Synthesis, Spectral and Structural Studies on Metal Complexes of Schiff Bases involving Vitamin B_6 and Histamine†

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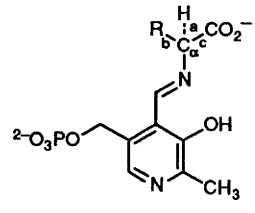
Six metal complexes of Schiff bases involving Vitamin B_6 and the decarboxylated amino acid histamine have been synthesised and characterized. Crystal structures have been determined for $[CuL^1(H_2O)Br]NO_3$ **1** (L^1 = pyridoxylidenehistamine) and $[Cu_2L^2_2(NO_3)_2]\cdot 6H_2O$ **2** (L^2 = 5′-phosphopyridoxylidenehistaminate). The crystal structure of complex **1** [space group $P\bar{1}$, $a = 8.161(2)$, $b = 10.368(2)$, $c = 11.110(2)$ Å, $\alpha = 105.18(1)$, $\beta = 102.12(1)$, $\gamma = 72.10(1)°$ and $Z = 2$; $R = 0.072$, $R' = 0.083$] consists of square-pyramidally co-ordinated copper with the tridentate Schiff base in the zwitterionic form, whereas in **2** [space group $P\bar{1}$, $a = 8.727(1)$, $b = 10.308(1)$, $c = 12.845(2)$ Å, $\alpha = 110.00(1)$, $\beta = 78.94(1)$, $\gamma = 114.35(1)°$ and $Z = 1$; $R = 0.035$, $R' = 0.034$] the copper has the same co-ordination geometry but the tetradentate Schiff-base ligand exists as a monoanion. The conformational parameters deduced from such structures are important for understanding the stereochemical aspects of Vitamin B_6-catalysed model reactions involving histidine.

All living organisms use pyridoxal (3-hydroxy-5-hydroxymethyl-2-methylpyridine-4-carbaldehyde) 5′-phosphate (PLP), the biologically functional derivative of Vitamin B_6, to synthesise, degrade and interconvert amino acids.[1] In the presence of the appropriate enzymes this cofactor plays a pivotal role in connecting carbon and nitrogen metabolism as well as providing an entry into the 'one-carbon pool' and catalysing the formation of biogenic amines.[1] All these reactions proceed through a Schiff base of PLP and amino acid.[2]

The mechanisms proposed for pyridoxal catalysis have mostly been derived from studies on model systems utilizing amino acid–pyridoxal and related Schiff bases and their metal complexes.[3] These reactions involve cleavage of one of the bonds to the amino acid α-carbon atom in the Schiff base **I**. While cleavage at a leads to racemization, transamination or β elimination, cleavage at b and c results in C_α–C_β bond cleavage and decarboxylation respectively. As first suggested by Dunathan,[4] ready cleavage of a bond to the amino acid α-carbon atom can be accomplished by orienting that bond orthogonal to the plane of the extended π system in order to optimize σ–π overlap. This stereoelectronic requirement enables pyridoxal-dependent enzymes to achieve reaction specificity and to enhance reaction rates by appropriate conformational orientation of the bond to be cleaved (or formed).[3c] Metal ions, in general, promote these reactions by maintaining the planarity of the conjugated system and by acting as 'superacids' drawing electrons away from the C_α–H bond through binding to the aldimine nitrogen.[5]

One of the important reactions, namely decarboxylation in model systems, is inhibited in binary complexes due to co-ordination of the carboxylate group of the amino acid to the metal ion.[6] This interaction draws the carboxylate group towards the plane of the extended π system and renders its orientation unfavourable for the reaction to occur. Martell[7] suggested that this difficulty could be overcome by using a ternary ligand, which by chelation to the metal prevents carboxylate co-ordination. Earlier attempts to prepare ternary Schiff-base complexes, however, were unsuccessful and further



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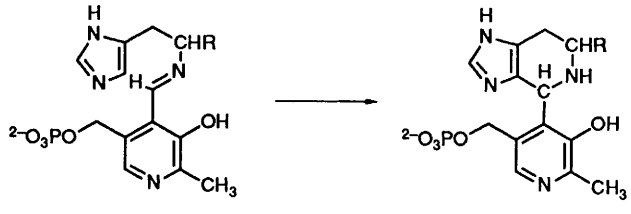

R = H (Histamine)
R = CO_2H (Histidine)

Cyclized Schiff base

Scheme 1

resulted in the unexpected oxidation of the Vitamin B_6 moiety.[8]

As an alternate step towards this end we have employed the decarboxylated amino acid histamine (1*H*-imidazole-4-ethanimine) to study the stereochemical aspects of these reactions. The pyridoxal (PL)–histidine– or PL–histamine–metal ion system is also of interest because metal ions like Cu^{2+} and Zn^{2+} are known to inhibit cyclization reactions between PL and histidine or histamine[9] (Scheme 1) which are believed to be detrimental to the functioning of Vitamin B_6-dependent enzymes. Here we report the synthesis and spectroscopic characterization of Schiff-base complexes of Zn, Cd and Cu from histamine with PL and PLP and the X-ray structures of $[CuL^1(H_2O)Br]NO_3$ **1** (L^1 = pyridoxylidenehistamine) and $[Cu_2L^2_2(NO_3)_2]\cdot 6H_2O$ **2** (L^2 = 5′-phosphopyridoxylidenehistaminate). The X-ray structure of $[Cu(L^1)Cl_2]$ **3** has been briefly reported by Aoki and Yamazaki[10] and we compare the present structures with this complex. In view of the absence of reports on ternary Schiff-

† *Supplementary data available:* see Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1991, Issue 1, pp. xviii–xxii.

Table 1 Summary of crystal data and intensity collection parameters[a]

Complex	1	2
Formula	$C_{13}H_{18}BrCuN_5O_6$	$C_{26}H_{44}Cu_2N_{10}O_{22}P_2$
M	483.54	1037.08
a/Å	8.161(2)	8.727(1)
b/Å	10.368(2)	10.308(1)
c/Å	11.110(2)	12.845(2)
α/°	105.18(1)	110.00(1)
β/°	102.12(1)	78.94(1)
γ/°	72.10(1)	114.35(1)
U/Å^3	845.8	987.6
Z	2	1
$F(000)$	486	534
D_c/g cm^{-3}	1.878	1.744
D_m/g cm^{-3} [b]	1.86	1.74
μ(Mo-Kα)/cm^{-1}	36.22	12.47
Transmission coefficients	0.79–1.01[c]	—
Colour	Green	Dark green
Crystal size (mm)	0.08 × 0.10 × 0.25	0.10 × 0.19 × 0.26
$2\theta_{max}$/°	50	52
Octant measured	$\pm h, \pm k, +l$	$\pm h, \pm k, \pm l$
No. of reflections measured	3259	7737
No. of unique reflections	2218 [$I > 2.0\sigma(I)$]	3764 [$I > 1.5\sigma(I)$]
R_{int}	0.043	0.035
No. refined parameters	291	368
Weighting scheme	$[\sigma^2(F_o) + 0.002\,144F_o^2]^{-1}$	$[\sigma^2(F_o) + 0.000F_o^2]^{-1}$
R[d]	0.072	0.035
R'[e]	0.083	0.034

[a] Details in common: crystal system, triclinic; space group $P\bar{1}$; CAD4 diffractometer; scan type ω–2θ; λ(Mo-Kα) 0.7107 Å; 294 K; maximum shift/e.s.d. <0.05. [b] By flotation in a mixture of $CHCl_3$ and $CHBr_3$. [c] Normalized to an average of unity. [d] $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [e] $R' = [\Sigma w(F_o - |F_c|)^2/\Sigma wF_o^2]^{\frac{1}{2}}$.

base metal complexes involving Vitamin B_6, attempts were also made to prepare ternary complexes involving histamine.

Copper and zinc are well known for their catalytic properties in these systems,[11] whereas Cd was selected because of its chemical similarity with zinc. The structures reported here give important conformational parameters that provide a basis for the understanding of stereochemical aspects of Vitamin B_6 model reactions involving histidine. The present study, for the first time employing related systems, provides a unique opportunity to compare the effects of PL and PLP moieties in these reactions. Since histidine is a frequently found metal-binding site in biological systems[12] and is involved in copper(II) transport in blood,[13] this study could throw some light on their mode of function.

Experimental

The compounds PL·HCl, histamine bis(hydrochloride) and PLP were purchased from Sigma Chemical Company and used as such. The salts $Cd(O_2CMe)_2{\cdot}2H_2O$, $Zn(O_2CMe)_2{\cdot}2H_2O$ and $Cu(NO_3)_2{\cdot}H_2O$ were from BDH India.

Electronic spectra were recorded using a Hitachi model U3400 spectrophotomer, infrared spectra with a Perkin-Elmer spectrometer using Nujol mulls in the 4000–400 cm^{-1} range and ^{1}H NMR spectra using a Bruker WH270 FT spectrometer operating at 270 MHz in CD_3SOCD_3 with $SiMe_4$ as internal standard. The elemental analysis was performed on a Perkin-Elmer 240 elemental analyser.

Preparation of Complexes.—In all preparations the Schiff-base ligand was first prepared by the following procedure. Equimolar amounts of PL·HCl or PLP and histamine bis(hydrochloride) were taken in water–methanol (1:1 v/v). This solution was then treated with 0.1 mol dm^{-3} NaOH to a final pH of ≈5.0. Part of the solution was tested for Schiff-base formation by monitoring the band at around 400 nm.[14] The Schiff-base solution was immediately treated with an equivalent amount of metal salt solution to avoid cyclization. The changes in the electronic spectra indicated complex formation. The resultant solution was concentrated on a water-bath and the complex was precipitated using dilute NH_3. The copper–PL–histamine complex was treated with 1 equivalent of NMe_4Br in an attempt to bring NMe_4^+ inside the crystal to vary the charge on the Schiff-base ligand.* However this attempt was unsuccessful. Single crystals of the complex suitable for X-ray analysis were obtained by slow evaporation after a number of trials. However, the Cu–PLP–histamine complex proved easier to crystallize.

These complexes could also be prepared by treating the histamine solution with the metal–Vitamin B_6 complex with stirring. The final pH had to be brought to nearly 5.0 by addition of 0.1 mol dm^{-3} NaOH. The copper complexes were treated with 2,2′-bipyridyl and imidazole in attempts to prepare ternary complexes.

Crystallography.—The lattice parameters were determined by least-squares refinement of the angular settings of 25 reflections in the range θ 7.0–17.7 for complex **1** and 19 reflections in the range θ 11.0–16.0 for **2**. Details of the data collection and processing are presented in Table 1. The data for complex **1** were corrected for Lorentz, polarization and absorption effects,[15] while no absorption correction was applied for complex **2**.

Solution and refinement of the structures. The structures were solved by conventional Patterson and Fourier techniques and refined by full-matrix least-squares treatment. The hydrogen atoms were located from difference electron-density maps and their positions and isotropic thermal parameters refined in the last few cycles. Even the hydrogens of the lattice water could be

* The charge on the Schiff-base ligand, in particular the protonation at the pyridine nitrogen, has been considered to be very crucial for *in vitro* reactions of Vitamin B_6. The customary way of changing the pH to vary the protonation states cannot be employed in these systems because an increase in pH favours cyclization.[9b]

Table 2 Fractional atomic coordinates ($\times 10^4$) for complex **1** with estimated standard deviations (e.s.d.s) in parentheses

Atom	*x*	*y*	*z*
Cu	1 282(1)	7 047(1)	1 733(1)
O(W)	3 089(9)	5 764(7)	2 727(7)
N(1)	−2 900(11)	10 266(9)	5 009(9)
C(1)	−1 582(12)	9 124(10)	4 686(9)
C(2)	−1 103(11)	8 844(9)	3 480(9)
C(3)	−2 100(12)	9 652(9)	2 613(9)
C(4)	−3 508(12)	10 802(10)	3 001(10)
C(5)	−3 828(13)	11 094(10)	4 219(9)
C(6)	−688(15)	8 275(12)	5 639(10)
C(7)	−4 553(15)	11 760(12)	2 135(11)
C(8)	−1 736(12)	9 370(9)	1 339(9)
O(1)	231(9)	7 785(7)	3 230(6)
O(2)	−3 628(11)	12 551(8)	1 838(8)
N(2)	−513(10)	8 384(8)	852(7)
C(9)	−382(13)	8 298(9)	−485(9)
C(10)	−569(15)	6 885(11)	−1 298(9)
C(11)	965(13)	5 731(10)	−1 052(9)
C(12)	1 751(16)	4 635(12)	−1 851(9)
N(3)	3 146(14)	3 916(9)	−1 185(10)
C(13)	3 236(13)	4 568(10)	31(10)
N(4)	1 884(11)	5 707(8)	156(8)
Br	3 536(2)	8 728(1)	2 056(1)
N(5)	3 148(8)	4 683(6)	5 316(6)
O(3)	3 770(11)	3 749(8)	5 901(7)
O(4)	2 309(14)	4 413(10)	4 227(8)
O(5)	3 322(12)	5 793(10)	5 697(8)

Table 3 Fractional atomic coordinates ($\times 10^5$ for Cu, $\times 10^4$ for the rest) for complex **2** with e.s.d.s in parentheses

Atom	*x*	*y*	*z*
Cu	1 240(3)	46 750(3)	24 916(2)
N(1)	3 803(2)	6 217(2)	5 845(2)
C(1)	3 339(3)	6 560(2)	5 073(2)
C(2)	2 137(3)	5 419(2)	4 314(2)
C(3)	1 526(3)	3 954(2)	4 394(2)
C(4)	2 074(3)	3 676(2)	5 240(2)
C(5)	3 199(3)	4 835(3)	5 950(2)
C(6)	4 092(3)	8 129(3)	5 020(2)
C(7)	1 473(3)	2 144(2)	5 370(2)
C(8)	313(3)	2 719(2)	3 634(2)
O(1)	1 705(2)	5 814(2)	3 600(1)
P	−934(1)	1 821(1)	6 942(1)
O(2)	−299(2)	1 589(2)	5 658(1)
O(3)	−2 790(2)	1 037(2)	6 943(1)
O(4)	−149(2)	955(2)	7 331(2)
O(5)	203(2)	6 562(2)	2 410(1)
N(2)	−386(2)	2 809(2)	2 884(2)
C(9)	−1 648(3)	1 391(3)	2 270(2)
C(10)	−1 385(4)	1 127(3)	1 026(2)
C(11)	−1 854(3)	2 141(3)	682(2)
C(12)	−2 819(4)	1 863(3)	−138(2)
N(3)	−2 857(3)	3 202(3)	−82(2)
C(13)	−1 962(3)	4 242(3)	761(2)
N(4)	−1 335(2)	3 643(2)	1 252(2)
N(5)	3 308(3)	3 601(3)	1 433(2)
O(6)	2 518(3)	4 082(2)	1 043(2)
O(7)	4 308(3)	4 462(3)	2 159(2)
O(8)	3 075(3)	2 266(2)	1 106(2)
O(W1)	5 836(3)	8 375(2)	7 301(2)
O(W2)	−2 047(3)	7 666(2)	1 218(2)
O(W3)	4 758(3)	7 380(2)	1 979(2)

located for complex **2**. The shifts in parameters for both compounds in the last cycle were less than 0.05 σ. Final residuals *R* and *R'* are 0.072 and 0.083 for complex **1** and 0.035 and 0.034 for **2**. The higher *R* values for **1** is due to the poor quality of the crystals, repeated attempts to get better quality crystals being unsuccessful. The final difference electron-density map for complex **1** revealed no significant electron density except for a few peaks of 0.9e Å^{-3} along some bonds. No peak higher than 0.3e Å^{-3} was observed in the map for complex **2**.

Table 4 Bond distances (Å) and angles (°) with e.s.d.s in parentheses

Complex **1**			
Cu–O(W)	2.011(7)	Cu–N(4)	1.977(8)
Cu–O(1)	1.902(7)	Cu–Br	2.813(2)
Cu–N(2)	1.971(8)		
O(W)–Cu–O(1)	85.6(3)	N(2)–Cu–Br	88.2(2)
O(W)–Cu–N(2)	176.6(3)	N(4)–Cu–Br	101.4(2)
O(W)–Cu–N(4)	89.6(3)	O(1)–Cu–N(4)	156.5(3)
O(W)–Cu–Br	90.9(2)	O(1)–Cu–Br	101.7(2)
O(1)–Cu–N(2)	91.4(3)	N(2)–Cu–N(4)	93.8(3)
Complex **2**			
Cu–O(1)	1.893(2)	Cu–N(4)	1.947(2)
Cu–O(5')	1.956(2)	Cu–O(6)	2.643(2)
Cu–N(2)	2.006(2)		
O(1)–Cu–O(5')	87.3(1)	O(5')–Cu–N(4)	88.7(1)
O(1)–Cu–N(2)	91.5(1)	O(5')–Cu–O(6)	105.2(1)
O(1)–Cu–N(4)	173.7(1)	N(2)–Cu–N(4)	93.6(1)
O(1)–Cu–O(6)	90.3(1)	N(2)–Cu–O(6)	89.0(1)
O(5')–Cu–N(2)	165.8(1)	N(4)–Cu–O(6)	86.0(1)

Major calculations were performed on a DEC1090 computer using the SHELX 76 system of programs[16] for Fourier and least-squares calculations and ORTEP II[17] and PLUTO 78[18] for diagrams. The scattering factors for H, C, N, O, P and Br atoms were used as available in the SHELX programs, and for Cu they were taken from ref. 19 (anomalous corrections applied). The final atomic coordinates for the compounds are given in Tables 2 and 3, selected bond distances and angles in Table 4.

Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom coordinates, thermal parameters, and remaining bond lengths and angles.

Results and Discussion

Spectral Studies.—The bands around 400 nm in the electronic spectra were used for the identification of the complex formation in solution. The IR spectra (Table 5) of all the complexes show a strong band at 1630–1640 cm^{-1} which is related to the stretching mode of the imine C=N bond.[9b] The complex [Cd(L^1 − H)] where L^1 − H is the monodeprotonated form of L^1, showed a very weak band around 1665 cm^{-1} indicating the presence of the cyclized tetrahydropyrido-[3,4-*d*]imidazole complex (Scheme 1) as an impurity.

In the ^{1}H NMR spectra (Table 5) of the zinc and cadmium complexes the azomethine proton signal is observed near δ 8.8.[20] The absence of a proton signal near δ 6 for both these complexes indicates the absence of a saturated 4-CH group characteristic of the cyclized product. The imidazole 5-CH signal was observed for these complexes at δ 7.1, confirming the absence of cyclization.

Attempts to prepare ternary Schiff-base complexes involving copper were unsuccessful. Spectral and preliminary X-ray studies showed that use of 2,2'-bipyridine results in the oxidation of PL, whereas similar attempts with imidazole resulted in its absence in the product.

X-Ray Structural Studies.—The molecular structures with atom labelling schemes for complexes **1** and complex **2** are shown in Figs. 1 and 2, respectively.

Complex **1**. As in complex **3** the tridentate Schiff-base ligand, existing as a zwitterion, is co-ordinated to the metal through phenolic oxygen, imino nitrogen and the imidazole nitrogen. The two co-ordinated chlorides in **3**, however, are replaced by a

water molecule in the basal plane and a bromide ion in the axial position resulting in a square-pyramidal co-ordination for copper. The bond lengths in the basal plane are in the range 1.902(7)–2.011(7) Å, whereas the axial bond [2.813(2) Å] is much longer. They are in agreement with values reported for similar complexes.[21] The *cis* bond angles in the basal plane range from 85.6(3) to 93.8(3)°. The four basal atoms show significant tetrahedral deviation [−0.216 to 0.228(9) Å]. The rings A, B and D (Fig. 1) are almost planar. The largest deviation from the best plane is 0.03(1), 0.040(8) and 0.004(11) Å for A, B and D, respectively. The chelate ring C is much less planar, the largest deviation from the best plane being 0.42(1) Å for C(9). All these features are similar to those of complex **3**. The torsion angles and asymmetry parameters[22] indicate that this ring assumes a conformation in between sofa and half-chair, whereas in **3** it is in the half-chair conformation.

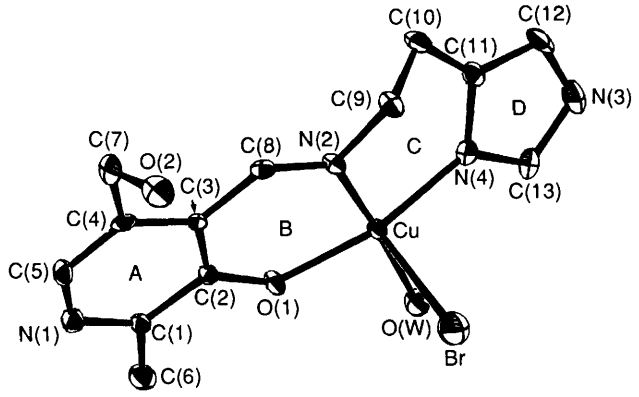

Fig. 1 Molecular structure of complex **1** with the atom labelling scheme, showing 30% probability ellipsoids

Complex **2**. Here two tetradentate Schiff-base ligands act as bridges between two coppers resulting in the formation of a dimeric structure. One half of the dimer is related to the other half (primed labels, Fig. 2) by a crystallographic centre of symmetry. The Schiff-base ligands are tridentate to one copper and monodentate to the other. As in complex **1** the geometry around the coppers is square pyramidal. The basal sites for each copper are occupied by a phenolic oxygen, imino nitrogen and

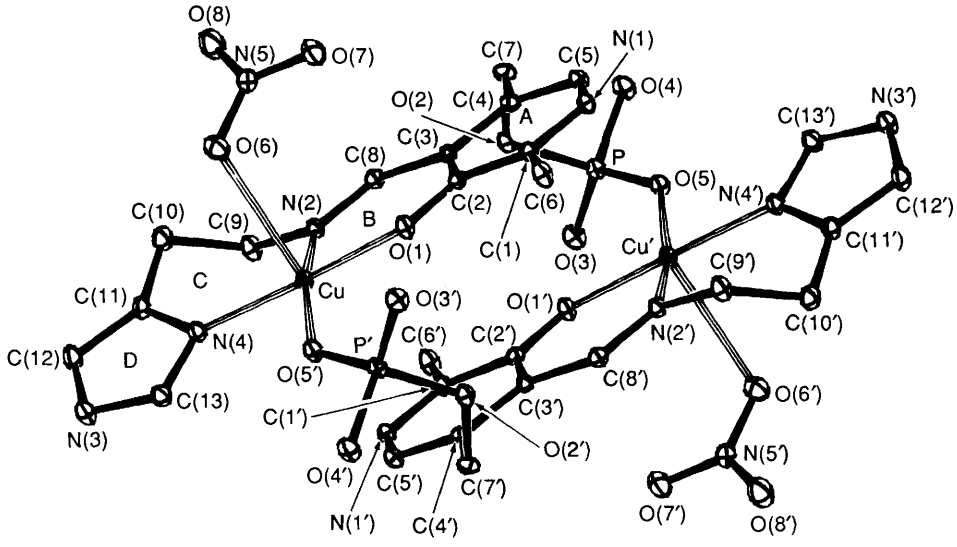

Fig. 2 Molecular structure of complex **2** with the atom labelling scheme, showing 15% probability ellipsoids. The atoms with primed labels are related to the unprimed ones by the crystallographic centre of symmetry

Table 5 Yields, analytical and spectroscopic data for the complexes

Compound	Colour	Yield (%)	Analysis[a] (%) C	H	N	IR (cm^{-1})[b]	^1H NMR (δ)[c]
$[Zn(L^1-H)(O_2CMe)]\cdot 2H_2O$	Yellow	69	43.5 (42.80)	4.9 (5.45)	13.8 (13.30)	3300(br) (OH), 1630s (C=N), 1500m (ring), 1305s (OPh)	8.7 (CH=N, s), 7.84 (imidazole 2-CH, s), 7.41 (PL 6-H, s), 7.17 (imidazole 5-CH, s), 4.7 (PL 5-CH_2, s), 3.77 (CH_2N=, br), 2.51 (PL 2-CH_3, s),[d] 2.10 (O_2CMe, s)
$[Cd(L^1-H)Cl]\cdot 2H_2O$	Yellow	61	35.8 (35.15)	5.1 (4.50)	13.2 (12.60)	3240s(br) (OH), (NH), 1630s (C=N), 1500s (ring), 1300s (OPh)	8.83 (CH=N, s), 7.82 (imidazole 2-CH, s), 7.31 (PL 6-H, s), 7.12 imidazole 5-CH, s) 4.61 (PL 5-CH_2, s), 3.75 (CH_2N=, m) 2.51 (PL 2-CH_3, s)[d]
$[CuL^1(H_2O)Br]NO_3$	Green	79	32.1 (32.25)	3.5 (3.70)	14.5 (14.50)	1630s (C=N), 1505(sh) (ring), 1300(br) (OPh)	
$[ZnL^2(O_2CMe)]\cdot 3H_2O$	Yellow	76	35.2 (34.80)	5.3 (4.85)	11.4 (10.80)	1640s (C=N), 1510w (ring), 1300w (OPh)	
$[CdL^2Cl]\cdot 3H_2O$	Brownish yellow	65	29.3 (28.85)	4.9 (4.05)	10.9 (10.35)	1645s (C=N), 1510(sh) (ring), 1310w (OPh)	
$[Cu_2L^2_2(NO_3)_2]\cdot 6H_2O$	Dark green	84	30.1 (30.10)	4.2 (4.25)	13.4 (13.50)	3300(br) (OH), 3150w (imidazole CH), 1620s (C=N), 1513w (ring)	

[a] Calculated values are given in parentheses. [b] s = Strong, br = broad, w = weak, sh = shoulder, m = medium. [c] The PLP complexes were insoluble in most solvents. In CD_3SOCD_3 using $SiMe_4$ as standard. s = singlet, m = multiplet and br = broad. [d] Obscured by solvent absorption.

Table 6 Selected structural parameters (lengths in Å, angles in °) for complexes **1–3**

	1	2	3
C(1)–C(6)	1.483(15)	1.494(3)	1.499(9)
C(2)–O(1)	1.304(12)	1.290(3)	1.283(7)
Cu–O(1)	1.902(7)	1.893(2)	1.922(5)
Cu–N(2)	1.971(8)	2.006(2)	2.031(5)
C(3)–C(8)	1.444(13)	1.460(3)	1.449(9)
C(8)–N(2)	1.282(12)	1.281(3)	1.271(8)
N(2)–C(9)	1.489(12)	1.480(3)	1.488(9)
H(8)–C(8)–N(2)–C(9)	−11(16)	4(2)	−3(3)
*X**	−0.66(10)	−0.87(3)	−0.80(5)
C(8)–N(2)–C(9)–H(9)	118(7)	−106(3)	−109(6)
C(9)–H(9)	0.79(10)	0.95(3)	0.92(6)
τ (%)	33.5	13.1	4.3

* *X* = Deviation (Å) of H(9) from the plane defined by atoms H(8), C(8), N(2) and C(9).

an imidazole nitrogen of one of the Schiff-base ligands and a phosphate oxygen from the other, while the axial site is occupied by a nitrate oxygen.

In contrast to complexes **1** and **3**, in this complex the Schiff-base ligand exists as a monoanion with the pyridine nitrogen protonated and the phenolic oxygen and one of the phosphate oxygens deprotonated.

The basal bond lengths are in the range 1.893–2.006(2) Å similar to those in complexes **1** and **3**, whereas the axial bond length is 2.643(2) Å. The *cis* bond angles in the plane range from 87.3 to 93.6(1)° and the *trans* angles are 173.7(1) and 165.8(1)°. The four basal atoms show significant tetrahedral deviations [−0.166 to 0.182(2) Å] from the least-squares plane through these atoms. As in complex **3** the six-membered chelate ring (C) in this complex assumes a half-chair conformation.

Comparison of the structures. The X-ray structures of complexes **1** and **2** show that, as in **3**, imidazole co-ordination inhibits the cyclization reaction. Because of the importance of these complexes in Vitamin B_6-catalysed reactions it is instructive to make a detailed comparison of their structures. Some relevant parameters for complexes **1–3** are given in Table 6. A perusal of the table shows that most parameters are unaffected by change in the Vitamin B_6 moiety. The changes in Cu–N(2) distance could be explained by invoking a decrease in charge concentration on the metal as we go from **1** and **3**. It is noteworthy that the percentage of trigonal distortion of the square-pyramidal geometry, τ,[23] decreases with increasing charge on the metal ion. The present study of closely similar systems gives structural support for the earlier proposal[24] that in non-enzymatic reactions there is no need for the entire coenzyme molecule, but for its 4-formyl-3-hydroxypyridine part. Furthermore, complex **2** gives very accurate structural parameters for these type of complexes.*

Comparison with Other PLP–Metal Complexes.—There are only four PLP–Schiff base–metal (Cu^{II}) complexes in the literature, involving the amino acids glycine,[21a] L-β-phenylalanine,[25a] DL-tyrosine[25b] and 1-aminocyclopropanecarboxylic acid.[25c] In contrast to the present structure, the Schiff-base ligands in these complexes exist as dianions with the additional negative charge on the carboxylate. The present complex **2** gives the first structural report on a PLP–Schiff base complex involving a decarboxylated amino acid. The dimeric nature shown by the present complex makes it unique among this group, other complexes having polymeric structures due to the axial phosphate–metal bonding. It is interesting that the co-ordination mode of phosphate and the dihedral angle, C(7)–O(2)–P–O(5), determine the nature of the complex. In the present complex phosphate oxygen occupies the equatorial position. Furthermore the dihedral angle is 54.1°, whereas in other complexes this is approximately 180° (178, 180, 177 and 198° for the above four complexes respectively).

Conclusion

The absence of cyclization in these systems is in agreement with the earlier report that the use of metal ions inhibits cyclization reactions.† In addition to Cu and Zn, Cd also shows similar effects. The absence of cyclization in these systems is confirmed by electronic, infrared and NMR spectroscopic techniques.

The close values of corresponding structural parameters obtained in the present study of related systems confirms the earlier proposal that in model systems pyridoxal and pyridoxal phosphate have similar reactivities. As discussed in the Introduction, electronic factors favour the elimination of a group oriented perpendicular to the pyridoxal π system. The structural parameters reported here show that the position of the hydrogen atom H(9), attached to the α-carbon, C(9), is perpendicular to the π system (Table 6). In histamine-like bound histidine residues, where the carboxyl group is expected to occupy the position H(9), it is almost perpendicular to the pyridoxal π system. Therefore, this conformer is expected to decarboxylate easily. The C_α–H bond cleavage can also lead to transamination. On the other hand, the co-ordination of imidazole to copper makes β elimination, involving C(10)–C(11) bond cleavage (Figs. 1 and 2), unfavourable.

Complex **2**, for the first time, gives structural parameters for a PLP complex involving a decarboxylated amino acid. It is interesting that, in contrast to the polymeric nature shown by PLP–amino acid complexes, the present complex exists as a dimer. The dimeric nature makes one face of the pyridoxal π system alone susceptible to reactions. In most of the enzymes, except the racemases found in bacteria, only one face of the enzyme is open to attack.[27]

* The Schiff bases involving Vitamin B_6 are difficult to crystallize, and most are not very stable, thus rendering accurate structure determination difficult.

† There is only one report on a complex involving a cyclized ligand.[26] This complex was prepared by treating the metal salt solution with the cyclized ligand.

References

1 D. E. Metzler, M. Ikawa and E. E. Snell, *J. Am. Chem. Soc.*, 1952, **76**, 648; D. E. Metzler, *Adv. Enzymol.*, 1979, **50**, 1; J. C. Vederas and H. G. Floss, *Acc. Chem. Res.*, 1980, **13**, 455.
2 V. M. Shanbag and A. E. Martell, *Inorg. Chem.*, 1980, **29**, 1023.
3 (*a*) *Pyridoxal Catalysis: Enzymes and Model Systems*, eds. E. E. Snell, A. E. Braunstein, E. S. Severin and Yu. M. Torchinsky, Interscience, New York, 1968; (*b*) C. M. Metzler, A. Cahill and D. E. Metzler, *J. Am. Chem. Soc.*, 1980, **102**, 6075; (*c*) L. Casella, M. Gullotti and G. Pacchioni, *J. Am. Chem. Soc.*, 1982, **104**, 2386 and refs. therein.
4 H. C. Dunathan, *Adv. Enzymol.*, 1971, **35**, 79.
5 S. E. Hamilton, S. R. Mason and B. Zerner, *J. Chem. Ed.*, 1984, **61**, 811.
6 A. E. Martell, *Acc. Chem. Res.*, 1989, **22**, 115.
7 A. E. Martell, in *Metal Ions in Biological Systems*, ed. H. Sigel, Marcel Dekker, New York, 1973, vol. 2, pp. 207–268.
8 S. P. S. Rao, H. Manohar, K. Aoki, H. Yamazaki and R. Bau, *J. Chem. Soc., Chem. Commun.*, 1986, 4; S. P. S. Rao, H. Manohar, K. Aoki and H. Yamazaki, *J. Chem. Soc., Dalton Trans.*, 1987, 1009.
9 (*a*) D. Heyl, S. A. Harris and K. Folkers, *J. Am. Chem. Soc.*, 1948, **70**, 3429; (*b*) L. Casella and M. Gullotti, *J. Am. Chem. Soc.*, 1981, **103**, 6338.
10 K. Aoki and H. Yamazaki, *J. Chem. Soc., Chem. Commun.*, 1984, 410.
11 D. E. Metzler and E. E. Snell, *J. Am. Chem. Soc.*, 1952, **74**, 979.
12 R. J. Sundberg and R. B. Martin, *Chem. Rev.*, 1974, **74**, 471; F. Schneider, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 583.
13 A. S. Brill, *Transition Metals in Biochemistry*, Springer, New York, 1977, ch. 2; *Inorganic Biochemistry*, The Chemical Society, London, 1979, vol. 1.
14 L. Casella and M. Gullotti, *Inorg. Chem.*, 1986, **25**, 1293.
15 A. T. C. North, C. C. Phillips and F. S. Mathews, *Acta Crystallogr., Sect. A*, 1968, **24**, 351.

16 G. M. Sheldrick, SHELX 76, Program for Crystal Structure Determinations, University of Cambridge, Cambridge, 1976.
17 C. K. Johnson, ORTEP II, Program for Thermal Ellipsoid Plotting, Oak Ridge National Laboratory, Oak Ridge, TN, 1976.
18 S. Motherwell and W. Clegg, PLUTO, Program for Drawing Crystal and Molecular Structures, University of Cambridge, Cambridge, 1978.
19 *International Tables for X-Ray Crystallography*, Kynoch Press, Birmingham, 1974, vol. 4.
20 G. N.Weinstein, M. J. O'Connor and R. H. Holm, *Inorg. Chem.*, 1970, **9**, 2104; O. A. Gansow and R. H. Holm, *J. Am. Chem. Soc.*, 1969, **91**, 573.
21 (*a*) S. P. S. Rao, H. Manohar and R. Bau, *J. Chem. Soc., Dalton Trans.*, 1985, 2051; (*b*) T. Ishida, K.-I. Hatta, S. Yamashita, M. Doi and M. Inoue, *Chem. Pharm. Bull.*, 1986, **34**, 3553.
22 W. L. Duax, C. M. Weeks and D. C. Rohrer, *Top. Stereochem.*, 1976, **9**, 279.
23 B. J. Hathaway, in *Comprehensive Coordination Chemistry*, ed. G. F. Wilkinson, Pergamon, 1987, vol. 5, pp. 607–609.
24 I. B. Black and J. Areaload, *J. Biol. Chem.*, 1969, **244**, 6124; G. Scholz and F. Kwok, *J. Biol. Chem.*, 1989, **264**, 4318.
25 (*a*) G. A. Bentley, J. M. Waters and T. N. Waters, *Chem. Commun.*, 1968, 988; I. I. Mathews and H. Manohar, *Polyhedron*, in the press; (*b*) I. I. Mathews, P. A. Joy, S. Vasudevan and H. Manohar, *Inorg. Chem.*, 1991, **30**, 2181; (*c*) N. Hu, K. Aoki and H. Yamazaki, personal communication.
26 H. M. Dawes and T. N. Waters, *J. Chem. Soc., Chem. Commun.*, 1982, 1390.
27 H. G. Floss and J. C. Vederas, *Acc. Chem. Res.*, 1980, **13**, 455.

Received 7th February 1991; *Paper* 1/00583I