



Note

The first vitamin B₆ zinc complex, pyridoxinato-zinc acetate: A 1D coordination polymer with polar packing through strong inter-chain hydrogen bonding

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ABSTRACT

The biologically important pyridoxinato(1⁻) ligand (anionic vitamin B₆) shows the rare phenolate-hydroxymethyl chelation plus bridging mode through the pyridine-nitrogen atom towards zinc(II) to give the one-dimensional (1D) coordination polymer {(acetato-κO)-aqua-μ-[2-methyl-3-oxy-4,5-di(hydroxymethyl)pyridine-κN:O,O']zinc(II)}-monohydrate with polar packing of adjacent chains along the polar c axis (in space group *Pc*) through strong inter-chain hydrogen bonding.

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1. Introduction

Pyridoxine [2-methyl-3-hydroxy-4,5-bis(hydroxymethyl)pyridine] (Scheme 1) the first isolated vitamin B₆ component, is essential in the diet for the metabolism of amino acids and the maintenance of body cells.

Metal complexes of vitamin B₆ have been reported to inhibit the growth as well as the biosynthesis of RNA, DNA and protein of *E. coli* B-766 [1]. Pyridoxine displays different metal coordination sites with different charges and hard/soft character [2]. Chelation through the phenolate oxygen and adjacent oxymethyl is common for pyridoxinato(2⁻) [3], (N)H-pyridoxinato(1⁻) [4,5] and zwitterionic N-protonated, phenol-deprotonated pyridoxine(0) (Scheme 2) [6–9].

Also reported for pyridoxine is the sole coordination through the pyridine-nitrogen (to palladium) [1,2,10]. In di- and polynuclear complexes phenolate-oxymethyl chelation plus bridging through the phenolate-O [11], through the 4-oxymethyl-O [3,5,12–14] and 5-hydroxymethyl-O [4] was observed while there is only one report on the phenolate-hydroxymethyl chelation plus bridging through the pyridine-nitrogen atom (towards Cu²⁺) (Scheme 3) [9].

In view of the essential biological catalytic and structural functionalities of zinc in a number of metalloproteins and biological

zinc complexes with proteins and nucleic acids [15–17] we report here the first zinc complex with vitamin B₆ and only the second example of pyridoxine chelation plus bridging through the pyridine-nitrogen atom.

2. Experimental

Pyridoxine and zinc acetate were purchased from Aldrich and used without further purification. Doubly distilled water was used in the preparation of all the solutions. The IR spectra were recorded with samples as KBr pellets on a Shimadzu FTIR 8400S spectrophotometer.

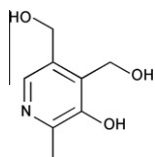
2.1. Synthesis of catena-[(acetato-κO)-aqua-μ-[2-methyl-3-oxy-4,5-di(hydroxymethyl)pyridine-κN:O,O']zinc(II)] monohydrate (1)

Pyridoxine (0.169 g, 1.0 mmol) in ethanol (10 mL) was added dropwise to a stirred solution of zinc acetate dihydrate (0.219 g, 1.0 mmol) in ethanol (10 mL) at room temperature. After the slow addition of the ligand was complete, the mixture was refluxed for 2 h with constant stirring and kept at room temperature for 1 day to give a clear solution. When the clear solution was saturated with petroleum ether in a closed vial colorless crystals were obtained. The crystals were collected by filtration, washed several times with ethanol and finally with diethyl ether until the washings became colorless. The product was dried in air and stored in a desiccator over anhydrous calcium chloride under vacuum (yield 0.28 g, 67%). The product is insoluble in water and in all the usual organic solvents, including DMSO and DMF but soluble in hot DMSO.

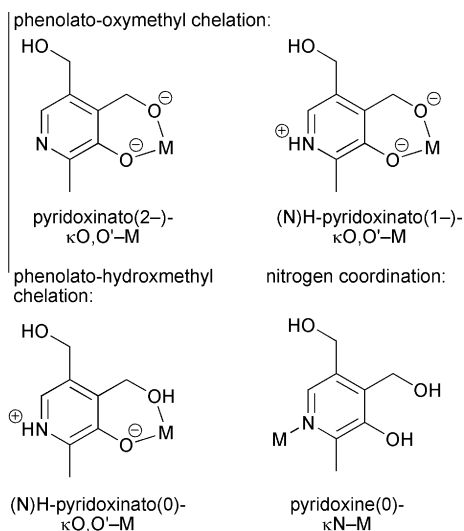
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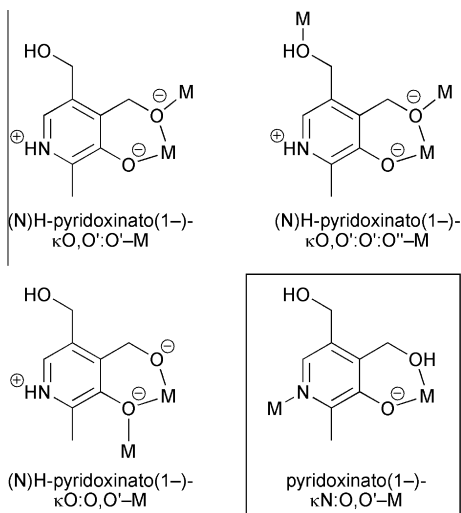
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Scheme 1. Pyridoxine [2-methyl-3-hydroxy-4,5-bis(hydroxymethyl)pyridine].



Scheme 2. Typical metal–pyridoxine coordination modes in mononuclear complexes.



Scheme 3. Chelating-bridging modes in di- and polynuclear metal–pyridoxine complexes. The only second case of the highlighted pyridine–nitrogen bridging mode is described here in the structure of **1**.

Elemental *Anal.* Calc. for $\text{C}_{10}\text{H}_{17}\text{NO}_7\text{Zn}$ (328.62): C, 36.55; H, 5.21. Found: C, 36.72; H, 6.22%. IR (KBr, cm^{-1}): 3441, 3333 and 3136 (sh, C–OH), 3100 (br, H_2O), 1606 (C=N), 1546 (C=C), 1579 ($\nu_{\text{as}}\text{COO}^-$), 1502 (phenolic–C–O), 1336 ($\nu_{\text{s}}\text{COO}^-$).

2.2. X-ray crystallography

Crystals were carefully selected under a polarizing microscope. *Data collection:* Bruker Apex2 AXS CCD, Mo $K\alpha$ radiation ($\lambda =$

Table 1
Crystal data and structure refinement for **1**.

Empirical formula	$\text{C}_{10}\text{H}_{17}\text{NO}_7\text{Zn}$
M (g mol^{-1})	328.62
Crystal size (mm)	$0.19 \times 0.18 \times 0.06$
Crystal appearance	isometric, colorless
2θ Range ($^\circ$)	4.28–51.7
h, k, l Range	$\pm 13, \pm 6, \pm 16$
Crystal system	monoclinic
Space group	Pc
a (\AA)	11.0881(14)
b (\AA)	5.1477(7)
c (\AA)	13.4316(17)
β ($^\circ$)	120.784(8)
V (\AA^3)	658.63(15)
Z	2
D_{calc} (g cm^{-3})	1.657
$F(000)$	340
μ (mm^{-1})	1.893
Maximum/minimum transmission	0.8949/0.7127
Reflections collected	12 794
Independent reflections (R_{int})	2545(0.0638)
Observed reflections [$I > 2\sigma(I)$]	2493
Parameters refined	190
Maximum/minimum $\Delta\rho^a$ (e \AA^{-3})	1.197/–0.755
R_1/wR_2 [$I > 2\sigma(I)$] ^b	0.0354/0.0832
R_1/wR_2 (all reflections) ^b	0.0360/0.0837
Goodness-of-fit (GOF) on F^2 ^c	1.058
Weight scheme $w; a/b^d$	0.0596/0.0000
Flack parameter ^e	0.012(13)

^a Largest difference peak and hole.

^b $R_1 = [\sum(|F_o| - |F_c|)] / \sum|F_o|$; $wR_2 = [\sum[w(F_o^2 - F_c^2)^2] / \sum[w(F_o^2)^2]]^{1/2}$.

^c Goodness-of-fit = $[\sum[w(F_o^2 - F_c^2)^2] / (n - p)]^{1/2}$.

^d $w = 1 / [\sigma^2(F_o^2) + (aP)^2 + bP]$, where $P = (\max(F_o^2 \text{ or } 0) + 2F_c^2) / 3$.

^e Absolute structure parameter [22].

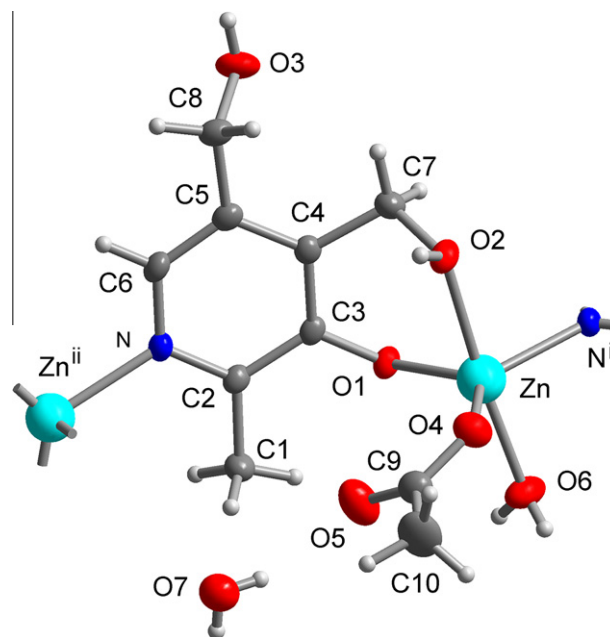


Fig. 1. Thermal ellipsoid plot (50% probability) of the asymmetric unit of **1**, also showing the full zinc coordination sphere and the ligand bridging action. Selected distances (\AA) and angles ($^\circ$): Zn–Nⁱ 2.081(3), Zn–O1 1.971(2), Zn–O2 2.187(3), Zn–O4 1.965(3), Zn–O6 2.069(3), Nⁱ–Zn–O1 107.5(1), Nⁱ–Zn–O2 89.6(1), Nⁱ–Zn–O4 126.2(1), Nⁱ–Zn–O6 86.9(1), O1–Zn–O2 86.6(1), O1–Zn–O4 126.1(1), O1–Zn–O6 96.3(1), O2–Zn–O4 88.7(1), O2–Zn–O6 176.0(1), O4–Zn–O6 91.8(1); symmetry transformations $i = x, -y, -0.5 + z$ and $ii = x, -y, 0.5 + z$.

0.71073 \AA), graphite monochromator, temperature 293(2) K, ω -scans, absorption correction with SADABS [18]. *Structural analysis*

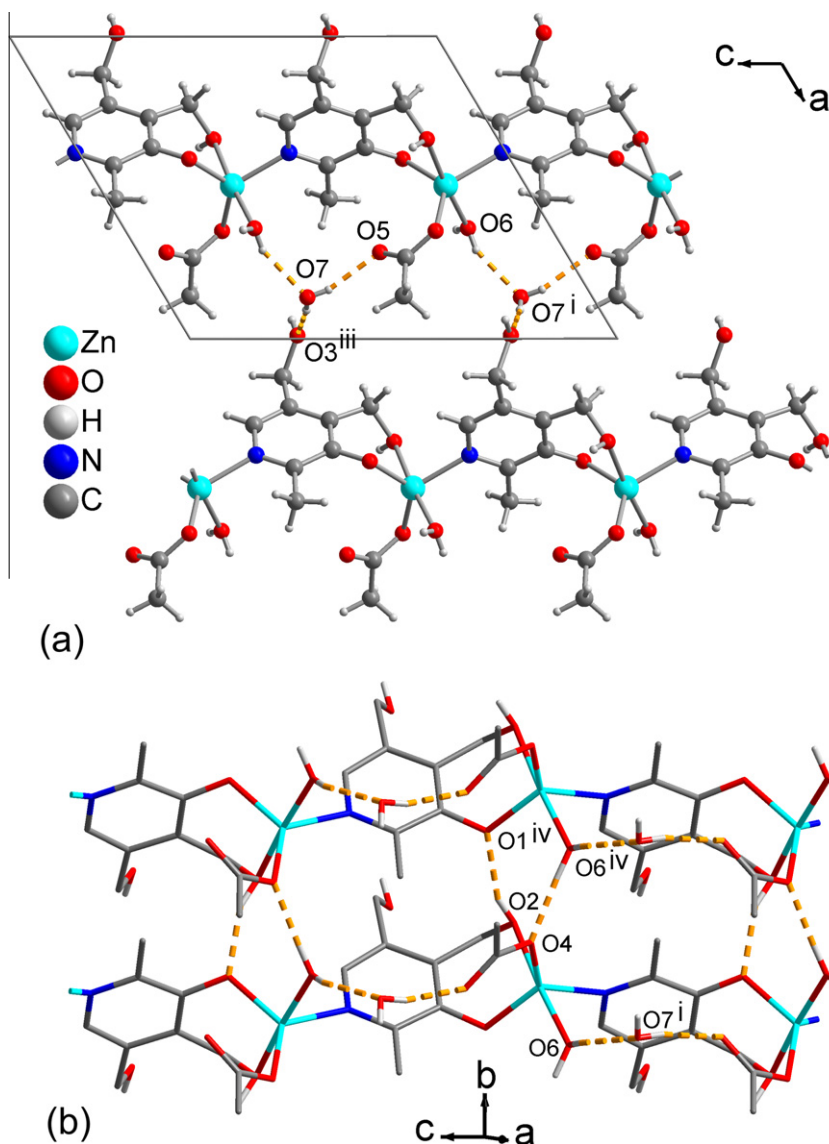


Fig. 2. Projection of the unit cell packing of **1** onto the (a) *ac* plane and (b) *bc* plane to illustrate the polar packing along the *c* axis, with hydrogen bonds shown as orange dashed lines. For clarity, the H atoms on carbon are omitted in the wire frame presentation in (b). See Table 2 for hydrogen bonding details.

Table 2
Hydrogen bonding interactions in **1**^a.

D–H···A	D–H (Å)	H···A (Å)	D···A (Å)	D–H···A (°)
O2–H2(A)···O1 ^{iv}	0.82(6)	1.88(6)	2.654(3)	155(5)
O3–H3···O7 ^v	0.84(4)	2.07(5)	2.830(4)	150(5)
O6 ^{iv} –H6A···O4	0.86(7)	1.78(7)	2.641(4)	177(6)
O6–H6B···O7 ⁱ	0.75(7)	2.06(8)	2.765(5)	157(7)
O7–H7A···O5	0.71(8)	2.01(8)	2.691(5)	160(8)
O7–H7B···O3 ⁱⁱⁱ	0.71(8)	2.19(8)	2.885(4)	166(7)

^a D = donor, A = acceptor. For found and refined atoms the standard deviations are given. Symmetry relation: i = *x*, –*y*, –0.5 + *z*; iii = 1 + *x*, –*y*, 0.5 + *z*; iv = *x*, 1 + *y*, *z*; v = –1 + *x*, 1 – *y*, –0.5 + *z*.

and refinement: the structure was solved by direct methods (SHELXS), refinement was done by full-matrix least squares on F^2 using the SHELXL program suite [19]; all non-hydrogen positions refined with anisotropic temperature factors; hydrogen atoms on carbon were positioned geometrically and refined using a riding model, with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$; H atoms on the aqua ligand and water of crystallization were found and refined with $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{O})$. Graphics

were obtained with DIAMOND [20]. Computations on the supramolecular π -interactions were carried out with PLANTON for Windows [21]. Crystal data and details on the structure refinement are given in Table 1.

3. Results and discussion

The pyridoxinato(1–) ligand in **1** shows phenolate-hydroxy-methyl chelation towards zinc plus bridging through the pyridine-nitrogen atom. An acetato and an aqua ligand conclude the close to trigonal-bipyramidal ($\tau = 0.83$ [23]) zinc coordination sphere (Fig. 1).

The bridging action of pyridoxinato(1–) between two zinc atoms leads to the formation of a 1D coordination polymeric chain in **1** [24]. Remarkably, compound **1** crystallizes in the non-centrosymmetric polar space group *Pc*. Accordingly; the molecules must all be oriented in the same direction along the polar *c* axis: With their nitrogen atoms, for example, the ligands are all pointing in the same direction (along the polar *c* axis in Fig. 2). This polar packing [25] within the chain and of adjacent chains in the crystal of **1**

probably originates from the inter-chain hydrogen bonding interactions (Fig. 2 and Table 2). The low solubility of **1** in water and in all the usual organic solvents, including DMSO and DMF is indicative of rather strong covalent intra-chain interactions and of a strong non-covalent (hydrogen bonding) inter-chain network.

Under biological conditions in aqueous solution at lower concentrations and with additional chelating ligands available, molecular pyridoxinato–metal complexes are a clear alternative and perhaps more likely to the formation of a coordination polymer. However, we note that when pyridoxine forms metal complexes with metal chlorides or metal sulfates in more acidic solutions (pH 2–3) the metal atom is coordinated in the phenolato-(hydr)oxymethyl mode and the nitrogen atom is protonated (Schemes 2 and 3) [26]. As a result, the heterocycle acquires a pyridinium character and the nitrogen atom is not available for further metal-bridging coordination so that the formation of polymeric compound is avoided. When pyridoxine forms a metal complex with metal acetate the solution is in a more physiological less acidic pH regime (pH 6–6.5). In this condition the pyridine-nitrogen is not protonated and, thus, it can coordinate to the metal ion and form an insoluble coordination polymer.

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Appendix A. Supplementary material

CCDC 782880 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.ica.2010.07.033](https://doi.org/10.1016/j.ica.2010.07.033).

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