X-Ray Crystal Structures of the Nickel(II) and Copper(II) Complexes of O-Phospho-DL-threonine–Pyridoxal Schiff Base

By Katsuyuki Aoki* and Hiroshi Yamazaki

(The Institute of Physical and Chemical Research, Wako-shi, Saitama 351, Japan)

Summary X-Ray structural analyses of two metal complexes of O-phospho-DL-threonine–pyridoxal Schiff base, [Ni(C$_{12}$H$_{15}$N$_2$O$_8$P)(H$_2$O)$_3$]·2H$_2$O (1) and [Cu(C$_{12}$H$_{15}$N$_2$O$_8$P)(H$_2$O)]·H$_2$O (2), show the nickel (II) complex (1) to be a monomer with the octahedral nickel ion bonded to the tridentate Schiff base and three water molecules, and the copper(II) complex (2) to be a dimer with the square-pyramidal copper ion bonded to the tetradentate Schiff base, involving a phosphate oxygen atom from a neighbouring molecule, and one water molecule

Pyridoxal phosphate (the cofactor form of vitamin B$_6$)-dependent enzymes catalyse a variety of metabolic reactions of amino acids such as decarboxylation, transamination, racemization, and carbon–carbon bond cleavage Many nonenzymatic model reactions also proceed by similar mechanisms in the presence of pyridoxal and a suitable metal ion [1] Murakami et al have reported the β-elimination of the phosphate group from O-phosphothreonine catalysed by pyridoxal and metal ions [2] We have undertaken X-ray investigations of metal complexes of O-phosphothreonine–pyridoxal Schiff base which have been considered to be reaction intermediates, in order to develop a better understanding of these reaction mechanisms We now report the crystal structures of the nickel(II) (1) and copper(II) (2) complexes, which are quite different from each other

The (pyridoxylidene-O-phospho-DL-threoninato) nickel(II) complex (1) (yellow-green plates) was prepared from pyridoxal HCl, O-phospho-DL-threonine, and Ni(NO$_3$)$_2$·6H$_2$O in an equimolar (0·2 mmol) ratio at pH ca 5 Crystal data [Ni(C$_{12}$H$_{15}$N$_2$O$_8$P)(H$_2$O)$_3$]·2H$_2$O, triclinic, space group P$\bar{1}$, a = 9·245(2), b = 14·243(9), c = 9·754(5) Å, α = 126 89(4), β = 79·63(3), γ = 109·97(3)°, Z = 2, U = 964·9 Å³, D$_m$ = 1·69, D$_c$ = 1·704 g cm^{-3} The final R is 0·052 for 1502 reflections [2θ ⩽ 45°, F$_0$ > 3σ(F$_0$), Rigaku diffractometer, Mo-K$_\alpha$ radiation] †

(1)

(2)

† The atomic co-ordinates for this work are available on request from the director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW Any request should be accompanied by the full literature citation for this communication
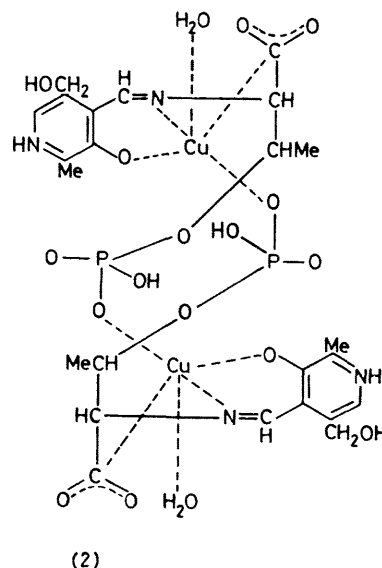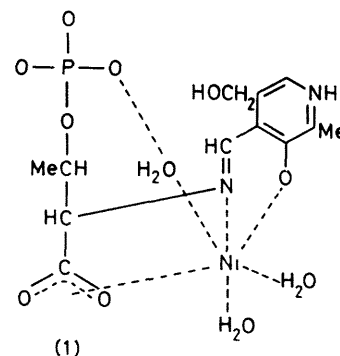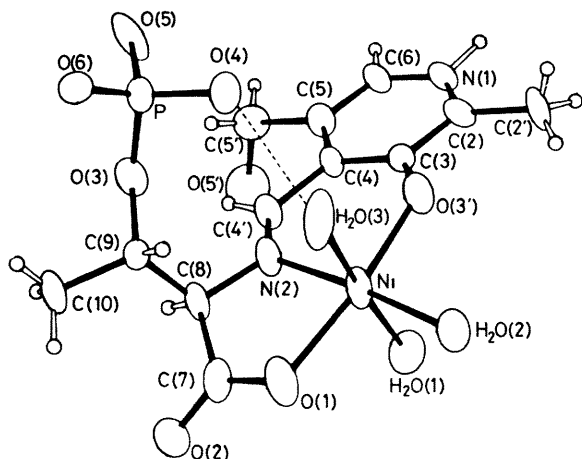
FIGURE 1. Crystal structure of the nickel complex (1).

FIGURE 2. Crystal structure of the copper complex (2).

Figure 1 shows the monomeric molecular structure of the nickel complex (1), in which the pyridoxal group forms a Schiff base with O-phosphothreonine, as expected. The Schiff base exists as a divalent anion with the carboxylate and the phosphate‡ amino acid substituents each providing one negative charge; the phenolic oxygen O(3′) of the pyridoxal group is deprotonated and the pyridoxal ring nitrogen N(1) is protonated instead. The tridentate Schiff base ligand co-ordinates to the octahedral nickel atom through the phenolic O(3′), the carboxylate oxygens, and the imino nitrogen N(2) of the amino acid, as do other known metal complexes of pyridoxal–amino acid Schiff bases, and the fourth co-ordination site in the equatorial plane and two axial positions are occupied by three water molecules. The pyridoxal–aldimine [pyridoxal + imino nitrogen N(2)] group involving the α-carbon C(8) is almost planar while the metal ion significantly deviates from this plane [0·35 Å towards the axial H₂O(3)]; the carboxylate group rotates around the C(8)–C(7) bond with an N(2)–C(8)–C(7)–O(1) torsion angle of 23·4°. Interestingly, in this structure the phosphate unit is not directly bound to the metal centre, but instead forms an intramolecular hydrogen bond (2·79 Å) with the axial water molecule; this stabilizes the molecular structure.

The dimeric (pyridoxylidene-O-phospho-DL-threoninato) copper(II) complex (2) (green columns) was prepared by a similar method to that used for (1), but at pH ca. 2. Crystal data: [Cu(C₁₂H₁₅N₂O₈P)(H₂O)]·H₂O, triclinic, space group PĪ, $a = 9·756(6)$, $b = 9·866(5)$, $c = 10·115(6)$ Å, $\alpha = 112·44(4)$, $\beta = 111·36(7)$, $\gamma = 89·08(9)$ °, $Z = 2$, $U = 829·5$ Å³, $D_m = 1·77$, $D_c = 1·785$ g cm⁻³. The final R is 0·044 for 2706 reflections [$2\theta \leqslant 55°$, $F_0 > 3\sigma(F_0)$; Rigaku diffractometer, Mo-K_α radiation].†

Figure 2 shows the molecular structure of the centrosymmetric dinuclear copper complex (2), where the charge distribution of the molecule is the same as that found in the nickel complex (1). The co-ordination sphere is approximately 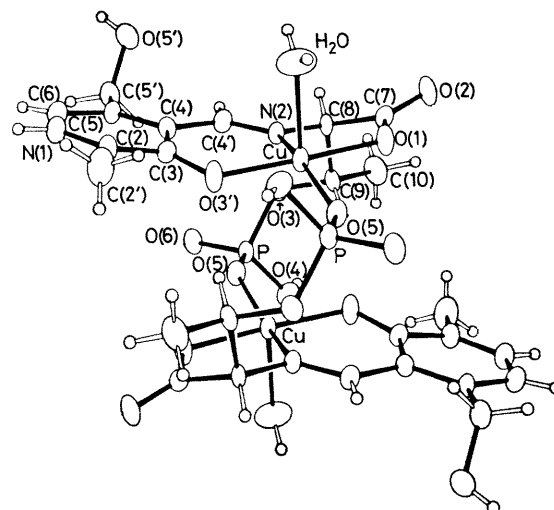square-pyramidal, with the equatorial plane defined by the phenolate and carboxylate oxygens and the imino nitrogen of the Schiff base, and also by a phosphate oxygen from a neighbouring molecule which produces the dimeric structure; the axial position is occupied by a water molecule. As in (1), the metal ion deviates from the pyridoxal–aldimine plane (0·25 Å towards the axial water molecule) and the distortion of the carboxylate group from the chelate plane is due to rotation around the C(8)–C(7) bond with a torsion angle N(2)–C(8)–C(7)–O(1) of 24·9°. It is of interest that the configuration as well as the dimensions of the Schiff base (including the side chain atoms) are very similar to those observed in the nickel complex (1) in spite of the different type of the molecular structure and metal ion–phosphate interactions; i.e., (1) is a monomer with indirect ('outer-sphere') attachment of the phosphate group to the metal ion through an intramolecular hydrogen bond involving a co-ordinated water molecule while (2) is a dimer with a direct ('inner-sphere') metal ion–phosphate bonding; torsion angles are C(4′)–N(2)–C(8)–C(9) −86·9 for (1) and −84·4° for (2), N(2)–C(8)–C(9)–O(3) 49·6 for (1) and 54·8° for (2), and C(8)–C(9)–O(3)–P −128·2 for (1) and −127·1° for (2). This configuration seems to avoid unfavourable steric and electrostatic repulsion between the charged COO⁻ and PO₃H⁻ groups.

The stereochemistry of the hydrogen atom at the α-carbon atom of the amino acid residue is of particular interest in connection with the mechanism of the β-elimination reaction of O-phosphothreonine catalysed by pyridoxal and metal ions, since the key step in this reaction is the elimination of the α-C-hydrogen atom of the substrate amino acid–pyridoxal Schiff base.[2] In the present compounds, the α-C-hydrogen atom is positioned almost in the pyridoxal–aldimine plane: torsion angle C(4′)–N(2)–C(8)–8-H 24·0° for (1) and 33·5° for (2). This observation seems to rationalize the fact[2] that the copper(II) ion under acidic conditions§ and the nickel(II) ion lack catalytic

‡ The hydrogen atom attached to the phosphate oxygen could not be located in the final Fourier map, but the P–O bond lengths are P–O(4) 1·542(5), P–O(5) 1·488(7), and P–O(6) 1·521(8) Å, so O(4) is the most probable site for the proton.

§ The copper(II) ion shows catalytic activity only in the alkaline region (pH >7). We have been unsuccessful in crystallizing the ion from alkaline solution, possibly because the catalytic reaction is over before the reaction intermediates can crystallize.

activity; Dunathan's hypothesis[3] for the α–C–H bond breaking process, states that the α-C–H bond must be perpendicular to the extended π system in order to optimize orbital interactions.

[1] D. E. Metzler and E. E. Snell, *J. Am. Chem. Soc.*, 1952, **74**, 979.
[2] Y. Murakami, H. Kondo, and A. E. Martell, *J. Am. Chem. Soc.*, 1973, **95**, 7138.
[3] H. C. Dunathan, *Proc. Natl. Acad. Sci. USA*, 1966, **55**, 712.