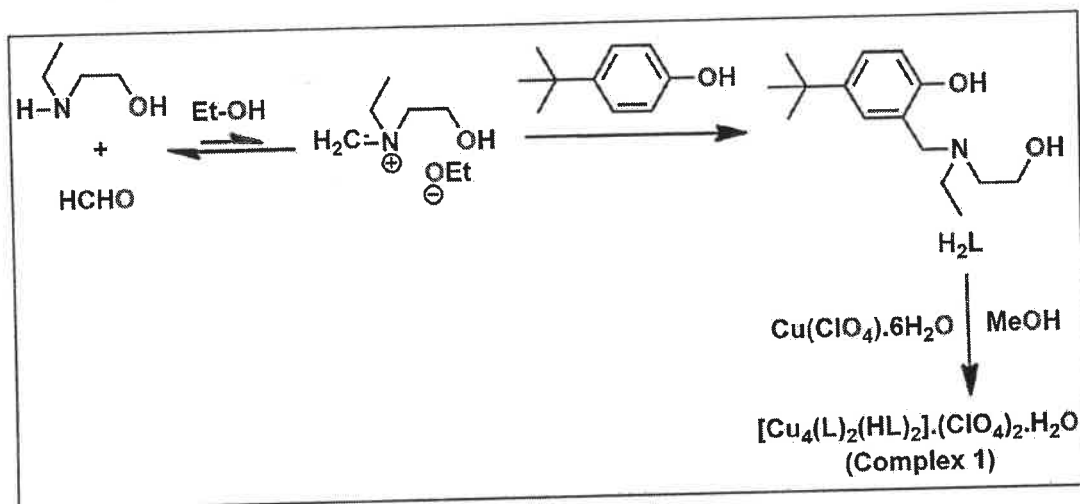
Elemental analyses (carbon, hydrogen, and nitrogen) were carried out using a Perkin–Elmer 240C elemental analyzer. Fourier Transform Infrared spectra were recorded on KBr disks and NaCl disks ( $400\text{--}4000\text{ cm}^{-1}$ ) and a Perkin–Elmer RXI FTIR spectrophotometer. Electronic spectra and kinetic studies ( $200\text{--}900\text{ nm}$ ) were measured at room temperature with a Shimadzu UV 3101PC instrument and dry DMF as solvents.  $^1\text{H}$  NMR spectra (300 MHz) were recorded in  $\text{d}_6\text{-DMSO}$  as solvents and TMSCl as standard at  $25\text{ }^\circ\text{C}$  with a Bruker AV300 Supercon NMR spectrometer and use of the solvent signal as the internal standard in a 5 mm BBO probe. Electrospray mass spectra were recorded on a WATERS Xevo G2-S Q ToF mass spectrometer using HRMS-grade acetonitrile as solvent. The cyclic voltammograms were obtained with a Basi C-3 cell voltameter under nitrogen with a glassy carbon electrode as working electrode, Ag/AgCl as reference electrode and tetrabutylammonium perchlorate as supporting electrolyte.

High-purity 4-(*tert*-butyl)phenol, 2-(ethylamino)ethanol and 37% (w/v) formalin solution, copper(II) perchlorate hexahydrate were purchased from commercial sources (Alfa Aesar, Sigma-Aldrich, Merck) and used as received. Solvents were dried by standard procedures and distilled prior to use.

**Caution!** Perchlorate salts are explosive. They should be handled with great care and in small amounts.

### 2.2. Synthesis of ligand ( $\text{H}_2\text{L}$ )

To an ethanolic solution of 4-(*tert*-butyl)phenol (25 mmol, 3.75 g), ethanolic solution of 2-(ethylamino)ethanol (25 mmol, 2.22 g) is added. Then 37% (w/v) formalin solution (25 mmol, 2.1 mL) has been added and the resulting yellow colored solution is refluxed for 10 h. The reaction mixture is evaporated under reduced pressure. The oil-like residue is extracted with brine solution and dichloromethane for three times. The organic layer has been collected and dried with anhydrous  $\text{MgSO}_4$ . The ligand has been collected after complete evaporation of dichloromethane. Yield: 90%; FT-IR (NaCl):  $\nu(\text{C}=\text{N})$   $1583\text{ cm}^{-1}$ ;  $\nu$  (skeletal vibration)  $1472\text{ cm}^{-1}$  (Fig. S1).  $^1\text{H}$  NMR (300 MHz,  $\text{d}_6\text{-DMSO}$ ,  $25\text{ }^\circ\text{C}$ ):  $\delta$  1.124 (s, 9H,  $\text{C}(\text{CH}_3)_3$ );  $\delta$  3.630 (s, 2H,  $\text{Ar-CH}_2\text{-N}$ );  $\delta$  2.463 (q, 2H,  $\text{N-CH}_2\text{-CH}_3$  and 2H,  $\text{N-CH}_2\text{-CH}_2\text{-OH}$ );  $\delta$  3.449 (q, 2H,  $\text{N-CH}_2\text{-CH}_2\text{-OH}$ );  $\delta$  0.899 (t, 3H,  $\text{N-CH}_2\text{-CH}_3$ );  $\delta$  3.630 (q, 1H,  $\text{N-CH}_2\text{-CH}_2\text{-OH}$ );  $\delta$  7.078 (d, 1H, Ar);  $\delta$  6.973 (d, 1H, Ar);  $\delta$  6.598 (d, 1H, Ar) (Fig. S2).  $^{13}\text{C}$



Scheme 1. Synthetic route of complex 1.



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**Collaborative Research in Analytical Coordination Chemistry**

**Number 48**

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Road, Kolkata 700009, India**

**Concerned Faculty: Prof. Debasis Das, Department of Chemistry**

**&**

**Institute 2: Ramakrishna Mission Residential College (Autonomous)**

**Concerned Faculty: Dr. Prasanta Ghosh, Dept of Chemistry**

**Period of Investigation: 20-3-2019 to 07-02-2020**

**Project: Bioactive Transition Metal Schiff Base Complexes**

**Output:** The result was published in a journal of international repute

**Publication: Unveiling the binding interaction of zinc (II) complexes of homologous Schiff-base ligands on the surface of BSA protein: A combined experimental and theoretical approach**

Tania Chowdhury, Kaushik Bera, Debabrata Samanta, Sandip Dolui, Suvendu Maity, Nakul C Maiti, Prasanta Ghosh and Debasis Das  
*Applied Organometallic Chemistry*, 2020, 34, 4, e5556, DOI: 10.1002/aoc.5556

**Prof. Debasis Das**

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## FULL PAPER

# Unveiling the binding interaction of zinc (II) complexes of homologous Schiff-base ligands on the surface of BSA protein: A combined experimental and theoretical approach

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## Funding information

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Four new zinc (II) complexes [Zn (HL<sup>1</sup>H)Br<sub>2</sub>] (1), [Zn (HL<sup>1</sup>H)Cl<sub>2</sub>] (2), [Zn<sub>2</sub>(HL<sup>2</sup>)Br<sub>3</sub>] (3), and [Zn (HL<sup>2</sup>)Cl] (4) have been synthesized by adopting template synthetic strategy and utilizing two homologous Schiff base ligands (H<sub>2</sub>L<sup>1</sup> = 4-bromo-2-[[2-(2-hydroxyethylamino)-ethylimino]-methyl]-6-methoxyphenol, H<sub>2</sub>L<sup>2</sup> = 4-bromo-2-[[3-(2-hydroxyethylamino)propylimino]methyl]-6-methoxyphenol), differing in one -CH<sub>2</sub>- unit in the ligating backbone, by adopting template synthetic strategy. All the complexes have been characterized by single crystal X-ray diffraction analysis as well as by other routine physicochemical techniques. Ligand mediated structural variations have been observed and rationalized by density functional theoretical (DFT) calculations. Interaction of the complexes 1–4 with Bovine Serum Albumin protein (BSA) has been studied by different spectroscopic techniques. A complete thermodynamic profile ( $\Delta H^\circ$ ,  $\Delta S^\circ$  and  $\Delta G^\circ$ ) was evaluated initially from the change in absorption and fluorescence spectra upon addition of BSA to the complexes. Appreciable binding constant values in the range  $\sim 0.94\text{--}4.51 \times 10^4 \text{ M}^{-1}$  indicate efficient binding tendency of the complexes to BSA with the sequence  $1 \cong 2 > 3 \cong 4$ . Circular dichroism (CD), isothermal calorimetric titration experiments, molecular docking and molecular dynamics have been performed to gain deep insight into the binding regions of complex 1 to BSA. Experimental evidences suggest an interaction of zinc complexes at the surface of BSA protein and this particular binding has been exploited to determine unknown concentration of BSA protein. For this purpose complex 1 was explored as a BSA protein quantification tool.

## KEYWORDS

BSA, homologous Schiff base, protein quantification tool, structurally diverse Zn-complex, surface binding

## 1 | INTRODUCTION

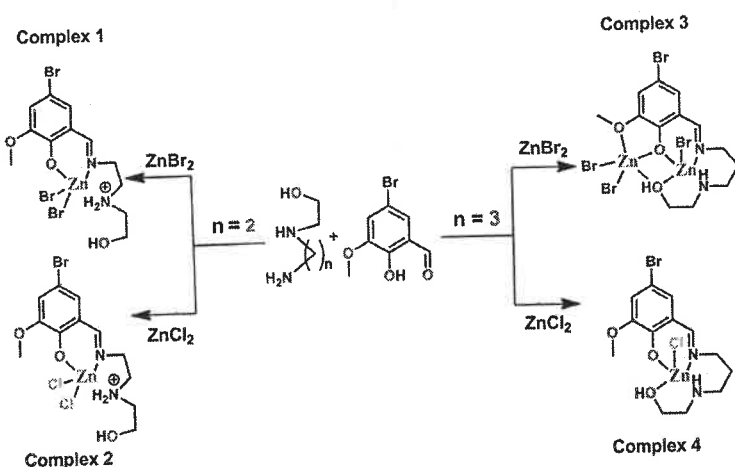
Over past few decades, the marked propensity to use metal complexes as bioactive substance has attracted

enormous interest in order to procure an alliance between chemistry and biology. Incorporation of transition metals to suitable heterocyclic moieties generates coordination compounds which possess enhanced

physicochemical and pharmacological properties. In the field of pharmacology designing of drugs as well as their interaction analysis with plasma proteins is a major determinant of drug disposition. Albumin, lipoproteins, and  $\alpha$ 1-acid-glycoprotein (AGP) are the proteins that commonly involved binding drugs, facilitating and helping their transport through the blood stream. The first discovered and most intensely studied protein is albumin, a plasma protein that is the most abundant in the vertebrates' organisms (about 60% of the total protein content of plasma). Human serum albumin has cylindrical structure with polar outer walls and a hydrophobic central core.<sup>[1]</sup> These multiple binding sites make it feasible for several organic heterocyclic aromatic molecules or their metal complexes to bind within the hydrophobic pocket as well as at the polar N-terminus.<sup>[2–5]</sup> Bovine serum albumin (BSA) is widely employed for model study due to its structural homology with human serum albumin (HSA).<sup>[6,7]</sup> An investigation of new metal complexes by varying their geometry, size and hydrophobicity appears useful to assess their binding to BSA protein. Protein-drug interaction is crucial for the drug efficiency as this interaction is most likely responsible to control absorption, transportation, distribution and metabolism of drugs.<sup>[8,9]</sup> The biological properties of the original drug could be enhanced or reduced due to binding to these proteins. Generally, a strong binding with protein will lead to reduce overall drug excretion due to having a low concentration of free drug in plasma, whereas for drugs interacting only via Van der Waals or H-bonding the drug-protein adduct breaks down before reaching to the targeted site. The protein binding assay may provide the pathway for drug transportation. Only a few studies have been reported on the binding of Schiff base-metal complexes with BSA protein.<sup>[10–12]</sup> Jun-Cheng et al. reported a Zn-Nd Schiff base complex that binds properly

with bovine serum albumin protein.<sup>[13]</sup> Hadadzadeh and his group prepared complex 5,6-diphenyl-3-(2-pyridyl)-1,2,4-triazine-Zn (II) that quenches fluorescence intensity of BSA.<sup>[14]</sup> Shrivastava et al. found that binding interaction of the Schiff-base ligand with BSA changes the protein helicity content.<sup>[15]</sup> Among the transition metals, zinc is a judicious choice in the context of metal-based pharmaceuticals due to its reactivity with wide range of organic ligands, superior Lewis acidity, flat coordination hypersurface and biocompatibility.<sup>[16–20]</sup> Moreover in proteins, zinc ions are regularly coordinated to the amino acid side chains of aspartic acid, glutamic acid, cysteine and histidine etc. Zinc is an inevitable component in controlling countless metabolic and signalling pathways within the body.<sup>[21–23]</sup> Superior Lewis acidity of  $Zn^{II}$  enables it to interact with albumin, a protein which is basic in nature.

To gain insights about how metal complexes can be administered intravenously to primary target molecules like serum albumins, herein, we designed a formulation process that includes the synthesis of four zinc (II) complexes (1–4) from two homologous Schiff base ligands (Scheme 1). Interestingly, the variation of a methylene group in the ligand backbone results in complexes of different the variation of nuclearity and the results of these experimental evidences were analysed by DFT calculations. Here, it is noteworthy that evaluation of actual binding mode of protein with drug is a matter of great challenge. However, detailed spectroscopic studies like absorption, emission, isothermal titration calorimetry (ITC) and circular dichroism (CD) studies may help to get a complete thermodynamic profile ( $\Delta G$ ,  $\Delta H$ , and  $\Delta S$ ) and thereby to shed light on the interaction mode. By using these spectroscopic techniques, in the present work we have thoroughly investigated the interaction of the synthesized zinc complexes as drug with



**SCHEME 1** Synthetic strategy of Complexes 1–4





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**Collaborative Research in Analytical Coordination Chemistry**

**Number 49**

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Road, Kolkata 700009, India**

**Concerned Faculty: Prof. Debasis Das, Department of Chemistry**

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**Institute 2: Ramakrishna Mission Residential College (Autonomous)**

**Concerned Faculty: Dr. Prasanta Ghosh, Dept of Chemistry**

**Period of Investigation: 20-09-2018 to 22-08-2019**

**Project: Transition Metal Complexes and Catecholase Activity**

**Output: The result was published in a journal of international repute**

**Publication: Exploration of catecholase-like activity of a series of  
magnetically coupled transition metal complexes of Mn, Co and Ni: new  
insights into the solution state behavior of Mn complexes**

**Abani Sarkar, Aratrika Chakraborty, Amit Adhikary, Suvendu Maity, Arnab  
Mandal, Debabrata Samanta, Prasanta Ghosh, Debasis Das**

***Dalton Trans.*, 2019,48, 14164-14177. DOI: 10.1039/C9DT02399B**

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## Exploration of catecholase-like activity of a series of magnetically coupled transition metal complexes of Mn, Co and Ni: new insights into solution state behavior of Mn complex

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### Abstract

A series of tri-nuclear complexes of general formula  $[M_3L_2(OAc)_4]$ , where M = Mn (**1**), Co (**2**) and Ni (**3**), (HL=(E)-4-bromo-2-(((2-morpholinoethyl)imino)methyl)phenol) have been synthesized. Single crystal X-ray crystallography reveals that each molecule contains three metal ions which are bridged by four acetate moieties. In solution phase, the complexes are present as mononuclear species. Amongst them, manganese atom of complex **1** switches the oxidation states from +II to +III with time, as confirmed by time dependent UV-Vis and EPR spectroscopic techniques. Further, complex **1** with Mn in both the oxidation states can oxidise 3,5-DTBC to 3,5-DTBQ through ligand centred radical formation pathway. It is remarkably observed that complex **1** in Mn<sup>II</sup> oxidation state shows abnormally high rate constant value in oxidation of 3,5-DTBC to 3,5-DTBQ. This difference in rate constant values for catechol oxidation reaction by complex **1** can be explained by considering the binding constant value of catechol with Mn<sup>II</sup> and Mn<sup>III</sup> respectively by experimental and theoretical aspect. Similar to that of complex **1**, complexes **2** and **3** also catalyses catechol oxidation following ligand centred imine radical formation pathways. Further, magnetic properties of all the complexes were explored. DC magnetic susceptibility studies of complexes **1** and **2** revealed that in both the complexes the metal centres are antiferromagnetically coupled with adjacent metal centres

whereas in case of complex **3**, weak ferromagnetic interaction occurs between the neighbouring  $\text{Ni}^{\text{II}}$  centres at low temperature range.

## Introduction

The use of transition metal complexes to gain insights into the nature of potential metallobiosites has attracted the interests of many researchers.<sup>1</sup> Such complexes mimicking the active sites of metallobiosites emerges as highly promising catalysts of industrial significance.<sup>2-4</sup> Oxidation reactions are one such important reactions of industrial significance and activation of molecular oxygen comes as a challenge to many. Model transition metal complexes with prowess to surpass this challenging task of activation of molecular oxygen has emerged to be highly popular.<sup>5,6</sup> As a part of synthesis of model transition metal compounds of various nuclearity, engineering the structural motifs of polynuclear metal complexes and administering their oxidation states has been a topic of immense interest over the past due to their widespread applicability in magnetism, catalysis, adsorption, fluorescence, sensors etc.<sup>7</sup> In recent times manganese ion clusters were found to be highly potent due to their raptness in oxygen-evolving center (OEC) of photosystem II in green plants and in multinuclear metallocofactors.<sup>11,12</sup> From literature reports it is evident that much efforts has already been devoted in developing protocols for synthesis of polynuclear compounds of transition metal complexes like manganese which can act as functional mimics for various metalloenzymes.<sup>13,14</sup> But the scope for Nickel and Cobalt complexes as functional mimics still remains a topic for extensive research since very limited studies has been reported concerning these two metals.<sup>15-18</sup> Catechol Oxidase, a naturally occurring Di-nuclear  $\text{Cu}^{\text{II}}$  enzyme with type-III active site catalyzes oxidation of catechol to quinone. Synthesis of quinone is a vital reaction to plant life considering the fact that quinone undergoes auto polymerization to form melanin which works as a shield in protecting the plant tissues from insects. Designing suitable transition metal complexes for mimicking of active sites of biologically relevant metalloenzymes like catechol oxidase have attracted enormous attention over the years.<sup>18-23</sup> Since the structure of the enzyme Catechol Oxidase accommodates an antiferromagnetically coupled dicopper(II) moiety, much study has already been devoted to mimic the enzyme with the help of dicopper(II) complexes.<sup>24-28</sup> Such in-depth probe of catecholase like activity by copper II complexes renders much space for synthesis of superior catalyst mimics comprising of non-copper complexes. In recent times our group has accentuated



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**Collaborative research in transition metal functional complexes**  
**Number 50**

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**Concerned Faculty: Dr. Sanchita Goswami, Department of Chemistry**  
**&**

**Institute 2: Ramakrishna Mission Residential College (Autonomous)**

**Concerned Faculty: Dr. Prasanta Ghosh, Dept of Chemistry**

**Period of Investigation: 18-01-2019 to 25-12-2019**

**Project: Mixed valence complexes of transition metal ions**

**Output: The result was published in a journal of international repute**

**Publication: Fascinating Structures of a Mixed Valence  $[Mn^{III}] \cdot [Mn^{II}Mn^{III}]$**

**Cocrystal and a  $Mn^{III}Na^I$  Complex: Slow Magnetic Relaxation and**  
**Theoretical Investigations**

**Riya Bag, Yeasin Sikdar, Pinaki Saha, Prasanta Ghosh, Michael G. B.**  
**Drew and Sanchita Goswami**

**Cryst. Growth Des. 2020, 20, 3, 1849–1858.**

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# Fascinating Structures of a Mixed Valence $[\text{Mn}^{\text{III}}]\cdot[\text{Mn}^{\text{II}}\text{Mn}^{\text{III}}]$ Cocrystal and a $\text{Mn}^{\text{III}}\text{Na}^{\text{I}}$ Complex: Slow Magnetic Relaxation and Theoretical Investigations

Riya Bag, Yeasin Sikdar, Pinaki Saha, Prasanta Ghosh, Michael G. B. Drew, and Sanchita Goswami\*



Cite This: *Cryst. Growth Des.* 2020, 20, 1849–1858



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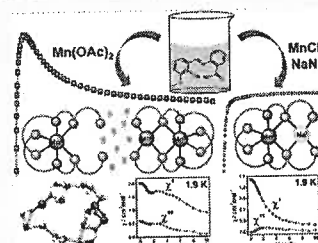
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**ABSTRACT:** Herein, a cocrystal, incorporating mixed valence manganese ions, namely,  $[\text{Mn}^{\text{III}}]\cdot[\text{Mn}^{\text{II}}\text{Mn}^{\text{III}}]$  formulated as  $[\{\text{Mn}^{\text{III}}(\text{Vaan})_2\}\cdot\{\text{Mn}^{\text{II}}\text{Mn}^{\text{III}}(\text{Vaan})_2(\text{H}_2\text{O})_3\}\cdot 14\text{H}_2\text{O}]$  (1) and a  $\text{Mn}^{\text{III}}\text{Na}^{\text{I}}$  compound  $[\text{Mn}^{\text{III}}\text{Na}^{\text{I}}(\text{Vaan})_2(\text{H}_2\text{O})_2\cdot\text{H}_2\text{O}]$  (2), are synthesized utilizing  $\text{Mn}^{\text{II}}$  precursor salts and a rarely used ligand, 2-[(2-hydroxy-3-methoxy-benzylidene)-amino]-benzoic acid ( $\text{H}_2\text{Vaan}$ ). Structure analyses illustrate that 1 contains a cationic dinuclear unit ( $\text{Mn}^{\text{II}}\text{Mn}^{\text{III}}$ ) and an anionic mononuclear unit  $\text{Mn}^{\text{III}}$  to generate the cocrystal, whereas a different recipe produces compound 2. Detailed descriptions of the prevailing supramolecular interactions within the systems have been provided. Interestingly, as far our knowledge goes, 1 is the first example of a cocrystal involving a mixed valence  $\text{Mn}^{\text{II}}/\text{Mn}^{\text{III}}$  species. Notably, dc and ac susceptibility measurements indicate the existence of slow relaxation of magnetization in both complexes. Furthermore, we have analyzed the nature of the magnetic interactions present using density functional theory based on the CASSCF-NEVPT2 methodology



## INTRODUCTION

Mixed-valence complexes, an outstanding class of compounds, with features such as interesting electronic structures, involvement in electron transfer reactions, unprecedented magnetic properties, promising catalytic activities, and so on, have attracted significant research attention.<sup>1–5</sup> Mixed valence compounds of manganese, in particular, have attracted immense interest because of their relevance in the field of single molecule magnetism after the fascinating report of  $[\text{Mn}^{\text{IV}}_4\text{Mn}^{\text{III}}_8(\text{CH}_3\text{COO})_{16}(\text{H}_2\text{O})_4\text{O}_{12}]\cdot 2\text{CH}_3\text{COOH}\cdot 4\text{H}_2\text{O}$  in 1991.<sup>6</sup> As a result, there is widespread research activity among chemists to generate single molecule/ion magnets (SMM/SIMs) as a promising avenue toward molecular memory devices.<sup>7–12</sup> However, successful construction of SMM/SIMs requires perfect synergy of two factors: (i) large spin multiplicity and (ii) maximizing the anisotropy of the system,<sup>13,14</sup> which can be achieved by using inherently anisotropic metals centers such as  $\text{Mn}^{\text{III}}$ ,  $\text{Co}^{\text{II}}$ , and  $\text{Ln}^{\text{III}}$ . Again, the existence of mixed valence manganese centers in the Kok cycle of photosystem II (PS II) has evoked interest among chemists to construct bioinspired water oxidation catalysts.<sup>15,16</sup> Therefore, giving inspiration because of these features, any mixed valence manganese species is worthy of investigation and provides an interesting challenge to a synthetic chemist.

Cocrystals or multicomponent molecular crystals, as described by Desiraju et al.,<sup>17,18</sup> are a type of crystalline single phase material, containing a stoichiometric ratio of two or more molecules bound together in crystal lattices through noncovalent interactions, which have greatly impacted crystal engineering and therefore the pharmaceutical industry,<sup>17–35</sup>

since organic cocrystals enhance bioavailability of drugs in physiological systems. Similarly, inorganic cocrystals may be very effective in optimizing catalytic outcomes.

In recent years, the ligand, 2-[(2-hydroxy-3-methoxy-benzylidene)-amino]-benzoic acid ( $\text{H}_2\text{Vaan}$ ) had been utilized by only a few research groups.<sup>36–40</sup> In this work, we have further explored the use of this ligand,  $\text{H}_2\text{Vaan}$ , and have obtained a mixed valence  $\text{Mn}^{\text{III}}\cdot\text{Mn}^{\text{II}}\text{Mn}^{\text{III}}$  cocrystal, namely,  $[\{\text{Mn}^{\text{III}}(\text{Vaan})_2\}\cdot\{\text{Mn}^{\text{II}}\text{Mn}^{\text{III}}(\text{Vaan})_2(\text{H}_2\text{O})_3\}\cdot 14\text{H}_2\text{O}]$  (1) and a  $\text{Mn}^{\text{III}}\text{Na}^{\text{I}}$ ,  $[\text{Mn}^{\text{III}}\text{Na}^{\text{I}}(\text{Vaan})_2(\text{H}_2\text{O})_2\cdot\text{H}_2\text{O}]$  (2) compounds using two different reaction methods. Thorough structural characterization and evaluation of the magnetic properties of 1 and 2 are described. As far our knowledge goes, a cocrystal containing mixed valence states of manganese ions as represented here by complex 1 has not previously been reported (Table S1). Both 1 and 2 offered slow magnetic relaxation phenomena at dc fields of 0 and 2000 Oe, respectively. We have also cultivated the nature of magnetic anisotropy of the  $\text{Mn}^{\text{III}}$  centers of 1 and 2 with the help of density functional theory (DFT).

## EXPERIMENTAL SECTION

**Materials and Apparatus.** *o*-Vanillin and anthranilic acid used in this study were obtained from Spectrochem, India, and Sigma-Aldrich

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*Cryst. Growth Des.* 2020, 20, 1849–1858

(product of USA) respectively. Manganese acetate tetrahydrate, Manganese chloride tetrahydrate, sodium azide, and triethylamine were obtained from Merck, India. Solvents were obtained from commercial sources and used without further purification. All manipulations were performed under aerobic conditions.  $H_2Va$ , 2-[(2-hydroxy-3-methoxy-benzylidene)-amino]-benzoic acid, was synthesized according to a published procedure.<sup>41</sup>

Elemental analyses for carbon, hydrogen, and nitrogen were carried out on a PerkinElmer 2400 II analyzer. Fourier transform (FT-IR) spectra were recorded on a PerkinElmer Spectrum 100 spectrophotometer on a KBr disk. Powder X-ray diffraction (PXRD) patterns were acquired using a PANalytical, XPERT-PRO diffractometer (Netherlands) operated at 40 kV, 30 mA, with graphite-monochromatized Mo-K $\alpha$  radiation of wavelength = 0.71073 Å and a nickel filter. ESI-MS was performed on a Waters Xevo G2S QTOF instrument in LC-MS grade solvent. All magnetization data were collected using a Quantum Design MPMS-XL7 SQUID magnetometer equipped with a 7 T magnet. Direct-current (dc) measurements were performed on polycrystalline samples of complexes in the temperature range from 1.9 to 300 K, with an applied field of 1000 Oe. The alternating-current (ac) measurements were investigated at different frequencies from 1 to 997 Hz, under a 3.0 Oe ac oscillating field and a zero dc field. Experimental magnetic data were corrected for the diamagnetism contribution of all the atoms estimated from Pascal's tables<sup>42</sup> and sample-holder calibration.

**Synthesis of  $\{[Mn^{III}(Va)]_2\} \cdot \{Mn^{III}(Va)(H_2O)_3\} \cdot 14H_2O$  (1).** A 15 mL  $CH_3CN/MeOH$  (1/1) solution containing  $H_2Va$  (0.2 mmol, 0.054 g) was dropwise added to a 20 mL  $CH_3CN/MeOH$  (1/1) solution of  $Mn(CH_3COO)_2 \cdot 4H_2O$  (0.4 mmol, 0.098 g) followed by addition of triethylamine (0.4 mmol, 55  $\mu$ L), and the solution was stirred for 1 h. Again, triethylamine (0.4 mmol, 55  $\mu$ L) was added, and stirring was continued for 2 h resulting in a deep brown solution. The solution was filtered to discard any insoluble particles and kept for slow evaporation. After 15 days, on evaporation nearly to dryness, large block-shaped brown crystals were obtained suitable for SC-XRD experiments. The crystals were manually separated by hand and washed with ice cold methanol–water and stored in a refrigerator. Yield: 0.005 g (1% w.r.t  $Mn(CH_3COO)_2 \cdot 4H_2O$ ). Anal. Calcd for  $C_{60}H_{73}Mn_3N_4O_{33}$  (1543.04 g/mol): C, 46.70; H, 4.77; N, 3.63; Found: C, 46.51; H, 4.32; N, 3.43. FT-IR (KBr,  $cm^{-1}$ ): 3390(O–H), 1590(C=O), 1547 (C=N), 1250(C–O).

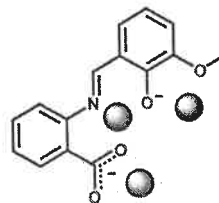
**Synthesis of  $\{[Mn^{III}Na(Va)]_2(H_2O)_2\} \cdot H_2O$  (2).** A 12 mL  $CH_3CN/MeOH$  (1/1) solution containing  $H_2Va$  (0.2 mmol, 0.054 g) was dropwise added to a 12 mL  $CH_3CN/MeOH$  (1/1) solution of  $MnCl_2 \cdot 4H_2O$  (0.2 mmol, 0.039 g) and  $NaN_3$  (0.2 mmol, 0.013 g) followed by addition of triethylamine (0.2 mmol, 27.6  $\mu$ L), and the solution was stirred for 4 h resulting in a deep green solution. The solution was filtered to discard any insoluble particles and kept for slow evaporation. After 10 days, on evaporation of the solution nearly to dryness, green flakes were obtained, which were further recrystallized in DMF/ $H_2O$  (4/1) solution. After 5 days, green block-shaped crystals were obtained suitable for SC-XRD experiment. The crystals were manually separated using tweezers and washed with ice cold methanol–water and stored in a refrigerator. Yield: 0.012 g (9% w.r.t  $MnCl_2 \cdot 4H_2O$ ). Anal. Calcd for  $C_{30}H_{28}MnN_2NaO_{11}$  (670.47 g/mol): C, 53.74; H, 4.21; N, 8.19; Found: C, 53.61; H, 4.35; N, 8.27. FT-IR (KBr,  $cm^{-1}$ ): 3440 (O–H), 1631 (C=N), 1115 (C–O).

**Single-Crystal XRD.** The single crystal X-ray diffraction data of 1 and 2 were collected with Mo-K $\alpha$  radiation using the Oxford Diffraction X-Calibur CCD System (at 150 K) and Bruker AXS D8 QUEST ECO diffractometer (at 296 K) respectively. Data analyses were carried out with the CrysAlis program for 1 and the APEX3 program suite for 2.<sup>43</sup> Crystal structures were determined by direct methods and subsequent difference Fourier syntheses, followed by full-matrix least-squares refinements on  $F^2$  using SHELXS and SHELXL-2016/6 software packages.<sup>44</sup> Absorption corrections were carried out using the ABSPACK<sup>45</sup> and SADABS<sup>46</sup> program for 1 and 2 respectively. The crystal parameters of complexes 1 and 2 are tabulated in Table S2.

## RESULTS AND DISCUSSION

**Ligand Design Aspects.** A typical synthetic procedure for mixed valence/polynuclear coordination complexes is based on

**Scheme 1.** Coordination Pockets in the Dianionic Ligand  $Va^{2-}$



the direct coordination of rationally chosen ligands and metal ions where the metal centers can be distinguished by their different affinities toward each coordination site of the ligand. We have chosen the potentially pentadentate ligand,  $H_2Va$ , 2-[(2-hydroxy-3-methoxy-benzylidene)-amino]-benzoic acid, which possesses several potentially donor groups, namely, phenoxo and carboxylate oxygens, methoxy oxygen, imine (C=N) nitrogen and carboxy (C=O) oxygen functionalities. It acts as a tripocket ligand system to chelate the metal centers (Scheme 1). Until now, this ligand has been seldom used to synthesize 3d-metal complexes that are suitable for studying magnetic properties. However, it has been used in the synthesis of lanthanide based  $Dy_4O_6$  and  $Dy_4O_4$  complexes which display slow magnetic relaxation or single molecule magnet phenomena.<sup>36</sup> The salicylaldehyde analogue of  $H_2Va$ , i.e., 2-[(2-hydroxy-benzylidene)-amino]-benzoic acid, has been used to synthesize a pentanuclear  $\{Co_2^{III}Co_3^{II}\}$  cluster,<sup>47</sup> and a mononuclear  $Mn^{III}$  bischelat.<sup>48</sup> The above reports show that the hard oxygen donor atom of the  $-COOH$  ligand binds with hard metal centers such as  $Mn^{III}$  and  $Co^{III}$ . Thus, our aim was to employ  $H_2Va$  to synthesize metal clusters containing  $Mn^{III}$  and  $Mn^{II}$  centers.

**Synthesis and Characterization.** The reaction of  $Mn-(CH_3COO)_2$  and  $H_2Va$  in a 2:1 ratio in triethylamine containing a mixed solvent of acetonitrile/methanol (1/1) afforded a few large block-shaped crystals of 1 along with a black smudge of unknown composition, and the reaction of  $MnCl_2$ ,  $NaN_3$ , and  $H_2Va$  in a 1:1:1 ratio in an alkaline mixed solvent acetonitrile/methanol (1/1) yielded green flakes of 2, which were further recrystallized in DMF/water (4/1) medium to afford green block-shaped crystals. Both 1 and 2 are highly soluble in hot solvents such as alcohol, dimethylformamide, and dimethyl sulfoxide but are insoluble in water.

The FT-IR spectrum of 1 shows the presence of a peak at 1547  $cm^{-1}$  attributed to the C=N stretching frequency, and the broad peak centered at 3390  $cm^{-1}$  was assigned to the O–H stretching frequency of a coordinated/uncoordinated water molecule. The strong peak at 1250  $cm^{-1}$  was identified as C–O stretching frequency (Figure S1). In the FT-IR spectrum of 2, two sharp peaks at 1631 and 1115  $cm^{-1}$  and a broad peak at 3440  $cm^{-1}$  are observed, corresponding to the stretching frequency of C=N, C–O, and O–H bonds, respectively (Figure S2). The phase purity of the synthesized complexes was confirmed by powder XRD, which shows good fits between the peak positions of experimental and calculated data (Figures S3–S4).





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**Collaborative research in transition metal functional complexes**

**Number 51**

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**Concerned Faculty: Dr. Prasanta Ghosh, Associate Professor, Dept of Chemistry**

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**Period of Investigation: 21-06-2018 to 27-02-2019**

**Project: Osazone complexes of transition metal ions and their activities**

**Output: The result was published in a journal of international repute**

**Publication: Palladium(II) and platinum(II) complexes of glyoxalbis(*N*-aryl)osazone: molecular and electronic structures, anti-microbial activities and DNA-binding study**

**Sarat Chandra Patra, Amit Saha Roy, Saswati Banerjee, Ananya Banerjee, Krishna Das Saha, Ranjan Bhadra, Kausikisankar Pramanik and Prasanta Ghosh**

**New J. Chem., 2019, 43, 9891-9901.**

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# Palladium(II) and platinum(II) complexes of glyoxalbis(*N*-aryl)osazone: molecular and electronic structures, anti-microbial activities and DNA-binding study†

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Palladium(II) and platinum(II) complexes of types  $[\text{Pd}(\text{L}^{\text{NHPh}}\text{H}_2)\text{Cl}_2]$  (**1**),  $[\text{Pd}(\text{L}^{\text{NH(CIPh)}}\text{H}_2)\text{Cl}_2]$  (**2**),  $[\text{Pt}(\text{L}^{\text{NHPh}}\text{H}_2)\text{Cl}_2]$  (**3**) and  $[\text{Pt}(\text{L}^{\text{NH(CIPh)}}\text{H}_2)\text{Cl}_2]$  (**4**) were successfully isolated, where  $\text{L}^{\text{NHPh}}\text{H}_2$  and  $\text{L}^{\text{NH(CIPh)}}\text{H}_2$  are osazone ligands. The molecular and electronic structures of **1–4** and their reduced analogues were confirmed by single crystal X-ray crystallography, EPR spectroscopy, and DFT calculations. Osazone is a redox non-innocent ligand and the redox activities of **1–4** were investigated by cyclic voltammetry. The redox activities of **1–4** are solvent dependent. In cyclic voltammetry, no redox wave of **1–4** is discernible in  $\text{CH}_3\text{CN}$ , while in the less polar  $\text{CH}_2\text{Cl}_2$  solvent, the cathodic waves of **3** and **4** gain some reversibility. Mulliken spin density analyses and EPR spectral data reveal that the unpaired electron of  $[\text{3}]^-$  and  $[\text{4}]^-$  ions is dominantly localized on the diimine fragment of the osazone ligands. Cell viability studied using MTT assay against leishmania promastigote shows that these compounds are strong leishmanicidal agents, while they have low anti-bacterial and anti-fungal activities. All the reported compounds are completely non-cytotoxic within the limit of 0–50  $\mu\text{M}$  up to 72 h revealing their potentiality as therapeutic agents. The leishmanicidal activity of **1** and **3** is found to be higher than the ligands as well as **2** and **4**. Furthermore, the interaction of **1** and **3** with DNA has been assessed as possibly intercalating in nature, which correlates with one of the requisite modes for anti-leishmanial activity.

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## Introduction

Square planar palladium(II) and platinum(II) complexes with heterocyclic  $\alpha$ -diimine ligands have been investigated over last few

decades owing to their attractive redox activity,<sup>1</sup> rich photoluminescence properties<sup>2</sup> and high antiproliferative profile.<sup>3</sup> Although their aliphatic analogues<sup>4</sup> are less documented in the literature, they have parallel remarkable chemistry. Osazones represent a special class of  $\alpha$ -diimine ligands containing a  $\text{RNN}=\text{CH}-\text{CH}=\text{NNR}$  moiety and the chemistry of them is different from that of  $\alpha$ -diimine ligands containing a  $\text{RN}=\text{CH}-\text{CH}=\text{NR}$  fragment. In our previous investigation on osazone complexes, we reported that osazones are redox active<sup>5</sup> and phenyl osazone ( $\text{L}^{\text{NHPh}}\text{H}_2$ ) is a better  $\pi$ -acceptor [ $E_{\pi^*}(\text{L}^{\text{NHPh}}\text{H}_2) = -2.613 \text{ eV}$ ] than the phenyl diimine ligand [ $E_{\pi^*}(\text{L}^{\text{Ph}}\text{H}_2) = -1.421 \text{ eV}$ ].<sup>5a</sup> Thus, osazones have been considered to generate tunable  $\text{Pd}^{\text{II}}\text{N}_2\text{Cl}_2$  and  $\text{Pt}^{\text{II}}\text{N}_2\text{Cl}_2$  coordination spheres. In the early 1970s, Vigato *et al.* reported some complexes of osazones<sup>6</sup> of the types  $[\text{M}^{\text{II}}(\text{L}_1)\text{Cl}_2]$ ,  $[\text{M}^{\text{II}}(\text{L}_2)\text{Cl}_2]$  ( $\text{M} = \text{Pd}, \text{Pt}$ ),  $[\text{Pd}_2(\text{L}_2)_2\text{Cl}_2]$ , and  $[\text{Pd}^{\text{II}}(\text{L}_2)\text{Cl}]$ , where  $\text{L}_1$  = cyclohexane-1, 2-dionebisphenylhydrazones, and  $\text{L}_2$  = biacetylbis(*N*-methyl, *N*-phenyl)hydrazones. However, detailed molecular and electronic structures of the complexes of general formula  $\text{M}^{\text{II}}(\text{N}^{\wedge}\text{N})\text{Cl}_2$  ( $\text{M} = \text{Pd}, \text{Pt}$ ) with parent osazones are under-explored. The  $-\text{C}=\text{NNHR}$  moiety in osazones closely resembles that of semicarbazone and thiosemicarbazones.

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† Electronic supplementary information (ESI) available: X-ray crystallographic CIF, materials and physical measurements, DFT calculations, cyclic voltammograms, EPR spectra of  $[\text{3}]^-$  and  $[\text{4}]^-$ , Mulliken spin density of  $[\text{3}]^+$ , gas phase optimized geometries, FMOs of **1–4**, comparative study of  $\text{IC}_{50}$  values, anti-leishmanial activity of the compounds **1** and **3**, minimum inhibitory concentration (MIC) of **1** and **3** in bacterial systems, antifungal activity (MIC) of **1** and **3**, and optimized coordinates. CCDC 1534727 and 1534728. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c9nj00223e

## Paper

The anti-leishmanial activity of platinum and palladium complexes containing bioactive nitrofuryl thiosemicarbazones<sup>7</sup> is well established and the same with hydrazone ligands<sup>8</sup> is rare. Navarro *et al.* reported a series of palladium(II) polypyridyl complexes<sup>9</sup> of types [PdCl<sub>2</sub>(phen)], [PdCl<sub>2</sub>(biquinoline)] and [PdCl<sub>2</sub>(phendiamine)] which exhibit leishmanistatic effects, particularly inhibiting the growth rate. [PdCl<sub>2</sub>(phendiamine)] was found to be the most effective, causing 58% growth inhibition. The investigation provides useful information that the heterocyclic  $\alpha$ -diimine complexes of palladium(II) and platinum(II) are potential leishmanicidal agents and in this study we have been persuaded to explore such activity with 1–4.

Leishmaniasis is still one of those major 'neglected tropical diseases' (NTD) considering drug discovery and development.<sup>10</sup> It is caused by a parasite belonging to the *Leishmania* genus and is spread by the female sandfly vector (*Phlebotomine* in the old world and *Lutzomyia* in the new world) showing broad spectrum clinical manifestations in humans, especially the poorest.<sup>11</sup> Among all three types of leishmaniasis viz. cutaneous (CL), mucocutaneous (MCL), and visceral (VL), the visceral form, also known as kala-azar in India, is most brutal and sometimes proves to be fatal if untreated. It is caused by the *Leishmania donovani* parasite.<sup>12</sup> Chagas disease, also known as American trypanosomiasis, is an infection caused by the parasite *Trypanosoma cruzi*. Visceral leishmaniasis is endemic in 65 countries, with over 600 million people at risk of infection and an estimated 50 000 to 90 000 new cases occurring worldwide each year.<sup>13</sup> More than 90% of new cases occurred in these countries: India (especially the Ganges and Brahmaputra plains), Bangladesh, Nepal, Brazil, Ethiopia, Kenya, Somalia, South Sudan and Sudan. Pentavalent antimony (e.g. sodium stibogluconate, SAG, Pentostan, GlaxoSmithKline) compounds were at first successful to address the challenge but they are almost resistant now.<sup>14</sup> In addition, numerous toxicities<sup>15</sup> like cardiotoxicity, pancreatitis, nephrotoxicity, and hepatotoxicity make them rather scarce in the market. Miltefosine is a recently used orally administered antileishmanial drug<sup>14</sup> but it has also some adverse side effects<sup>15</sup> like vomiting and diarrhoea, nephrotoxicity, hepatotoxicity and teratogenicity. Thus, there has been an increased urge for designed synthesis of alternative drugs or new formulations of old ones. Unfortunately the issues that are composed of high toxicity, resistance, high prices, high concentrations and long treatment duration or mode of administration have not been completely resolved.

G. Lowe *et al.* synthesized a series of (2,2':6',2''-terpyridine)-platinum(II) complexes and studied their antiprotozoal activity against the closely related hemiflagellate protozoa *Leishmania donovani*, *Trypanosoma cruzi*, and *Trypanosoma brucei*.<sup>16</sup> These complexes exploit the intercalative DNA properties of the terpyridine ligand along with the covalent binding ability of the Pt(II) center. The effective compounds cause 100% inhibition of growth of the intracellular amastigote forms of *L. donovani* at a concentration of 0.03  $\mu$ M. But there is not any single report of complexes containing osazone ligands that show antileishmanial activity. In fact the bioactivity of osazone complexes is still to be explored. Palladium(II) and platinum(II) Schiff base<sup>17a,b</sup> and

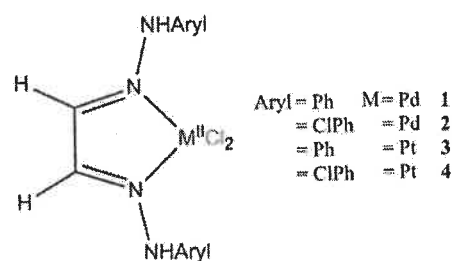


Chart 1

phenanthroline complexes<sup>17c</sup> are also promising antibacterial and antifungal agents. The present demand of alternate antileishmanial agents provoked us to synthesize a new family of palladium(II) and platinum(II) osazone complexes [Pd<sup>II</sup>(L<sup>NHPh</sup>H<sub>2</sub>)Cl<sub>2</sub>] (1), [Pd<sup>II</sup>(L<sup>NH(ClPh)</sup>H<sub>2</sub>)Cl<sub>2</sub>] (2), [Pt<sup>II</sup>(L<sup>NHPh</sup>H<sub>2</sub>)Cl<sub>2</sub>] (3) and [Pt<sup>II</sup>(L<sup>NH(ClPh)</sup>H<sub>2</sub>)Cl<sub>2</sub>] (4) (Chart 1) and investigate the antimicrobial activities of 1–4 and also the title ligands. The antileishmanial activity of the ligands L<sup>NHPh</sup>H<sub>2</sub> and L<sup>NH(ClPh)</sup>H<sub>2</sub> and complexes 1–4 was compared with the standard drugs, miltefosine and SAG. A DNA binding study was also carried out to explore the basis of the anti-protozoal activity. In addition, the cytotoxicity of these compounds is scrutinized against RAW 264.7 macrophages for their plausible usefulness as therapeutic agents.

1–4 were characterized by different spectral means (IR, UV-vis, NMR and mass) and the molecular geometries of the representative complexes (2 and 4) were authenticated by single crystal X-ray crystallography. Electron transfer phenomena were studied by cyclic voltammetry. DFT calculations at the B3LYP level were performed to elucidate their electronic structure. This has been further substantiated by EPR study of the electrogenerated [3]<sup>−</sup> and [4]<sup>−</sup> ions.

## Results and discussion

### Syntheses

The complexes reported in this article are summarized in Chart 1. L<sup>NHPh</sup>H<sub>2</sub> and L<sup>NH(ClPh)</sup>H<sub>2</sub> were synthesized using the reported procedures.<sup>5c</sup> Complexes 1–4 were synthesized by refluxing a methanolic solution of the osazone ligands with [M(DMSO)<sub>2</sub>Cl<sub>2</sub>]<sup>18</sup> (M = Pd, Pt) in acetonitrile solution. Detailed syntheses are presented in the Experimental section. The complexes were characterized by elemental analyses, and IR, mass, and <sup>1</sup>H NMR spectra. Antiprotozoal studies were performed with the chromatographically pure ligands and crystalline complexes. All the compounds are non-luminescent in the solid state and in solution at 298 K and even at 130 K.

### Molecular geometries

2 crystallizes in the *Pnma* space group. The crystals are weakly diffracting, however a reasonable solution was achieved. The molecular geometry of 2 in the crystals with the atom labeling scheme is illustrated in Fig. S1 (ESI†). The crystallographic data are provided in Table S1 (ESI†). Significant bond parameters are



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Collaborative research in transition metal functional complexes

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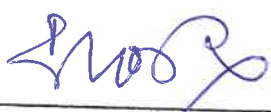
Period of Investigation: 01-04-2019 to 31-03-2020

Project: Transition metal complexes catalyzed organic transformations

Output: The result was published in a journal of international repute

Publication: Ligand directed synthesis of a unprecedented tetragonalbipyramidal copper  
(II) complex and its antibacterial activity and catalytic role in oxidative dimerisation of  
2-aminophenol

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Appl. Organomet. Chem, 2020, 34, Issue 11, e5935. DOI: 10.1002/aoc.5935

		
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# Ligand directed synthesis of a unprecedented tetragonalbipyramidal copper (II) complex and its antibacterial activity and catalytic role in oxidative dimerisation of 2-aminophenol

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## Funding information

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In pursuit of the significant contribution of copper ion in different biological processes, this research work describes the synthesis, X-ray structure, Hirshfeld surface analysis, oxidative dimerization of 2-aminophenol and antibacterial activity of a newly designed copper (II)-Schiff base complex, [Cu(L)<sub>2</sub>] (1), [Schiff base (HL) = 2-(2-methoxybenzylideneamino)phenol]. X-ray structural analysis of 1 reveals that the Cu (II) complex crystallizes in a cubic crystal system with Ia-3d space group. The Cu (II) centre adopts an unprecedented tetragonal bipyramidal geometry in its crystalline phase. The Schiff base behaves as a tridentate chelator and forms an innermetallic chelate of first order with Cu (II) ion. The copper (II) complex has been tested in the bio-mimics of phenoxazinone synthase activity in acetonitrile and exhibits good catalytic activity as evident from high turnover number, 536.4 h<sup>-1</sup>. Electrochemical analysis exhibits the appearance of two additional peaks at -0.15 and 0.46 V for Cu (II) complex in presence of 2-AP and suggests the development of AP<sup>-</sup>/AP<sup>•-</sup> and AP<sup>•-</sup>/IQ redox couples in solution, respectively. The presence of iminobenzosemiquinone radical at g = 2.057 in the reaction mixture was confirmed by electron paramagnetic resonance and may be considered the driving force for the oxidative dimerisation of 2-AP. The existence of a peak at m/z 624.81 for Cu (II) complex in presence of 2-AP in electrospray ionization mass spectrum ensures that the catalytic oxidation proceeds through enzyme-substrate adduct formation. The copper (II) complex exhibits potential antibacterial properties against few pathogenic bacterial species like *Staphylococcus aureus*, *Enterococcus* and *Klebsiella pneumonia* and scanning electron microscope studies consolidates that destruction of bacterial cell membrane accounts on the development of antibacterial activity.

Shreya Mahato and Nishith Meheta have equal contribution.

**KEYWORDS**

aminophenol oxidation activity, antibacterial property, copper (II), electrochemical analysis, X-ray structure

## 1 | INTRODUCTION

In this modern age of science, Schiff base as polydentate chelators have been widely used in the development of coordination compounds of varied functionality.<sup>[1–3]</sup> Among the transition metal ions, copper ion has been considered as an essential metal ion in living system and it also plays significant role in designing advance functional materials.<sup>[4–7]</sup> In nature, copper ions are integrated with different bio-ligands in the functional sites of various metallo-enzymes such as catechol and galactose oxidase, phenoxazinone synthase, superoxide dismutase, lysine oxidase, N<sub>2</sub>O reductase etc.<sup>[8–11]</sup> It pursuit of deep understanding of different biological oxidation processes in nature, synthetic coordination chemists have been stepped forward to tune electronic and geometric factors of the ligands in engineering bio-inspired coordination driven compounds.<sup>[12–15]</sup> It is well documented that the bio-inspired synthetic analogues also serve as magic catalysts in several catalytic oxidation reactions of laboratory and industrial significance.<sup>[14–16]</sup> Among the different oxidase enzymes, phenoxazinone synthase has drawn special attention<sup>[14,15]</sup> as the oxidized product, aminophenoxazinone acts as an antineoplastic agent named actinomycin D (questiomycin A) which is usually recommended in the treatment of certain types of cancer.<sup>[17–20]</sup> Furthermore, 2-aminophenoxazin-3-one and 3-aminophenoxazin-2-one compounds show potential antimicrobial, antiviral, and antitumor activities against different pathogens.<sup>[21–24]</sup> Aminophenoxazinone compounds have also been reported in different forms like *Streptomyces parvulus* and wood rotting fungi metabolites, oxidative coupling products of *o*-aminophenols with bovine erythrocyte hemolyzate, and bio-conversion products of *Pseudomonas putida* grown on nitroarenes.<sup>[24–28]</sup>

In light of incessant emergence for new antibiotics with potential resistance against microorganisms, it is of great importance to design novel antibiotics, which would destroy the lipid layer as well as the cell membrane of the pathogen with high selectivity.<sup>[29,30]</sup> In this perspective, copper based coordination compounds hold a great promise to provide future alternatives to the existed antibiotics.<sup>[30,31]</sup> In the context of newly designed copper (II) complexes with high catalytic activities and potential therapeutic values, this research study deals with the synthesis, structural characterization and catalytic oxidase activity of a new copper (II)-Schiff base

complex. The antibacterial property of this copper (II) complex towards different bacterial species has also been delineated.

## 2 | EXPERIMENTAL

### 2.1 | Preparation of the Schiff base and dinuclear copper (II) complex

#### 2.1.1 | Chemicals, solvents and starting materials

Highly pure *o*-anisidine (Sigma Aldrich, Missouri, Texas, USA), salicylaldehyde (Sigma Aldrich, Missouri, Texas, USA) and cupric acetate monohydrate (SRL, Gurugram, Haryana, India) were purchased from the respective concerns and used as received. All other chemicals and solvents were of analytical grade and used as received without further purification.

#### 2.1.2 | Synthesis of the Schiff base and copper (II) complex

The Schiff base, HL was synthesized following a reported method.<sup>[32]</sup> The Schiff base was synthesized through condensation reaction between *o*-anisidine (0.123 g, 1 mmol) and salicylaldehyde (0.122 g, 1 mmol) in ethanol under reflux for 8 hr. Then, the yellowish brown coloured gummy product was extracted and stored *in vacuo* over CaCl<sub>2</sub> for use. Yield: 0.201 g (~88.5%). Anal. Calc. for C<sub>14</sub>H<sub>13</sub>NO<sub>2</sub> (HL): C, 73.99; H, 5.77; N, 6.16; Found: C, 73.93; H, 5.72; N, 6.19. IR (KBr, cm<sup>-1</sup>; Figure S1): 3372 ( $\nu_{OH}$ ), 1615, 1590 ( $\nu_{C=N}$ ); UV-Vis ( $\lambda_{max}$ , nm; Figure S2): 230, 270, 346; <sup>1</sup>H NMR ( $\delta$  ppm, 400 Mz, CDCl<sub>3</sub>; Figure S3)  $\delta$  = 13.88 (s, 1H), 8.63 (s, 1H), 7.26–6.82 (Ar-H, 7H), 3.79–3.83 (t, 3H) ppm. <sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>; Figure S4): 162.06 (HC=N); 153.03, (Ar-OH); 137.05 (Ar-N=C); 132.94, 132.05, 127.95, 127.13, 119.64, 118.46, 117.40, 115.05, (Ar-C); 77.49, 77.17, 76.85 (-OCH<sub>3</sub>).

The copper (II)-Schiff base complex was prepared by drop wise addition of acetonitrile solution of Cu (OAc)<sub>2</sub> (0.199 g, 1 mmol) to the methanolic solution of HL (0.454 g, 2 mmol). The yellow coloured Schiff base solution was instantly turned to green coloured solution.





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**Collaborative research in coordination chemistry of organic radicals**  
**Number 53**

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**781039, Assam, India**

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**Institute 2: Ramakrishna Mission Residential College (Autonomous)**  
**Concerned Scholar:** Dr. Suwendu Maity, Dept of Chemistry

**Period of Investigation:** 01-04-2018 to 30-04-2019

**Project:** Organic radical complexes of Oxidovanadium(IV/V)

**Output:** The result was published in a journal of international repute

**Publication:** An Iminosemiquinone-Coordinated Oxidovanadium(V)  
**Complex:** A Combined Experimental and Computational Study

Prasenjit Sarkar, Manas Kumar Mondal, Amrit Sarmah, Suwendu Maity and  
Chandan Mukherjee

*Inorg. Chem.* 2017, 56, 14, 8068–8077. DOI: 10.1021/acs.inorgchem.7b00789

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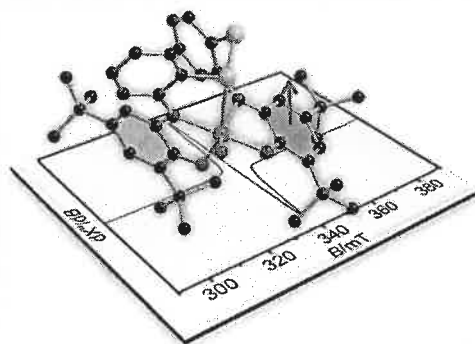


## An Iminosemiquinone-Coordinated Oxidovanadium(V) Complex: A Combined Experimental and Computational Study

Prasenjit Sarkar,<sup>†</sup> Manas Kumar Mondal,<sup>†</sup> Amrit Sarmah,<sup>‡</sup> Suwendu Maity,<sup>§</sup> and Chandan Mukherjee<sup>\*,†</sup><sup>†</sup>Department of Chemistry, Indian Institute of Technology Guwahati (IITG), Guwahati 781039, Assam, India<sup>‡</sup>Department of Molecular Modelling, Institute of Organic Chemistry and Biochemistry ASCR, Flemingovo nám. 2, CZ-16610 Prague 6, Czech Republic<sup>§</sup>Department of Chemistry, R. K. Mission Residential College, Narendrapur, Kolkata 700103, India

## Supporting Information

**ABSTRACT:** Ligand  $H_4Sar^{(AP/AP)}$  contained two terminal amidophenolate units that were connected by a disulfane bridge. The ligand reacted with  $VOSO_4 \cdot 5H_2O$  in the presence of  $Et_3N$  under air and provided a mononuclear octahedral oxidovanadium complex (1). X-ray crystal structure analysis of complex 1 revealed that the oxidation state of the V ion was V and the  $VO^{3+}$  unit was coordinated to an iminosemiquinone radical anion. An isotopic signal at  $g = 1.998$  in the X-band electron paramagnetic resonance (EPR) spectrum and the solution magnetic moment  $\mu_{eff} = 1.98 \mu_B$  at 298 K also supported the composition. The formation of complex 1 preceded through the initial generation of a diamagnetic  $VO^{2+}$ –iminosemiquinone species, as established by time-dependent UV–vis–near-IR (NIR), X-band EPR, and density functional theory studies. The UV–vis–NIR spectrum of complex 1 consisted of four ligand-to-metal charge-transfer transitions in the visible region, while an intervalence ligand-to-ligand charge transfer appeared at 1162 nm. The cyclic voltammogram of the complex showed four oxidation waves and one reduction wave. Spectroelectrochemical studies at fixed potentials revealed that the oxidation and reduction processes were ligand-based.



## INTRODUCTION

Over the last 2 decades, significant attention has been given to the synthesis and spectroscopic understanding of first-row transition-metal-radical complexes because of the ubiquity of first-row transition-metal-radical species in metalloenzymes' active sites and enzymatic activities.<sup>1</sup> In this context, non-innocent ligands have been employed for the successful syntheses of radical-coordinated transition-metal complexes under the solo use of molecular oxygen as the oxidant.<sup>2</sup> Although radical-containing copper, nickel, cobalt, iron, and manganese complexes are common, radical-containing vanadium complexes are indeed very rare.<sup>3</sup> The plausible reason is that the amount of energy required to oxidize closed-shell, fully reduced non-innocent ligands to the corresponding radical forms is higher compared to the energy required for oxidation of the V ion.<sup>4</sup> In radical-containing  $VO^{2+}$  complexes,<sup>3a–c</sup> apart from noninnocent ligands,  $\pi$ -interacting ligands are also present in the coordination environment. Stabilization of the V atom in the IV oxidation state, due to metal-to-ligand  $\pi$  interaction, energetically favors oxidation of the closed-shell, noninnocent ligands to their corresponding radical states. Thus, radical-containing  $VO^{2+}$  complexes are successfully synthesized. Further oxidation of the radical-containing  $VO^{2+}$  complexes does not provide radical-coordinated  $VO^{3+}$  complexes because oxidation of the radical center is favored compared to the  $\pi$ -interaction-stabilized  $VO^{2+}$

centers. Hence, radical-coordinated  $VO^{3+}$  complexes are yet to be reported in the literature.

Herein, we have taken the initiative for the plausible synthesis of a radical-coordinated  $VO^{3+}$  complex. In this endeavor, a noninnocent ligand, which will be denoted here as  $H_4Sar^{(AP/AP)}$ ,<sup>5</sup> has been designed. Ligand  $H_4Sar^{(AP/AP)}$  can exist in various oxidation states in coordination complexes (Scheme 1). In the ligand backbone, a disulfane unit has been incorporated. We envisaged that the S atom in the disulfane, which is not a strong  $\pi$ -donor or acceptor, would undergo weak coordination with the V center and would stabilize the V atom in the IV oxidation state via the weak metal-to-ligand ( $d\pi-d\pi$ ) and ligand-to-metal ( $p\pi-d\pi$ ) interactions. The interactions would initially facilitate the ligand-centered oxidation, and, hence, the formation of a radical-coordinated  $VO^{2+}$  species was expected. Further oxidation of the species would preferably promote the formation of  $VO^{3+}$  species from  $VO^{2+}$  species because the IV oxidation state for the V atom is not greatly stabilized by the S atom. Thus, radical-coordinated  $VO^{3+}$  species could be synthesized and characterized geometrically as well as spectroscopically.

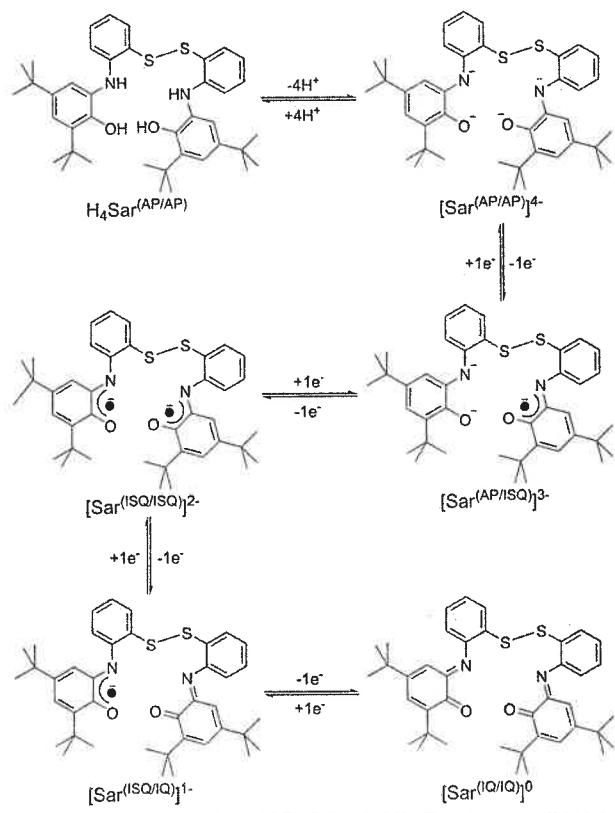
In this regard, ligand  $H_4Sar^{(AP/AP)}$  was reacted with a stoichiometric amount of  $VOSO_4 \cdot 5H_2O$  under air, thus

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**Scheme 1.** Various Plausible Oxidation States of Ligand  $H_4Sar^{(AP/AP)}$

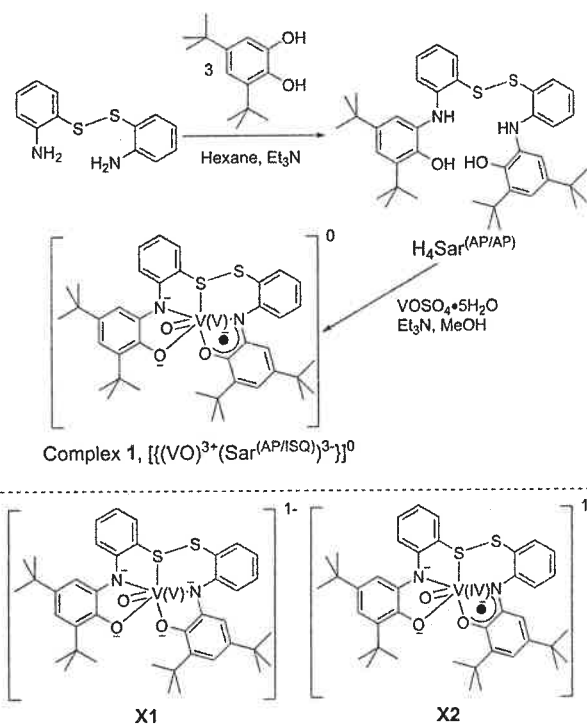


providing mononuclear complex **1**. X-ray crystallographic analysis of complex **1** showed that the central  $VO^{3+}$  unit contained an iminosemiquinone radical in its coordination sphere. The Evan's method room temperature magnetic moment measurement ( $\mu_{\text{eff}} = 1.98 \mu_B$ ) and ligand-centered  $g = 1.998$  X-band electron paramagnetic resonance (EPR) signal also supported the formation of the unprecedented radical-coordinated  $VO^{3+}$  complex. Time-dependent UV-vis-NIR and X-band EPR studies and density functional theory (TDDFT)-based calculation indicated that complex **1** was formed via the initial generation of a green diamagnetic  $VO^{2+}$ -iminosemiquinone species (intermediate **X**). Furthermore, TDDFT calculations were performed for a better understanding of the UV-vis-NIR spectra of the intermediate and complex **1**. Herein, we put forward the synthesis, characterization, and theoretical studies of  $H_4Sar^{(AP/AP)}$ , intermediate **X**, and complex **1**.

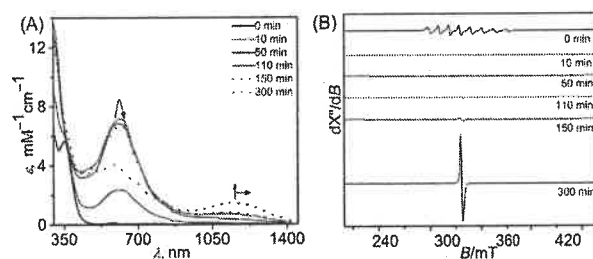
## RESULTS AND DISCUSSION

A schematic diagram for the syntheses of ligand  $H_4Sar^{(AP/AP)}$  and complex **1** is presented in Scheme 2. The organic 1,2-diphenyldisulfane-bridged ligand  $H_4Sar^{(AP/AP)}$  was synthesized in 73% yield by the condensation of 1:3 2,2'-disulfanediyl dianiline and 3,5-di-*tert*-butylcatechol in hexane in the presence of triethylamine ( $Et_3N$ ). The synthesis of complex **1** was carried out by reacting the ligand with an equivalent amount of  $VOSO_4 \cdot 5H_2O$  in the presence of  $Et_3N$  in methanol (MeOH) under air. Interestingly, a time-dependent change in the color of the reaction solution was observed. Initially, the color of the solution was green, which persisted for about 1 h. After that, the green

**Scheme 2.** (I) Schematic Representation for the Syntheses of  $H_4Sar^{(AP/AP)}$  and Complex **1** and (II) Two Possible Electronic Structures (X1 and X2) of Intermediate **X**



solution became blue and the complex started to precipitate out slowly. A detailed procedure is given in the Experimental Section. The time-dependent and simultaneous UV-vis-NIR and EPR spectra were recorded for a better understanding of the formation of complex **1** via the initial generation of the green intermediate **X**. In this context, the ligand, the metal salt, and  $Et_3N$  were added in MeOH. The UV-vis-NIR and X-band EPR spectra were recorded instantaneously. No appreciable peak in the absorption spectrum in the 400–1600 nm region was observed, while the X-band spectrum exhibited an eight-line spectrum (Figure 1B), which was typical for  $V^{IV} 3d^1$  species.<sup>6</sup> The X-band EPR spectrum appeared because of the presence of  $VOSO_4 \cdot 5H_2O$  salt in the solution. The EPR signal vanished within 10 min, and in the absorption spectrum, a new peak at around 615 nm appeared. It is worth noting that, in the absence of the metal salt, no change in the absorption spectrum was realized. This result further concluded that the presence of



**Figure 1.** Time-dependent UV-vis-NIR (A) and simultaneous X-band EPR (B) spectral changes that occur during the formation of complex **1**. X-band EPR spectra were measured at frequency = 9.45 GHz, power = 0.995 mW, modulation frequency = 100 kHz, amplitude = 10 G, and temperature = 298 K.



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**Collaborative research in coordination chemistry of organic radicals**  
**Number 54**

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**Institute 2: Ramakrishna Mission Residential College (Autonomous)**

**Concerned Scholar:** Dr. Suvendu Maity, Dept of Chemistry

**Period of Investigation:** 01-04-2018 to 30-04-2019

**Project:** Organic radical complexes of copper(II/I)

**Output:** The result was published in a journal of international repute

**Publication:** Geometry-Driven Iminosemiquinone Radical to Cu(II)  
**Electron Transfer and Stabilization of an Elusive Five-Coordinate Cu(I)**  
**Complex: Synthesis, Characterization, and Reactivity with  $\text{KO}_2$**

Ganesh Chandra Paul, Kanu Das, Suvendu Maity, Samiyara Begum, Hemant  
Kumar Srivastava and Chandan Mukherjee

*Inorg. Chem.* 2019, 58, 3, 1782–1793. DOI: 10.1021/acs.inorgchem.8b01931

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# Geometry-Driven Iminosemiquinone Radical to Cu(II) Electron Transfer and Stabilization of an Elusive Five-Coordinate Cu(I) Complex: Synthesis, Characterization, and Reactivity with $\text{KO}_2$

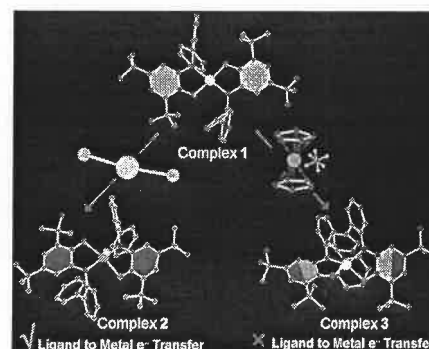
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## Supporting Information

**ABSTRACT:** The noninnocent ligand  $\text{H}_2\text{L}^{\text{AP(Ph)}}$  contained a bulky phenyl substituent at the *ortho* position to the aniline moiety. The ligand reacted with 0.5 equiv of  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$  in the presence of  $\text{Et}_3\text{N}$  under air and provided the corresponding Cu(II)-bis(iminosemiquinone) complex (1). The complex upon oxidation by a stoichiometric amount of ferrocenium hexafluorophosphate ( $\text{FcPF}_6$ ) yielded the four-coordinate [Cu(II)-(iminosemiquinone)-(iminoquinone)] $\text{PF}_6$  complex (3), while the oxidation by an equivalent amount of  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$  produced the five-coordinate Cu(I)-bis(iminoquinone)Cl complex (2). Thus, a ligand-based oxidation followed by ligand-to-metal electron-transfer was realized for the latter oxidation process. Removal of the  $\text{Cl}^-$  ion from complex 2 rendered the four-coordinate complex 4. The oxidation state of both Cu(I) and iminoquinone moieties remained unaltered upon the change in the coordination number. All the complexes were characterized by X-ray crystallography. Complexes 2, 3, and 4 were diamagnetic with an  $S_0 = 0$  ground state as evident by electron paramagnetic resonance (EPR) and  $^1\text{H}$  NMR measurements. The UV–vis–NIR spectra of all the complexes were dominated by charge-transfer transitions. Two oxidations and two reductions waves were noticed in the cyclic voltammogram (CV) of complex 1. Complex 2 and complex 3 underwent one oxidation and three reductions. Unlike complex 3, which experienced ligand-based oxidation, in complex 2 the oxidation was metal-centered [oxidation of Cu(I)-to-Cu(II)]. UV–vis–NIR spectral changes during the fixed-potential coulometric one-electron oxidation and thereafter EPR analysis consolidated the metal-based oxidation in complex 2. Complex 2 was air stable; however, it oxidized  $\text{KO}_2$  to oxygen molecule, and complex 1 was formed in due course as evident by UV–vis–NIR spectral changes and EPR measurements. Time dependent density functional theory calculations have been incorporated to assign the transitions that appeared in the UV–vis–NIR spectra of the complexes.



## INTRODUCTION

Investigation of radical-containing copper complexes has emerged as a research interest over recent years because of the involvement of copper-radical species in various biological oxidation and oxygenation processes.<sup>1–6</sup> The processes are mainly governed by (I) the geometry of the copper center; and (II) interactions between the redox-active copper (ranging between +I and +II) and the radical centers (phenolate/phenyl, catecholate/semiquinone/quinone,  $\text{O}_2^0/\text{O}_2^{\cdot-}/\text{O}_2^{2-}$ ).<sup>6</sup> Thus, the understanding of metal–ligand interactions in the geometry-dependent electron transfer processes and the employment of radical-containing copper complexes as biomimetic models and/or catalysts for various organic transformations are the imperative objectives.

In this context, the geometry, electronic structure, and biomimetic reactivity of Cu(II)-bis(radical) and Cu(II)-bis(quinone) complexes have been extensively studied. For example, Cu(II)-bis(radical) complexes have been successfully

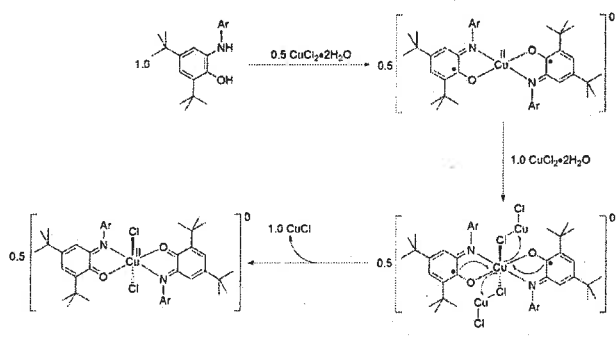
employed to mimic the function of GOase;<sup>7</sup> Cu(II)-bis(quinone) complexes have been utilized as catalysts for  $-\text{CF}_3$  transferring reactions, C–N coupling reactions, and  $\text{H}_2$  gas production from  $\text{NaBH}_4$  in dry acetonitrile.<sup>8</sup> While Cu(II)-bis(radical) and Cu(II)-bis(quinone) complexes are familiar in the literature, structurally characterized Cu(II)-monoradical systems with two coordinating noninnocent ligands of two different oxidation states remain elusive<sup>2g,j</sup> and demands special attention for understanding ligand–ligand and metal–ligands interactions, and their possible use as biomimetic catalysts.

Special Issue: Applications of Metal Complexes with Ligand-Centered Radicals

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2-Aminophenol derivatives have been well documented as being stabilized mainly in its one-electron oxidized iminosemiquinone ( $\text{ISQ}^{\cdot-}$ ) radical form in the corresponding  $\text{Cu(II)}$  complexes.<sup>7</sup> Recently, we have developed a new method where a bis(iminoquinone)-coordinated  $\text{Cu(II)}$  complex can directly be synthesized in one pot by employing  $\text{CuCl}_2$  as the oxidant.<sup>8d</sup> The mechanistic investigation (Scheme 1) suggests

**Scheme 1. Proposed Mechanism for the  $\text{CuCl}_2$  Mediated Oxidation of a  $\text{Cu(II)}$ -bis(radical) Complex to the Corresponding  $\text{Cu(II)}$ -bis(quinone) Complex<sup>8d</sup>**



that two chlorine atoms of two individual  $\text{CuCl}_2$  molecules bind at the axial positions to the  $\text{Cu(II)}$  center of the initially formed four-coordinate  $\text{Cu(II)}$ -bis(iminosemiquinone) complex, and subsequent two electrons transfer from two  $\text{Cu(II)}$ -coordinated iminosemiquinone units to the axially bound two  $\text{CuCl}_2$  molecules renders a six-coordinate  $\text{Cu(II)}$ -bis(iminoquinone) complex with two axial chloride ions.  $\text{CuCl}$  is the byproduct of the process.

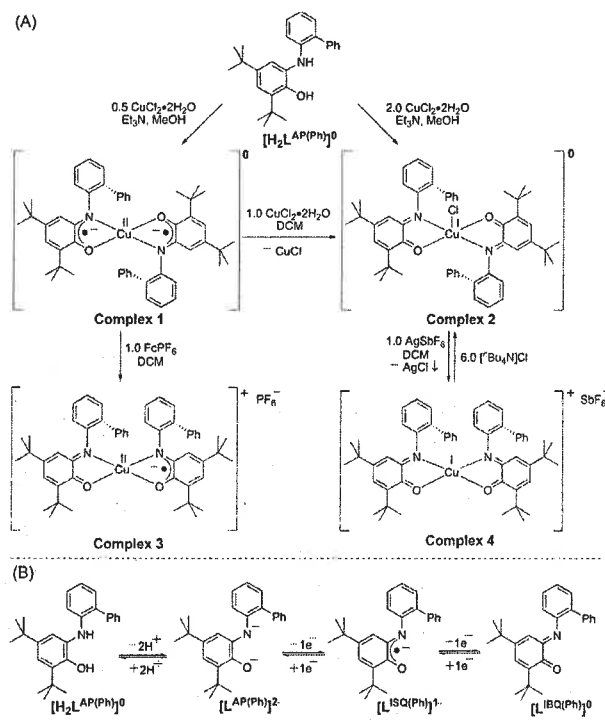
In this study, the aforementioned oxidation method has been examined on the  $\text{Cu(II)}$ -bis(iminosemiquinone) complex  $\{\text{Cu}^{\text{II}}[\text{L}^{\text{ISQ(Ph)}}]_2\}^0$  (1) of ligand  $\text{H}_2\text{L}^{\text{AP(Ph)}}$  for the *in situ* synthesis of the corresponding five-coordinate, chloride-bound  $\text{Cu(II)}$ -(iminosemiquinone)(iminoquinone) complex. In complex 1, two phenyl rings, which are attached at the *ortho* position to the aniline moiety, are situated *cis* to each other (*vide infra*). The steric hindrance created by the *cis* orientation of the two phenyl rings would block one of the two axial positions and hence would favor the approach of only one  $\text{CuCl}_2$  molecule along the open axial position to the  $\text{Cu(II)}$  center of complex 1. The  $\text{CuCl}_2$  molecule would then oxidize complex 1 by one electron to provide the expected complex. Interestingly, instead of the expected complex formation, a five-coordinate chloride-bound  $\text{Cu(I)}$ -bis(iminoquinone) complex  $\{\text{Cu}^{\text{I}}[\text{L}^{\text{IBQ(Ph)}}]_2\text{Cl}\}^0$  (2) was generated via a ligand-iminosemiquinone-to-metal[ $\text{Cu(II)}$ ] electron transfer during the  $\text{CuCl}_2$ -promoted oxidation process. To enlighten the geometry dependence on the electron transfer process, outersphere, one-electron oxidation of complex 1 has been carried out by employing ferrocenium hexafluorophosphate ( $\text{FcPF}_6$ ) as the oxidant. Thus, formed four-coordinate  $\text{Cu(II)}$ -complex  $\{\text{Cu}^{\text{II}}[\text{L}^{\text{ISQ(Ph)}}][\text{L}^{\text{IBQ(Ph)}}]\text{PF}_6\}$  (3) refrained from such electron transfer phenomenon. Furthermore, a four-coordinate  $\{\text{Cu}^{\text{I}}[\text{L}^{\text{IBQ(Ph)}}]_2\}\text{SbF}_6$  (4) complex was synthesized from complex 2 to extend the investigation on the geometry-dependent metal-to-ligand electron transfer process. All the complexes were subjected to react with  $\text{KO}_2$ ; while complex 2 and complex 3 reacted slowly and provided complex 1 and molecular oxygen as the final products, complex 4 remained indifferent to  $\text{KO}_2$ . Thus, geometry and oxidation state-

dependent reactivity studies are included, herein. Density functional theory (DFT) and time-dependent-DFT (TD-DFT)-based studies have been performed to investigate the geometry and to assign the UV-vis-NIR transitions observed in the complexes.

## RESULTS AND DISCUSSION

A schematic diagram for the syntheses of complexes 1, 2, 3, and 4 is presented in Scheme 2A. Ligand  $\text{H}_2\text{L}^{\text{AP(Ph)}}$  was

**Scheme 2. (A) A Schematic Representation for the Syntheses of Complexes 1, 2, 3, and 4 and (B) Possible Oxidation States of the Ligand**



synthesized in 88% yield by the condensation of 1:1 2-phenylaniline and 3,5-di-*tert*-butylcatechol in hexane in the presence of triethylamine ( $\text{Et}_3\text{N}$ ) under air. The three possible oxidation states of the ligands are shown in Scheme 2B. Complex 1 was obtained in 62% yield by reacting the ligand with half equivalent amount of  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$  in the presence of triethylamine ( $\text{Et}_3\text{N}$ ) in methanol ( $\text{MeOH}$ ) under air. The reaction of the ligand and excess amounts of  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$  (1:2 molar ratio) in the presence of  $\text{Et}_3\text{N}$  under air in  $\text{MeOH}$  provided complex 2 ( $\{\text{Cu}^{\text{I}}[\text{L}^{\text{IBQ(Ph)}}]_2\text{Cl}\}^0$ ) in 72% yield. Noteworthy, complex 2 has also been synthesized by reacting complex 1 ( $\{\text{Cu}^{\text{II}}[\text{L}^{\text{ISQ(Ph)}}]_2\}^0$ ) with 1 equiv of  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ . Thus, the formation of complex 1 and thereafter, oxidation of the complex by  $\text{CuCl}_2$ , was established. The removal of the axial chloride ion in complex 2 by employing an equivalent amount of  $\text{AgSbF}_6$  produced the four-coordinate complex 4 ( $\{\text{Cu}^{\text{I}}[\text{L}^{\text{IBQ(Ph)}}]_2\}\text{SbF}_6$ ). The feasibility of the regeneration of complex 2 from complex 4 in the presence of chloride anion was examined. In this regard, 1 equiv of complex 4 was allowed to react with 6 equiv of tetrabutylammonium chloride [ $(\text{tBu})_4\text{NCl}$ ] in dichloromethane ( $\text{DCM}$ ) for 4 h. Recrystallization of the isolated product, obtained by the removal of  $\text{DCM}$ ,





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**Collaborative research in functional coordination complexes**

**Number 55**

**Institute 1: Ramakrishna Mission Residential College (Autonomous)**

**Concerned Faculty: Dr. Prasanta Ghosh, Dept of Chemistry**

**&**

**Institute 2: Department of Chemistry, Dinabandhu Andrews College,**

**Kolkata, West Bengal, India.**

**Concerned Faculty: Dr. Madhusudan Shit, Department of Chemistry**

**Dinabandhu Andrews College, Kolkata, West Bengal, India**

**Period of Investigation: 01-10-2019 to 20-10-2020**


**Project: Functional nickel complexes**


**Output:** The result was published in a journal of international repute

**Publication: Nickel (II) di-aqua complex containing water cluster:  
Synthesis, X-ray structure and catecholase activity**

Madhusudan Shit, Suvendu Maity, Sachinath Bera, Prafulla Kumar Mudi,  
Bhaskar Biswas, Thomas Weyhermueller and Prasanta Ghosh

*New J. Chem., 2021, Accepted Manuscript. DOI: 10.1039/D0NJ05238H*

  
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### Nickel (II) di-aqua complex containing water cluster: Synthesis, X-ray structure and catecholase activity

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### Abstract

A trans-diaqua nickel(II) complex of the type  $[L2-NiII(H_2O)_2] \cdot nH_2O$  ( $1 \cdot nH_2O$ ) was isolated where LH2 is (E)-2-(2-((2-hydroxyphenylimino)methyl)phenoxy)acetic acid (LH2), a tetradentate ligand. The molecular geometry of  $1 \cdot nH_2O$  was confirmed by single crystal X-ray structure determination. It is observed that in the crystal, coordinated water, bulk water and ligand oxygen atoms form six membered water clusters by  $OH \cdots H$  interaction.  $1 \cdot nH_2O$  has been emerged as a catalyst for the oxidation of 3,5-di-tert-butylcatechol to 3,5-di-tert-butyl-o-benzoquinone with turnover number (kcat) as  $4.46 \times 10^2 \text{ h}^{-1}$  in  $CH_3OH$ . During oxidation, the coordination of catechol to the nickel(II) centre and the formation of a o-benzosemiquinone intermediate were confirmed by a nickel based EPR signal, ESI mass spectrometry and UV-Vis spectra.  $1 \cdot nH_2O$  exhibits an irreversible anodic peak at 0.83 V versus  $Fc^+/Fc$  couple due to phenoxyl/phenolato redox couple, authenticated by DFT calculations.

