



# Structural characterization and biological properties of a new dinuclear oxidovanadium(IV) *N*-(phosphonomethyl)iminodiacetate complex with the 4-amino-2-methylquinolinium cation



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## ABSTRACT

The crystal and molecular structures of a new dinuclear oxidovanadium(IV) complex with the *N*-(phosphonomethyl)iminodiacetate (pmida) ligand and the 4-amino-2-methylquinolinium ([amqH]<sup>+</sup>) cation of the molecular formula [amqH]<sub>4</sub>[V<sub>2</sub>O<sub>2</sub>(pmida)<sub>2</sub>]6H<sub>2</sub>O have been determined. The phosphonate groups in the two pmida<sup>4-</sup> ligands form two bridges between adjacent V<sup>4+</sup> atoms, resulting in the formation of a [V<sub>2</sub>O<sub>2</sub>(pmida)<sub>2</sub>]<sup>4-</sup> dimer with a V<sub>2</sub>O<sub>4</sub>P<sub>2</sub> eight-membered ring. This is the first example of a quinoline derivative complex containing the [V<sub>2</sub>O<sub>2</sub>(pmida)<sub>2</sub>]<sup>4-</sup> ion. The susceptibility curve for the complex exhibits a maximum at approximately 10 K, indicating the presence of antiferromagnetic interactions transmitted in the crystal lattice. Furthermore, the biological properties of the complex in the concentration range 1–100 μM were investigated in relation to its cytoprotective activity against oxidative damage generated exogenously using hydrogen peroxide in the hippocampal neuronal HT22 cell line (MTT tests). The obtained results were subsequently referred to the [amqH][VO(nta)(H<sub>2</sub>O)]H<sub>2</sub>O analogue as well as trolox and ascorbic acid, used as known antioxidants. It has been established that the title compound effectively protects HT22 from oxidative damage and is a potentially good candidate for further evaluation of the mechanism of its action.

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## 1. Introduction

*N*-(phosphonomethyl)iminodiacetic acid (H<sub>4</sub>pmida), a phosphonic derivative of nitrilotriacetic acid (H<sub>3</sub>nta), is a multidentate chelating ligand. The presence of two flexible chelating arms containing carboxylic acid groups, a central N-donor atom and a phosphonate group, with additional flexible coordination properties, enables the construction of organic–inorganic hybrid materials

(including heterometallic systems) with intriguing architectures and new framework topologies [1–6]. For these reasons, much attention has been focused on the synthesis and structural characterization of multi-dimensional coordination polymers which incorporate the pmida<sup>4-</sup> ligand. Among these complexes some oxidovanadium(IV) *N*-(phosphonomethyl)iminodiacetate crystal structures have been reported [8–13].

It has been found that in the solid state pmida<sup>4-</sup> has a great tendency to induce the formation of discrete binuclear oxidovanadium(IV) complexes of the [V<sub>2</sub>O<sub>2</sub>(pmida)<sub>2</sub>]<sup>4-</sup> type. The anionic [V<sub>2</sub>O<sub>2</sub>(pmida)<sub>2</sub>]<sup>4-</sup> units are stabilized by alkali metals, e.g. Na<sub>4</sub>[V<sub>2</sub>O<sub>2</sub>(pmida)<sub>2</sub>]10H<sub>2</sub>O and Na<sub>8</sub>[V<sub>2</sub>O<sub>2</sub>(pmida)<sub>2</sub>]216H<sub>2</sub>O [7]. The replacement of the Na<sup>+</sup> counterions with transition metal cations leads to the formation of mixed-metal-center hybrid materials under hydrothermal conditions [8]. The tetranuclear neutral [M<sub>2</sub>-V<sub>2</sub>O<sub>2</sub>(pmida)<sub>2</sub>(H<sub>2</sub>O)<sub>10</sub>] species (where M<sup>2+</sup> denotes Mn<sup>2+</sup>, Co<sup>2+</sup>, Zn<sup>2+</sup> or Cd<sup>2+</sup>) comprise two [M(H<sub>2</sub>O)<sub>5</sub>]<sup>2+</sup> moieties that coordinate

*Abbreviations:* Pmida, *N*-(phosphonomethyl)iminodiacetate ligand; Nta, nitrilotriacetate ligand; Amq, 4-amino-2-methylquinoline; Phen, 110'-phenantroline; 4,4'-bpy, 4,4'-bipyridine; Pyr, pyrazine; RNOS, reactive nitrogen and oxygen species; trolox, 6-hydroxy-2,5,7,8-tetramethylchromane-2-carboxylic acid; AA, ascorbic acid; acac, acetylacetonate; HT22, hippocampal neuronal cell line; MTT, (4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; FBS, fetal bovine serum; SF, serum-free medium.

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to the *exo*-P–O bonds of the phosphonate groups [9–11]. The aqua ligands can be easily displaced from  $[M(H_2O)_5]^{2+}$  by a bridging ligand, such as 4,4'-bpy, resulting in the formation of one-dimensional  $[M(4,4'\text{-bpy})(H_2O)_4]_n^{2n+}$  ( $M^{2+} = Mn^{2+}$  or  $Co^{2+}$ ) [12] or  $[M(4,4'\text{-bpy})(H_2O)_2]_n^{2n+}$  ( $M^{2+} = Co^{2+}$  or  $Cd^{2+}$ ) cationic polymers [9]. The inclusion of pyr, a smaller ditopic bridging organic ligand, has allowed the coordination polymer  $\{[Co(H_2O)_6][CoV_2(pmida)_2(pyr)_2(H_2O)_2]2H_2O\}_n$  [13] to be obtained, which contains a two-dimensional anionic  $[CoV_2O_2(pmida)_2(pyr)(H_2O)_2]_n^{2n-}$  layer which alternates with the  $[Co(H_2O)_6]^{2+}$  complexes and water molecules of crystallisation. The layer is formed by the anionic binuclear  $[V_2O_2(pmida)_2]^{4-}$  unit directly connected to the  $Co^{2+}$  metal centres of the  $[Co(pyr)(H_2O)_2]_n^{2n+}$  cationic polymers via *exo*-P–O bonds.

In the course of our ongoing studies on oxidovanadium(IV) complexes containing polycarboxylate ligands [14–17], we have focused our research on the synthesis and structural characterization of a novel oxidovanadium(IV) complex which incorporates the *N*-(phosphonomethyl)iminodiacetate ( $pmida^{4-}$ ) ligand and the 4-amino-2-methylquinolinium ( $[amqH]^+$ ) cation.

Our previous studies have shown that the oxidovanadium(IV) complex, containing a discrete mononuclear  $[VO(nta)(H_2O)]^-$  coordination unit and the 1,10-phenanthroline cation,  $[phenH][VO(nta)(H_2O)](H_2O)_{0.5}$ , exhibits a protective activity against oxidative damage induced by  $H_2O_2$  in the mouse hippocampal neuronal HT22 cell line [14]. Therefore, it seemed worthy to investigate how modification of the coordination sphere of the oxidovanadium(IV) ion, by replacing the  $nta^{3-}$  ligand with the  $pmida^{4-}$  ligand, affects the cytoprotective properties of the oxidovanadium(IV) complexes. Generally, the type of ligands in the coordination sphere of the oxidovanadium(IV) ion, as well as their coordination mode, governs the biological activity of the complexes [18]. To estimate the influence of the ligands ( $pmida^{4-}$  and  $nta^{3-}$ ) on the biological properties of the oxidovanadium(IV) complexes we have examined the protective activities of  $[V_2O_2(pmida)_2]^{4-}$  and  $[VO(nta)(H_2O)]^-$ , namely  $[amqH]_4[V_2O_2(pmida)_2]6H_2O$  and  $[amqH][VO(nta)(H_2O)]H_2O$ , against hydrogen peroxide-induced oxidative damage in the mouse hippocampal neuronal HT22 cell line. As far as we are concerned,

there are no reports on the biological activity of *N*-(phosphonomethyl)iminodiacetate oxidovanadium(IV) complexes. Consequently, this was the reason that prompted us to embark on these studies.

## 2. Experimental

### 2.1. Synthesis

A mixture of  $VO(acac)_2$  (2.63 g, 0.01 mmol) and  $H_3nta$  (1.91 g, 0.01 mmol) or  $H_4pmida$  (2.27 g, 0.01 mmol) in water  $H_2O$  (200 mL) was provided by rotary evaporation. The mixture was heated under vacuum at 70 °C in order to eliminate Hacac. In the next step, to the obtained concentrated reaction mixture an ethanol solution of 4-amino-2-methylquinoline (*amq*) (0.01 mmol) was added. The mixture was left for crystallization in a fridge. After 2–5 days bluish crystals of  $[amqH]_4[V_2O_2(pmida)_2]6H_2O$  and a blue precipitate of  $[amqH]_4[VO(nta)(H_2O)]H_2O$  were obtained. The filtered crystals and powder were air-dried at room temperature. The compositions of the compounds were established based on their carbon and hydrogen elemental analyses (Vario EL analyzer Cube CHNS). *Anal. Calc.* for  $[amqH]_4[V_2O_2(pmida)_2]6H_2O$ : C, 45.32; H, 5.18; N, 10.57, Found: C, 43.50; H, 5.30; N, 10.16%. *Anal. Calc.* for  $[amqH]_4[VO(nta)(H_2O)]H_2O$ : C, 42.86; H, 4.73; N, 9.37, Found: C, 42.43; H, 4.83; N 9.27%.

### 2.2. X-ray measurements

Good-quality single-crystal specimens of the title compound were selected for the X-ray diffraction experiments at  $T = 295(2)$  K. Diffraction data were obtained on an Oxford Diffraction Gemini R Ultra Ruby CCD diffractometer, using a  $MoK\alpha$  radiation source ( $\lambda = 0.71073$  Å). The lattice parameters were obtained by a least-squares fit to the optimized setting angles of the reflections by means of CrysAlis CCD [19]. Data were reduced using the CrysAlis RED software [19]. The structural resolution procedure was carried out with the SHELXS-97 package, solving the structure by direct methods and carrying out refinements by full-matrix least-squares on  $F^2$  using the SHELXL-97 program [20].

All H atoms bound to O(water) atoms were located on the Fourier difference map and refined with restraints  $U_{iso}(H) = 1.5$ . All H atoms bound to N atoms were located on the Fourier difference map and refined using a riding model where  $U_{iso}(H) = 1.2$ . All H atoms bound to C atoms were placed geometrically and refined using the riding model with C–H = 0.97 Å and  $U_{iso}(H) = 1.2 U_{eq}(C)$  (C–H = 0.96 Å and  $U_{iso}(H) = 1.5 U_{eq}(C)$  for the methyl group).

The molecular packing in the crystal structure was prepared by the ORTEP-3 [21] and MERCURY [22] programs. The computational material for publication was prepared using the PLATON program [23]. Details concerning the crystal data and refinement are given in Table 1.

### 2.3. Magnetic properties

The magnetic measurements were conducted using a Quantum Design SQUID-VSM magnetometer. The magnetic susceptibility data of a powdered sample were measured over the temperature range 4–300 K at a magnetic induction of 0.1 T. The SQUID magnetometer was calibrated with a palladium rod sample. Corrections for the sample holder and diamagnetism of the constituent atoms, the last calculated from Pascal constants [24,25], were taken into account. The effective magnetic moment values were calculated from the equation:

$$\mu_{\text{eff}} = 2.83(\chi_m \cdot T)^{1/2}$$

**Table 1**

The crystal data and structure refinement for  $[amqH]_4[V_2O_2(pmida)_2]6H_2O$ .

Chemical formula	$(C_{10}H_{12}V_2P_2N_2O_{16})^{4-} \cdot 4(C_{10}H_{11}N_2)^+ \cdot 6(H_2O)$
FW (g mol <sup>-1</sup> )	1324.96
Crystal system	monoclinic
Space group	$P2_1/c$
<i>a</i> (Å)	11.011(2)
<i>b</i> (Å)	10.847(2)
<i>c</i> (Å)	24.924(5)
$\alpha$ (°)	90
$\beta$ (°)	91.21(3)
$\gamma$ (°)	90
<i>V</i> (Å <sup>3</sup> )	2976.2(9)
<i>Z</i>	2
<i>T</i> (K)	295(2)
$\lambda_{Mo}$ (Å)	0.71073
$\rho_{\text{calc}}$ (g cm <sup>-3</sup> )	1.479
$\mu$ (mm <sup>-1</sup> )	0.453
<i>F</i> (000)	1380
$\theta$ range for data collection (°)	3.27–50.00
Completeness $2\theta$ (%)	99.8
Reflections collected	19624
Reflections unique	5221 [ $R_{\text{int}} = 0.0333$ ]
Data/restraints/parameters	5221/9/408
Goodness-of-fit (GOF) on $F^2$	1.038
Final $R_1$ value ( $I > 2\sigma(I)$ )	0.0357
Final $wR_2$ value ( $I > 2\sigma(I)$ )	0.0821
Final $R_1$ value (all data)	0.0462
Final $wR_2$ value (all data)	0.0865
CCDC number	CCDC 1535864

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