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Registry No. *trans*-[Cr^{II}(nic-*N*)$_2$(H_2O)$_4$], 89230-21-7; *trans*-[Zn^{II}(nic-*N*)$_2$(H_2O)$_4$], 34383-87-4.

Supplementary Material Available: Listings of anisotropic parameters for *trans*-[Cr^{II}(nic-*N*)$_2$(H_2O)$_4$] and *trans*-[Zn^{II}(nic-*N*)$_2$(H_2O)$_4$] (2 pages). Ordering information is given on any current masthead page.

Contribution from the Department of Chemistry, Thimann Laboratories, University of California, Santa Cruz, California 95064, and Department of Chemistry and Biochemistry, University of Windsor, Windsor, Ontario, Canada N9B 3P4

Synthetic Analogue Approach to Metallobleomycins. 1. Syntheses, Structures, and Properties of the Copper Complexes of Two Peptides Related to Bleomycins

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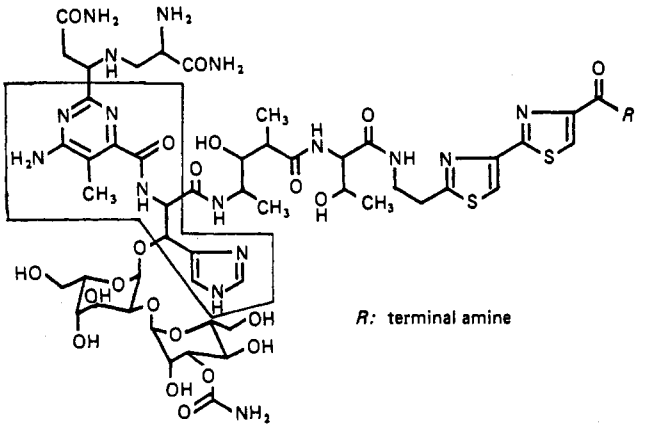
As part of a synthetic analogue approach to metallobleomycins, copper complexes of two peptides, PypepH and PmpepH, resembling fragments of the metal-chelating section of bleomycins (BLM) have been isolated. The structures of two synthetic analogues have been determined by X-ray crystallography. [Cu(Pypep)(CH_3COO)]$_2$·1.46H_2O (**4**) crystallizes in the monoclinic space group $C2/c$ with a = 17.360 (2) Å, b = 14.207 (4) Å, c = 13.418 (3) Å, β = 112.61 (1)°, V = 3055 (1) Å^3, and Z = 4. The structure of **4** was refined to R = 5.15% on the basis of 1594 unique data ($F_o^2 > 3\sigma(F_o^2)$). The acetate ions in **4** bridge between the two copper centers through one oxygen atom. The coordination geometry around copper is approximately square pyramidal. [Cu(Pmpep)(CH_3COO)(H_2O)] (**5**) crystallizes in the space group $P2_1/c$ with a = 7.130 (2) Å, b = 10.918 (3) Å, c = 21.686 (7) Å, β = 105.59 (2)°, V = 1626.2 (9) Å^3, and Z = 4. On the basis of 1593 unique data, the structure of **5** was refined to R = 4.32%. The acetate ion in **5** is bidentate, and the sixth coordination site is occupied by the water molecule. Due to the small "bite" of the acetate group, the coordination geometry around copper is highly distorted. Steric crowding of substituents on the pyrimidine ring in PmpepH does not allow formation of a dimeric copper complex. In methanol and DMF solutions, both **4** and **5** give rise to a monomeric tetragonal Cu(II) EPR spectrum. The g and $A_\parallel$ values for **4** are remarkably similar to those of Cu(II)-BLM. Similarities among various spectroscopic properties of **4**, **5**, and Cu(II)-BLM raise questions regarding the structure of the coordination sphere of copper in Cu(II)-BLM proposed on the basis of preliminary structural data on the P3A peptide complex of copper.

Introduction

The activation of bleomycins (BLM), a family of glycopeptide antibiotics (**1**), in the presence of metal ions like Fe^{2+} and Cu^{2+} and molecular oxygen and subsequent catalytic cleavage of double-stranded DNA have drawn much attention in recent years.[1-4] A metal ion cofactor is now believed to be a requirement



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for the drug action,[5] and this realization has initiated active research in the coordination chemistry of BLM[1,6] and the interaction of BLM-metal chelates with DNA.[7] The coordination centers around Cu(II) in Cu(II)-BLM have been assigned on the basis of the preliminary X-ray crystallographic data on a Cu(II) complex of P-3A, the nitrogen-containing fragment of BLM.[8] Certain anomalies, however, still exist. For example, the absorption spectrum, EPR parameters, and half-wave potential of Cu(II)-P-3A are distinctly different from those of Cu(II)-BLM.[9] Also, P-3A does not contain a CH_3 group on the pyrimidine ring next to the peptide junction which might interfere (CPK model studies) with the participation of the pyrimidine ring nitrogen in the coordination sphere of the central metal atom.

Studies on metal complexes of BLM analogues have so far been scarce and retricted to measurements in solutions where the metalated species were generated in situ and their spectral properties were compared with those of metallobleomycins (M-BLMs).[6d,9-11] The structural and chemical complexities of the

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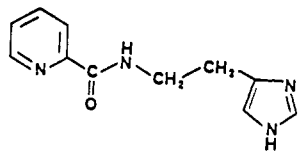
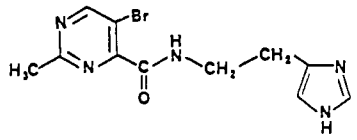
systems studied so far maintained ambiguity in the interpretations of the spectroscopic data, particularly in absence of any crystallographic information. Recently, we have initiated a "synthetic analogue approach"[12] to M–BLMs where we attempt to synthesize and structurally characterize metal complexes of smaller organic frameworks that resemble or consist of portions of the metal-chelating part of BLM. These tailored ligands of varying complexity are carefully designed such that the coordination spheres of the resultant complexes will match the proposed coordinations around M in M–BLMs. Our building-block approach will be extremely helpful in deciding the minimum structural requirements for the free-radical-forming metal centers in M–BLMs and the reaction conditions to synthesize and crystallize such species. Also, step-by-step construction of the metalated species and their structural characterization by crystallography will determine the role of various groups in BLM and other added components in the coordination chemistry of BLM.

In this paper, the syntheses, structures, and spectroscopic properties of copper complexes of two peptides resembling portions of BLM (boxed in **1**) are reported. The two peptides, *N*-(2-(4-imidazolyl)ethyl)pyridine-2-carboxamide (**2**) and *N*-(2-(4-imidazolyl)ethyl)-2-methyl-5-bromopyrimidine-4-carboxamide (**3**)



PypepH (**2**)



PmpepH (**3**)

will be abbreviated hereafter as PypepH and PmpepH, respectively (the dissociable H is the amide H). These peptides are the simplest fragments in our list of synthetic analogues and mimic three of the five proposed donor centers in Cu(II)–BLM. Both of the copper complexes, namely $[Cu(Pypep)(CH_3COO)]_2 \cdot 1.46H_2O$ (**4**) and $[Cu(Pmpep)(CH_3COO)(H_2O)]$ (**5**) contain acetate ion in their coordination sphere. The corresponding chloro and bromo species have also been synthesized and structurally characterized and will be reported in a subsequent paper.[13]

Experimental Section

Preparation of Compounds. Ethyl picolinate, mucobromic acid, acetamidine hydrochloride, and histamine (free base) were procured from Aldrich Chemical Co. and were used without further purification. Copper(II) acetate hydrate and copper(II) perchlorate hexahydrate were purchased from Mallinckrodt, Inc.

PypepH (2). A 6.79-g (45-mmol) amount of ethyl picolinate was mixed with 5.0 g (45 mmol) of histamine in 50 mL of benzene, and the mixture was refluxed for 18 h. After removal of solvent, the crude product was recrystallized from hot water to yield 7.78 g (80%) of white needles, mp 85 °C dec. ^1H NMR ($CDCl_3$, 300 MHz): δ 2.94 (t, J = 7.8 Hz, 2 H, CH_2), 3.72 (m, 2 H, CH_2), 6.84 (s, 1 H, Im), 7.34 (t, 1 H, py), 7.60 (s, 1 H, Im), 7.74 (t, 1 H, py), 7.88 (s, br, 1 H, CONH), 8.1 (d, 1 H, py), 8.45 (d, 1 H, py), 8.50 (t, 1 H, Im). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 26.83, 39.21, 116.51, 121.75, 125.94, 134.51, 134.91, 137.04, 147.86, 149.28, 164.42. MS: m/e 217 (M + 1), 216 (M). Selected IR bands (KBr pellet, cm^{-1}): 3240 (vs, br), 2900 (m), 1650 (ν_{CO}, vs), 1550 (vs), 1320 (m), 1205 (m), 1100 (m), 860 (s), 755 (s), 700 (vs), 630 (s), 520 (m). Electronic spectrum (λ_{max}, nm (ϵ_M), in methanol): 260 (5000), 215 (13 000). Anal. Calcd for $C_{11}H_{12}N_4O$: C, 61.10; H, 5.59; N, 25.91. Found: C, 60.81; H, 5.71; N, 25.73.

PmpepH (3). A 7.43-g (30-mmol) amount of ethyl 2-methyl-5-bromo-pyrimidinecarboxylate[14] was heated wtih 3.33 g (30 mmol) of histamine in benzene (60 mL) under reflux for 8 h. Removal of solvent and recrystallization of the crude product from hot water afforded 8.41 g (90%) of pale cream-colored needles, mp 141 °C dec. ^1H NMR ($CDCl_3$, 300 MHz): δ 2.70 (s, 3 H, Me), 2.97 (t, J = 7.4 Hz, 2 H, CH_2), 3.74 (m, 2 H, CH_2), 6.88 (s, 1 H, Im), 7.61 (s, 1 H, Im), 8.41 (t, br, 1 H, Im), 8.87 (s, 1 H, Pm). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 25.17, 27.01, 39.60, 114.80, 116.05, 134.97, 135.86, 153.38, 162.71, 165.95. MS: m/e 312, 310 (M + 1), 311, 309 (M). Selected IR bands (KBr pellet, cm^{-1}): 3525 (vs), 2740 (s, br), 1665 (ν_{CO}, vs), 1621 (s), 1427 (s), 1270 (s), 950 (s), 820 (s), 671 (s), 623 (s), 432 (m). Electronic spectrum (λ_{max}, nm (ϵ_M), in methanol): 273 (4200), 215 (16 000) nm. Anal. Calcd for $C_{11}H_{12}N_5OBr$: C, 42.59; H, 3.87; N, 22.59. Found: C, 42.51; H, 4.03; N, 22.71.

$[Cu(Pypep)(CH_3COO)]_2 \cdot 1.46H_2O$ (4). A solution of 200 mg (1 mmol) of copper acetate hydrate in 8 mL of water was slowly added with stirring to 216 mg (1 mmol) of PypepH in 10 mL of methanol. The resulting deep blue mixture was filtered to remove any suspended particles, and the filtrate was allowed to evaporate at room temperature until a volume of ~3 mL was left. At this stage 8 mL of acetonitrile was added, and the deep blue solution was stored in a stoppered flask at room temperature. Dark blue blocks appeared within 8 h. The crystals were collected by filtration, washed with 5 mL of cold acetonitrile, and dried in air: yield 284 mg (80%); mp 165–169 °C dec. Anal. Calcd for $C_{13}H_{15.46}N_4O_{3.73}Cu$: C, 44.46; H, 4.44; N, 15.97; Cu, 18.11. Found: C, 44.59; H, 4.51; N, 15.84; Cu, 18.04. Selected IR bands (KBr pellet, cm^{-1}): 3425 (s), 3160 (m), 2920 (s), 1585 (ν_{CO}, vs), 1395 (s), 1040 (m), 820 (s), 770 (m), 700 (m), 630 (m).

$[Cu(Pmpep)(CH_3COO)(H_2O)]$ (5). A 310-mg (1-mmol) amount of PmpepH in 6 mL of methanol was slowly added with stirring to a solution of 200 mg (1 mmol) of copper acetate hydrate in 8 mL of water. The resultant bluish green solution was allowed to stand at room temperature. Green blocks were deposited within 24 h. The crystals were collected by filtration, washed with 10 mL of cold water, and dried in air: yield 340 mg (75%); mp 182–185 °C (dec). Anal. Calcd for $C_{13}H_{16}N_5O_4BrCu$: C, 34.70; H, 3.59; N, 15.58; Cu, 14.13. Found: C, 34.48; H, 3.54; N, 15.61; Cu, 14.01. Selected IR bands (KBr pellet, cm^{-1}): 3230 (s, br), 2917 (m), 1620 (ν_{CO}, vs), 1543 (m), 1425 (s), 1221 (m), 1055 (m), 828 (s), 696 (m), 625 (m), 567 (m).

Self-Assembly Reactions. $[Cu(Pypep)(CH_3COO)]_2 \cdot 1.46H_2O$ (4). A solution of 370 mg (1 mmol) of copper perchlorate hexahydrate in 6 mL of methanol was slowly added to a stirred mixture of 216 mg (1 mmol) of PypepH in 6 mL of methanol and 272 mg (2 mmol) of sodium acetate trihydrate in 5 mL of water. The volume of the resulting deep blue solution was reduced to ~3 mL by slow evaporation at room temperature. Next 10 mL of acetonitrile was added, and the mixture was filtered. The filtrate was kept at 4 °C for 24 h. A 284-mg (80%) amount of dark blue blocks was isolated. Both IR and analytical data confirmed the identity of the product.

$[Cu(Pmpep)(CH_3COO)(H_2O)]$ (5). To an aqueous solution (6 mL) of 370 mg (1 mmol) of copper perchlorate hexahydrate was slowly added with stirring a mixture of 310 mg (1 mmol) of PmpepH in 8 mL of methanol and 272 mg (2 mmol) of sodium acetate trihydrate in 5 mL of water. The bluish green mixture was then stored in a stoppered flask at room temperature. Dark green blocks appeared within 20 h. The crystals were collected by filtration, washed with 10 mL of cold water, and dried in air: yield 360 mg (80%). The identity of the product was confirmed by IR spectroscopy and copper analysis.

X-ray Data Collection and Reduction. Deep blue blocks of $[Cu(Pypep)(CH_3COO)]_2 \cdot 1.46H_2O$ (**4**) were grown from ethanol/propionitrile solution. Dark green blocks of $[Cu(Pmpep)(CH_3COO)(H_2O)]$ (**5**) were obtained by slow evaporation of the reaction mixture in aqueous methanol. The crystals were sealed in glass capillaries before data collection. Diffraction experiments were performed on a four-cycle Syntex $P2_1$ diffractometer using either graphite-monochromatized or Nb-filtered Mo Kα radiation. The initial orientation matrices for both compounds **4** and **5** were obtained from 15 machine-centered reflections selected from

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(13) The chloro-bridged dimer $[Cu(Pypep)(Cl)(H_2O)]_2$ crystallizes in space group $P2_1/n$ with a = 10.134 (2) Å, b = 14.141 (4) Å, c = 9.198 (4) Å, β = 95.01 (3)°, and Z = 4. The structure has been refined to R = 2.99% by using 1581 unique data ($F_o^2 > 3\sigma(F_o^2)$). Selected bond distances are as follows: Cu–N(py) = 2.014 (3) Å; Cu–N(pep) = 1.972 (3) Å; Cu–N(Im) = 1.973 (3) Å; Cu–Cl1 = 2.319 (1) Å; Cu–Cl2 = 2.831 (1) Å; Cu–Cu = 3.693 (1) Å. In methanol glass, the complex exhibits a strong g = 2.085 EPR transition. A weak $\Delta M_S = \pm 2$ transition is also observed at g = 4.583. Magnetic susceptibility data in the temperature range 6–300 K yield $J = -2.32$ cm^{-1}. In methanol glass, $[Cu(Pmpep)(Br)]_2$ exhibits EPR transitions at g = 4.711 ($\Delta M_S = \pm 2$) and 2.105 ($\Delta M_S = \pm 1$). $[Cu(Pmpep)(Cl)]_2$ dissociates into monomers in methanol or DMF (EPR data).

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Table I. Summary of Crystal Data, Intensity Collection, and Structure Refinement Parameters for $[Cu(Pypep)(CH_3COO)]_2 \cdot 1.46H_2O$ (**4**) and $[Cu(Pmpep)(CH_3COO)(H_2O)]$ (**5**)

	4	**5**
formula (mol wt)	$C_{26}H_{30.92}N_8Cu_2O_{7.46}$ (701.28)	$C_{13}H_{16}N_5CuBrO_4$ (449.60)
a, Å	17.360 (2)	7.130 (2)
b, Å	14.207 (4)	10.918 (3)
c, Å	13.418 (3)	21.686 (7)
β, deg	112.61	105.59 (2)
crystl syst	monoclinic	monoclinic
space group	$C2/c$	$P2_1/c$
vol, Å^3	3055 (1)	1626.2 (9)
d_{calcd}, g/cm^3	1.52	1.84
d_{obsd},[a] g/cm^3	1.53	1.83
Z	4	4
cryst dimens, mm	0.38 × 0.42 × 0.46	0.61 × 0.50 × 0.31
abs coeff, μ, cm^{-1}	13.87	37.16
cryst faces		(001), (00$\bar{1}$), (110), (1$\bar{1}$0), ($\bar{1}$00), (010), (0$\bar{1}$0)
radiation (λ, Å)	Mo Kα (0.710 69) (graphite monochromator)	Mo Kα (0.710 69) (Nb filtered)
temp, °C	24	24
scan speed, deg/min	2.0–5.0 ($\theta/2\theta$ scan)	2.0–5.0 ($\theta/2\theta$ scan)
scan range, deg	1.0 below Kα_1 to 1.0 above Kα_2	1.0 below Kα_1 to 1.0 above Kα_2
bkgd/scan time ratio	0.5	0.5
data collected	2224	2332
no. of unique data ($F_o^2 > 3\sigma(F_o^2)$)	1594	1593
no. of variables	142	158
R, %	5.15	4.32
R_w, %	6.29	5.04
max Δ/σ in final least-squares cycle	0.013	0.033
largest residual electron density, e/Å^3	0.9 (assoc with O5[b])	0.7 (assoc with Br)

[a] Determined by flotation in CCl_4/cyclohexane and $CHBr_3/CCl_4$, respectively. [b] Associated with H_2O molecule (partial occupancy) in the lattice.

rotation photographs. These data were used to determine the crystal systems. Partial rotation photographs around each axis were consistent with monoclinic crystal systems in both cases. Ultimately, 30 high-angle reflections ($15 < 2\theta < 35°$) were used to obtain the final lattice parameters and the orientation matrix for **4**; in the case of **5**, 60 such reflections were used. Machine parameters, crystal data, and data collection parameters are summarized in Table I. The observed extinctions for **4** and **5** were consistent with the space groups Cc or $C2/c$ and $P2_1/c$, respectively. Successful refinement confirmed that **4** crystallized in the space group $C2/c$, while for **5**, $P2_1/c$ was uniquely determined. $\pm h,+k,+l$ data were collected in one shell ($4.5 < 2\theta < 45°$) for each compound. Three standard reflections were recorded every 197 reflections. Their intensities showed no statistically significant change over the duration of data collection. The data were processed by using the SHELX-76 program package.[15] The total of reflections with $F_o^2 > 3\sigma(F_o^2)$ for each compound is listed in Table I. The absorption coefficient of compound **4** is 13.81 cm^{-1}. ψ-scan data showed a standard deviation of only 1.6% of the mean intensity; thus no absorption correction was applied. In the case of **5**, where μ = 37.16 cm^{-1}, an analytical absorption correction was applied to the data employing the program ABSORB.

Structure Solution and Refinement. Non-hydrogen atomic scattering factors were taken from literature tabulations.[16] The Cu atom positions were determined in both cases with use of the heavy-atom (Patterson) method. The remaining non-hydrogen atoms were located from successive difference Fourier map calculations. Refinement was carried out by using full-matrix least-squares techniques on F, minimizing the function $\sum w(|F_o| - |F_c|)^2$, where the weight w is defined as $4F_o^2/\sigma^2(F_o^2)$ and F_o and F_c are the observed and calculated structure factor amplitudes. In the refinement, all non-hydrogen, non-carbon atoms were assigned anisotropic temperature factors while all carbons atoms were assigned isotropic thermal parameters. For compound **4**, the water molecules of crystallization were not of full site occupancy. Following refinement of the oxygen atom positions, site occupancies were refined. The data were consistent with one water molecule with site occupancy of 0.60 (W_1) and a second water molecule, located on a special position (0.5, y, 0.25), with site occupancy of 0.13 (W_2). Methylene and methine hydrogen atom positions were calculated by assuming a C–H bond length of 0.95 Å. Hydrogen atom temperature factors were fixed at 1.10 times the isotropic temperature factor of the carbon atom to which the hydrogen is bonded. Methyl groups were treated as rigid rotors. All other hydrogen atoms (amino and water hydrogens) were located from difference Fourier map calculations. Ultimately all hydrogen atom contributions were included but not refined. Final R and R_w values ($R = \sum||F_o| - |F_c||/\sum|F_o|$, $R_w = (\sum w(|F_o| - |F_c|)^2/\sum wF_o^2)^{1/2}$) and maximum Δ/σ values on any of the parameters in the final cycle of refinement are given in Table I. Final difference Fourier map calculations showed no peaks of chemical significance in either case. The magnitudes and locations of the largest residual peaks are described in Table I. The following data are tabulated: positional parameters (Table II) and selected bond distances and angles (Table III). Thermal parameters (Table S1) and hydrogen atom parameters (Table S2) have been deposited as supplementary material.

Other Physical Measurements. Both ^1H and ^{13}C NMR spectra were recorded on a General Electric 300-MHz GN-300 spectrometer using $Si(CH_3)_4$ as reference. Infrared spectra were monitored with a Nicolet MX-S FT spectrophotometer. Absorption spectra were obtained with a Hitachi Model 100-80 spectrophotometer. A Finnigan 4000 mass spectrometer was used to record the mass spectra of the peptide ligands. Electrochemical measurements were performed with standard Princeton Applied Research instrumentation with a glassy-carbon or Pt working electrode; all potentials were obtained at ~25 °C vs. a saturated calomel electrode as reference. EPR spectra were recorded on a Varian E-3 spectrometer connected to a Digital PDP 11 computer for data manipulation. Samples were run at 9 GHz (X-band) in the temperature range 77–298 K. Elemental analyses were performed by Atlantic Microlab Inc., Atlanta, GA.

Results and Discussion

The peptide bonds in PypepH (**2**) and PmpepH (**3**) have been synthesized in high yield via the ester route. Both ligands can coordinate through three N centers, an aromatic N, a peptide N and an imidazolyl N, and thus resemble part of the metal-chelating region of BLM (**1**). PmpepH is a better analogue in the sense that it contains a pyrimidine ring. Also in PmpepH, C_2 and C_5 of the pyrimidine ring have CH_3 and Br group as substituents—in BLM, the corresponding C_2 and C_5 are connected to a β-aminoalanine moiety and CH_3 group, respectively. This kind of substitution in PmpepH is sufficient to generate enough steric hindrance so as to yield the mononuclear copper complex **5**. PypepH, on the other hand, gives rise to the binuclear species **4**, where two acetate ions form weak one-atom bridges between the two copper centers. The copper complexes have been synthesized directly from copper acetate and by self-assembly reaction using copper perchlorate and sodium acetate. Since coordination of the peptide nitrogen to copper liberates 1 equiv of proton,[17] the stoichiometries of these reactions are properly selected to provide 1 equiv of free acetate to neutralize it.

Structure of $[Cu(Pypep)(CH_3COO)]_2 \cdot 1.46H_2O$ (4). The crystal structure is made up of unit cells each containing eight [Cu(Pypep)(CH_3COO)] fragments as well as 5.84 molecules of water. The copper-containing fragments pair up to result in centrosymmetric acetate-bridged dimers. An ORTEP drawing of the dimeric molecule is shown in Figure 1. The closest approach of two dimers is 1.858 Å (O1–HN4) through hydrogen bonding. Additional hydrogen bonding between the water molecules (partial occupancy) in the asymmetric unit is evidenced by the $W_1O–HW_2$ distance of 1.519 Å. The W_1 water molecule is located in the vicinity of the peptide oxygen O1 and the imidazole nitrogen N4 ($O1–H_aW_1$ = 2.797 Å and $N4–H_bW_1$ = 2.707 Å). Selected interatomic distances and angles are listed in Table III.

The geometry about the copper atom can be described as essentially a distorted square-based pyramid. The three nitrogens of the peptide ligand are in the equatorial plane with the pyridine

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Table II. Positional Parameters[a]

atom	x	y	z	atom	x	y	z
			Compound **4**				
Cu	2893 (1)	1436 (1)	−0307 (1)	O1	3007 (3)	−1369 (2)	0114 (4)
O2	3305 (2)	2742 (3)	0093 (3)	O3	0588 (3)	2762 (4)	0181 (4)
O4	4427 (4)	7429 (6)	1101 (7)	O5	5000 (1)	6309 (15)	2500 (1)
N1	3474 (3)	0932 (3)	1210 (4)	N2	2578 (3)	0109 (3)	−0610 (4)
N3	2450 (3)	1738 (3)	−1873 (4)	N4	2219 (3)	2376 (4)	−3455 (4)
C1	3877 (4)	1401 (4)	2141 (5)	C2	4251 (4)	0957 (4)	3114 (5)
C3	4223 (4)	−0034 (4)	3152 (5)	C4	3830 (4)	−0513 (5)	2194 (5)
C5	3457 (3)	−0020 (4)	1238 (4)	C6	2991 (3)	−0486 (4)	0176 (4)
C7	2091 (4)	−0308 (5)	−1639 (5)	C8	1461 (4)	0393 (5)	−2357 (5)
C9	1834 (4)	1214 (5)	−2659 (5)	C10	1687 (4)	1628 (5)	−3633 (6)
C11	2666 (4)	2415 (5)	−2393 (5)	C12	1001 (4)	2125 (5)	−0012 (5)
C13	0687 (5)	1142 (6)	−0151 (7)				
			Compound **5**				
Br	−2681 (1)	−2732 (1)	0967 (1)	Cu	−2787 (1)	2359 (1)	1587 (1)
O1	−6524 (7)	2758 (4)	1065 (2)	O2	−3907 (6)	3695 (4)	0977 (2)
O3	0833 (6)	2605 (4)	1711 (2)	O4	−2361 (6)	−1192 (4)	2117 (2)
N1	−2453 (6)	1070 (4)	0940 (2)	N2	−2373 (7)	0298 (5)	−0073 (2)
N3	−2692 (7)	0914 (5)	2113 (2)	N4	−2668 (7)	3503 (4)	2293 (2)
N5	−2028 (7)	5136 (5)	2904 (3)	C1	−5748 (8)	3640 (5)	0886 (3)
C2	−6884 (10)	4690 (7)	0549 (4)	C3	−1800 (11)	2463 (6)	0131 (4)
C4	−2237 (9)	1207 (6)	0345 (3)	C5	−2542 (9)	−0828 (6)	0135 (3)
C6	−2586 (9)	−1070 (6)	0758 (3)	C7	−2555 (8)	−0087 (5)	1159 (3)
C8	−2545 (8)	−0159 (5)	1861 (3)	C9	−2627 (9)	0908 (6)	2791 (3)
C10	−3727 (9)	1971 (6)	2978 (3)	C11	−2951 (8)	3207 (6)	2873 (3)
C12	−2550 (9)	4211 (6)	3254 (3)	C13	−2124 (8)	4676 (6)	2323 (3)

[a] Multiplied by 10^4.

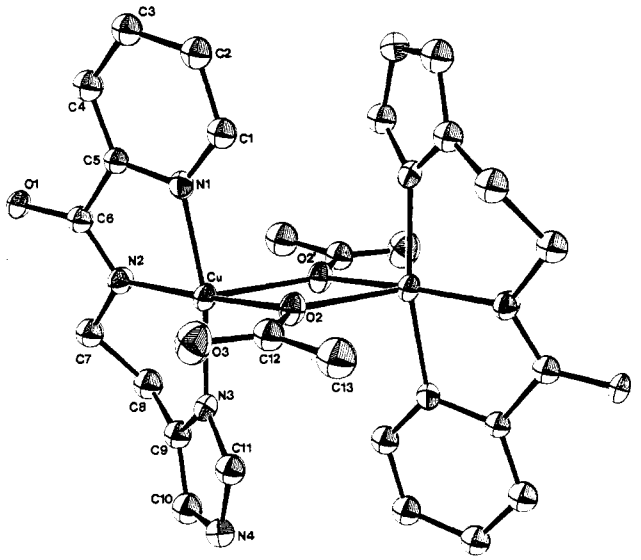

Figure 1. ORTEP drawing of $[Cu(Pypep)(CH_3COO)]_2 \cdot 1.46H_2O$ (**4**) showing 50% probability ellipsoids and the atom-labeling scheme. Hydrogen atoms and the lattice water molecules (partial occupancy) are omitted for clarity.

and the imidazole N atoms being trans to one another. The peptide N is trans to a bridging acetate O atom. The second bridging O atom occupies the axial position. The four coordinating atoms in the basal plane of copper are essentially coplanar. The copper atom also lies in this plane. Since the peptide nitrogen is deprotonated, the ligand is tridentate and anionic. Peptide coordination of this type has been observed previously.[13,18-21] The Cu–N(peptide) and Cu–N(imidazole) distances in copper complexes of glycyl-L-histidine[22] and glycyl-L-histidylglycine[19,20] fall in the narrow range of 1.93–1.98 and 1.93–1.99 Å, respectively. The typical Cu–N(pyridine) distance is 2.00–2.05 Å.[23] Thus, the Cu–N bond lengths in **4** are quite comparable to other related compounds. Interestingly, very similar Cu–N(imidazole) and Cu–N(pyridine) bond lengths are also observed in the copper complex of the Schiff base derived from 2-pyridinecarbaldehyde and histamine.[24]

The acetate ions in **4** bridge between two copper centers through one oxygen atom. In a common mode of acetate bridging between transition-metal atoms, the acetate group links adjacent metal centers via the two different acetate oxygen atoms to form a three-atom bridge. However, a one-atom bridge via one of the oxygen atoms of an acetate ligand has been found in a few Schiff base,[25] peptide,[19] and amino acid[26] complexes of copper. In all these compounds and **4**, each bridging O atom simultaneously occupies an equatorial position on Cu1 and an apical position on Cu2. The axial Cu–O2′ bond in **4** is considerably longer than the Cu–O2 bond in the equatorial plane (2.497 (4) vs. 1.987 (4) Å). This difference of 0.4–0.5 Å in two types of Cu–O distances is rather common in dimeric copper complexes; e.g., in the blue-violet form of the glycine-L-histidylglycine complex of copper, the two Cu–O bond distances are 2.00 and 2.53 Å. In the recently reported structure of a trimeric copper complex of the tridentate Schiff base *N*-methyl-*N*′-(4-methoxysalicylidene)-1,3-propanediamine,[27] both one-atom and three-atom acetate bridges between adjacent copper centers have been observed. In contrast to the case for the three-atom bridge, the one-atom acetate bridge is highly asymmetric and the Cu–O distances (2.000 (5) and 2.377

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Table III. Selected Bond Distances and Angles

Compound **4**

Distances (Å)

Cu–O2	1.987 (4)	Cu–O2′	2.497 (4)	Cu–N1	2.024 (5)
Cu–N2	1.962 (5)	Cu–N3	1.987 (5)	O1–C6	1.258 (7)
O2–C12	1.263 (7)	O3–C12	1.242 (8)	C12–C13	1.490 (1)
N1–C1	1.349 (8)	N1–C5	1.354 (7)	C1–C2	1.368 (9)
C2–C3	1.326 (8)	C3–C4	1.380 (9)	C4–C5	1.384 (8)
C5–C6	1.496 (8)	C6–N2	1.326 (7)	N2–C7	1.440 (8)
C7–C8	1.518 (9)	C8–C9	1.465 (9)	C9–N3	1.394 (9)
C9–C10	1.360 (1)	C10–N4	1.367 (9)	N4–C11	1.336 (8)
C11–N3	1.325 (8)	Cu···O3	2.817 (4)	Cu···Cu	3.542 (2)

Angles (deg)

O2–Cu–O2′	66.0 (2)	O2–Cu–N1	94.2 (2)	O2–Cu–N2	175.1 (2)
O2–Cu–N3	92.0 (2)	O2′–Cu–N1	99.5 (2)	O2′–Cu–N2	107.1 (2)
O2′–Cu–N3	91.1 (2)	N1–Cu–N2	81.9 (2)	N1–Cu–N3	168.7 (2)
N2–Cu–N3	91.4 (2)	Cu–O2–C12	143.5 (4)	O2–C12–O3	123.7 (6)
O2–C12–C13	116.4 (6)	O3–C12–C13	119.8 (6)	Cu–N1–C1	129.5 (4)
Cu–N1–C5	112.0 (4)	C1–N1–C5	118.4 (5)	N1–C1–C2	122.9 (6)
C1–C2–C3	118.9 (4)	C2–C3–C4	118.1 (6)	C3–C4–C5	120.0 (6)
C4–C5–N1	121.6 (5)	C4–C5–C6	123.2 (5)	C5–C6–O1	119.1 (5)
C5–C6–N2	113.9 (5)	O1–C6–N2	127.0 (5)	C6–N2–Cu	115.2 (4)
C6–N2–C7	116.0 (5)	N2–C7–C8	110.7 (5)	C7–C8–C9	114.2 (5)
C8–C9–C10	132.0 (6)	C8–C9–N3	120.5 (6)	N3–C9–C10	107.6 (6)
C9–N3–C11	106.3 (5)	Cu–N3–C9	123.9 (4)	Cu–N3–C11	129.8 (5)
C9–C10–N4	107.7 (6)	C10–N4–C11	107.2 (5)	N4–C11–N3	111.4 (6)

Compound **5**

Distances (Å)

Cu–O1	2.636 (5)	Cu–O2	1.987 (4)	Cu–O3	2.518 (4)
Cu–N1	2.046 (5)	Cu–N3	1.937 (5)	Cu–N4	1.960 (5)
O1–C1	1.225 (7)	O2–C1	1.275 (7)	C1–C2	1.479 (9)
N1–C4	1.348 (8)	N1–C7	1.359 (8)	N2–C4	1.329 (8)
N2–C5	1.326 (8)	C3–C4	1.506 (9)	C5–C6	1.385 (9)
C6–Br	1.876 (6)	C6–C7	1.378 (8)	C7–C8	1.523 (8)
N3–C8	1.309 (8)	C8–O4	1.248 (7)	N3–C9	1.458 (7)
C9–C10	1.516 (9)	C10–C11	1.498 (9)	N4–C11	1.365 (7)
N4–C13	1.335 (8)	N5–C12	1.372 (8)	N5–C13	1.340 (8)
C11–C12	1.356 (9)				

Angles (deg)

O1–Cu–O2	54.1 (2)	O1–Cu–O3	157.7 (1)	O1–Cu–N1	96.3 (2)
O1–Cu–N3	105.0 (2)	O1–Cu–N4	93.2 (2)	O2–Cu–O3	103.8 (2)
O2–Cu–N1	98.5 (2)	O2–Cu–N3	159.1 (2)	O2–Cu–N4	88.7 (2)
O3–Cu–N1	83.0 (2)	O3–Cu–N3	97.0 (2)	O3–Cu–N4	88.9 (2)
N1–Cu–N3	81.5 (2)	N1–Cu–N4	170.3 (2)	N3–Cu–N4	94.1 (2)
Cu–O1–C1	77.0 (3)	O1–C1–O2	121.5 (5)	Cu–O2–C1	106.3 (3)
O1–C1–C2	122.2 (6)	O2–C1–C2	116.4 (5)	Cu–N1–C4	130.1 (4)
Cu–N1–C7	111.9 (4)	C4–N1–C7	117.9 (5)	N1–C4–C3	118.8 (6)
N1–C4–N2	124.3 (6)	N2–C4–C3	117.0 (6)	C4–N2–C5	117.2 (5)
N2–C5–C6	122.5 (6)	C5–C6–Br	115.6 (5)	C5–C6–C7	117.8 (6)
C6–C7–N1	119.8 (5)	C6–C7–C8	125.8 (5)	C7–C8–O4	117.6 (5)
C7–C8–N3	113.0 (5)	C8–N3–Cu	118.5 (4)	C8–N3–C9	115.6 (5)
C9–N3–Cu	125.7 (4)	N3–C9–C10	112.8 (5)	C9–C10–C11	114.2 (5)
C10–C11–N4	108.1 (5)	C10–C11–C12	131.5 (5)	C11–N4–Cu	125.7 (4)
C11–N4–C13	107.1 (5)	C13–N4–Cu	126.9 (4)	C11–C12–N5	107.6 (6)
C12–N5–C13	106.9 (5)	N4–C13–N5	110.3 (6)		

(7) Å) are comparable to those found in **4**. Finally, there is a sixth interaction in **4**, albeit a weak one (2.817 Å), between the copper atom and the noncoordinated oxygen (O3) atom of the bridging acetate group.

The Cu–Cu distance of 3.542 Å in **4** is very similar to that found in other single O atom acetate-bridged complexes of copper. When this distance is compared to the Cu–Cu distances in copper carboxylates (2.62–2.89 Å),[28] no metal–metal bonding is evident in such complexes. Since **4** dissociates quite easily into monomeric units in solution (vide infra), the single O atom bridge appears to be a weak one.

Structure of [Cu(Pmpep)(CH_3COO)(H_2O)] (5). Crystals of **5** are made up of unit cells each containing four [Cu(Pmpep)(CH_3COO)(H_2O)] units. These units are discrete monomers, although hydrogen bonding between the coordinated water (O3) molecule of one unit and the peptide oxygen (O4) of the next one is indicated by the O4–H_aO3 distance 1.904 Å. An ORTEP drawing of the molecule is shown in Figure 2. Selected interatomic distances and angles are collected in Table III.

The disposition of donor atoms around copper in **5** can be described as distorted octahedral. Here again the three nitrogen atoms of the peptide ligand are in the equatorial plane of copper with the pyrimidine and the imidazole N atoms being trans to one another. Also, the peptide N is trans to an acetate O atom. The second O atom of the *same* acetate ion occupies an axial position while a water molecule fills the sixth coordination site. The Cu–N distances and the equatorial Cu–O bond length in **5** are very similar to those seen in **4**. In cytosine and cytidine complexes of copper, the Cu–N(pyrimidine) distances are found to lie in the narrow range of 1.95–2.05 Å.[29] Thus, the Cu–N(pyrimidine) distance of 2.046 (5) Å in **5** is quite normal. The

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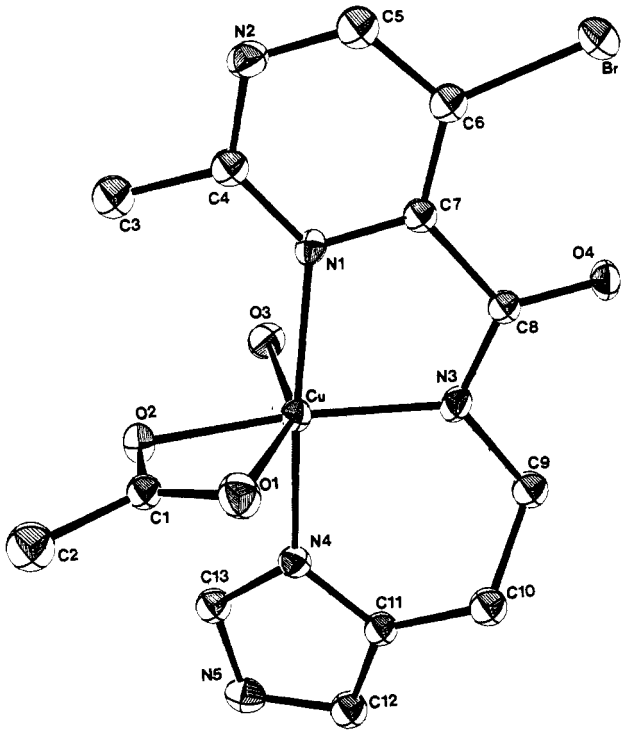

Figure 2. ORTEP drawing of $[Cu(Pmpep)(CH_3COO)(H_2O)]$ (**5**) showing 50% probability ellipsoids and the atom-labeling scheme. Hydrogen atoms are omitted for clarity.

axial Cu–O bonds are considerably longer and are typical of Jahn–Teller-distorted copper complexes.

Bidentate coordination by the acetate group has been observed in Cu(gly-L-hisgly)($NaClO_4$)(H_2O)[20] and Cu(gly-L-his)·$6H_2O$.[22] The Cu–O1 distance in **5** is, however, noticeably shorter (stronger interaction) than that noted for these peptide complexes. Without exception, the sixth coordination site of copper in these compounds is occupied by a water molecule at a distance of 2.40–2.75 Å. Quite contrary to this characteristic, no such water molecule is found in the single O atom acetate-bridged complexes, including **4**. In the latter class of compounds, weak axial interaction between the nonbonding O atom of the bridging acetate ion and copper might prevent the water molecule from ligation.

Because of the small "bite" of the carboxylic group (O1–Cu–O2 = 54.1 (2)°), the copper atom in **5** is displaced 0.157 Å out of the plane containing three nitrogens of the peptide ligand in the direction of the apical O1 atom. For the same reason, the equatorial oxygen atom (O2) lies 1.015 Å above the plane of the ligand nitrogens. The coordination geometry around copper is thus severely distorted from an octahedral one.

EPR Spectra. In the polycrystalline state, both **4** and **5** exhibit axial EPR spectra in the temperature range 77–300 K. The observed spectral parameters are presented in Table IV. The solid-state spectra provide very little structural information and hence will not be discussed any further. In frozen aqueous solution, a broad featureless transition with $g \approx 2.09$ is observed for **4** and **5**. A low-field resonance corresponding to the $\Delta M_S = \pm 2$ transition is also recorded. This transition is characteristic of magnetically coupled binuclear copper(II) complexes and is in agreement with the crystal structure of **4**. The one-atom acetate bridge in **4** apparently remains intact in a frozen aqueous glass. In the case of **5**, formation of a dimer in a low-temperature glass could take place through either one oxygen atom of the carboxylate anion (as in **4**) or the conversion of the bidentate acetate ion of the monomer to regular bridging (three-atom) acetate groups between two units. The single O atom bridge seems unlikely in view of structural data. It appears that there is a small difference in energy between the two types of acetate coordination in peptide complexes. Indeed, in the case of glycyl-L-histidylglycinato complexes of copper, two crystalline solids containing the two types of acetate coordination as in **4** and **5** have been isolated.[19,20]

Table IV. EPR Parameters for $[Cu(Pypep)(CH_3COO)]_2 \cdot 1.46H_2O$ (**4**) and $[Cu(Pmpep)(CH_3COO)(H_2O)]$ (**5**)[a]

complex	$g_\parallel$	$g_\perp$	$A_\parallel$, G
$[Cu(Pypep)(CH_3COO)]_2 \cdot 1.46H_2O$			
solid, 298 K	2.241	2.085	
solid, 77 K	2.221	2.064	
soln in MeOH, 77 K	2.207	2.053	181
soln in DMF, 77 K	2.198	2.051	180
soln in H_2O, 77 K[b]	2.085, 4.702		
$[Cu(Pmpep)(CH_3COO)(H_2O)]$			
solid, 298 K	2.223	2.085	
solid, 77 K	2.198	2.064	
soln in MeOH, 77 K	2.224	2.031	163
soln in DMF, 77 K	2.240	2.043	170
soln in H_2O, 77 K[b]	2.091, 4.711		
Cu(II)–BLM[c]	2.203	2.058	184
Cu(II)–BLM[d]	2.211	2.055	183.0
Cu(II)–P-3A[d]	2.214	2.133, 2.078	167.3
Cu(II)–PYML-1[d]	2.206	2.048	179.4
Cu(II)–PEML[d]	2.237	2.250	170.8
Cu(II)–AMPHIS[e]	2.204	2.050	177.5

[a] Spectral data for Cu(II)–BLM, Cu(II)–P-3A, and a few synthetic analogues from previous reports are also included for the purpose of comparison. [b] Spectrum obtained is that of the dimeric species. [c] Conditions: aqueous solution, pH 7.5, 77K. [d] Reference 9. [e] Reference 11.

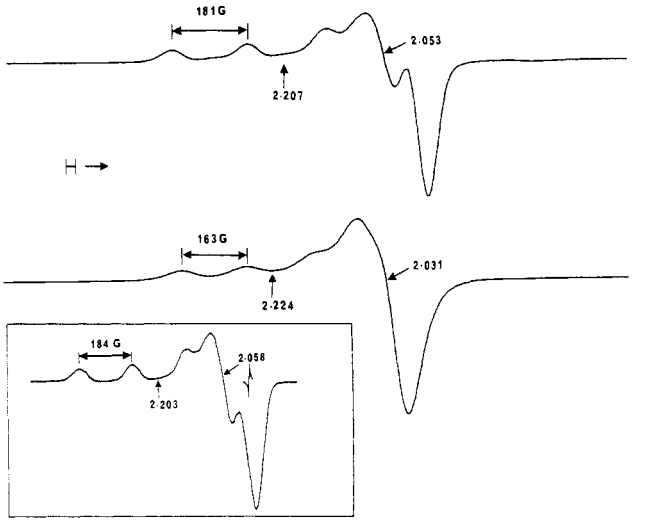

Figure 3. X-Band EPR spectra (77 K) of **4** (top) and **5** (bottom) in methanol (concentrations 2 mM). Inset: X-band EPR spectrum (77 K) of Cu(II)–BLM in aqueous solution (1 mM) at pH 7.5. Selected g and $A_\parallel$ values are indicated. Spectrometer settings: microwave frequency, 9.19 GHz; microwave power, 10 mW; modulation frequency, 100 kHz; modulation amplitude, 2.0 G.

EPR spectra of **4** and **5** in frozen methanol or DMF glass are, however, typical of a monomeric tetragonal Cu(II) complex with a $d_{x^2-y^2}$ ground-state doublet (Figure 3). The copper is bonded to one O and three N atoms in the basal plane of such monomeric Cu(II) species. Weak axial coordination by the second oxygen atom of the acetate ion is not ruled out in these monomers. EPR data for **4** and **5** are listed in Table IV. Parameters for Cu(II)–BLM, Cu–P-3A, and the copper complexes of three BLM analogues are also included in the table for the purpose of comparison. Even though no well-resolved superhyperfine coupling to inner-sphere coordination centers is detected in either **4** or **5**, features of the coordination geometry in each case can be extracted from the EPR parameters of the complexes presented in Table IV. The observed tendencies for $A_\parallel$ to increase and $g_\parallel$ to decrease have been taken as parameters for the measure of the strength of in-plane ligand fields under tetragonal geometry in copper complexes.[30] Larger $A_\parallel$ values in the case of **4** suggest that the

Table V. Electronic Spectral Data for $[Cu(Pypep)(CH_3COO)]_2 \cdot 1.46H_2O$ (**4**) and $[Cu(Pmpep)(CH_3COO)(H_2O)]$ (**5**)[a]

solvent	λ_{max}, nm (ϵ)	
	complex **4**[b]	complex **5**
MeOH	600 (68), 290 sh (4000), 260 sh (6900)	660 (98), 320 sh (4000), 295 (4900), 250 sh (7300)
DMF	575 (72), 320 sh (2700)	640 (107), 320 (2800)
H_2O	615 (65), 280 sh (4000), 260 (5400)	670 (90), 290 (4300), 240 (7100)

[a] For Cu(II)–BLM *in water* (pH 6.5; λ_{max}, nm (ϵ)): 595 (120), 292 (17 400) (bithiazole absorption), 320 (4000), 250 (23 000).[33,36] [b] ϵ values are quoted per Cu atom.

in-plane crystal field strength of PypepH is greater than that of PmpepH in **5**. Since high $g_\parallel$ and small $A_\parallel$ values are indicative of off-planar distortion,[31] a pseudotetragonal geometry is evident around copper in **5**. Both these features are supported by the absorption spectra of the complexes (vide infra).

The spectral characteristics of the Cu(II) complexes of two BLM analogues, namely PYML-1[9,10] and AMPHIS,[11] are comparable to those of Cu(II)–BLM (Table IV). In both complexes, a square-pyramidal N_5 coordination around copper has been predicted. In the absence of any structural data, a tetragonal geometry with four nitrogens in the basal plane of copper is also possible. It is important to note that both **4** and **5**, for which N_3O coordination in the equatorial plane of copper has been established, also exhibit EPR parameters very similar to those of Cu(II)–BLM. In fact, inspection of Figure 3 reveals that the spectrum of **4** is almost identical with that of Cu(II)–BLM. Following a comparison of the observed $g_\parallel$ and $A_\parallel$ values for a large number of Cu(II) compounds[32] and the bleomycin complex, the Cu(II)–BLM spectrum has previously been assigned to be a borderline case between N_4 and N_3O coordination.[33,34] In the present study, spectral similarities in Figure 3 clearly indicate that the Cu(II)–BLM spectrum could arise from structures other than the $Cu^{II}N_5$ chromophore. The proposed coordination sphere of copper in Cu(II)–BLM is largely based on the structure of Cu(II)–P-3A. However, the latter complex exhibits higher g anisotropies, suggesting a rhombic distortion of the ligand field. Also, the half-wave potential of Cu(II)–P3A is ~200 mV more positive that that of Cu(II)–BLM.[9] These differences in EPR and electrochemical data do not allow one to establish unambiguously the structure of the coordination sphere of copper in Cu(II)–BLM.

Absorption Spectra. The absorption spectra of **4** and **5** in methanol are shown in Figure 4; the peak positions and extinction coefficients in various solvents are presented in Table V. In each case, a single broad d–d band is obtained in the visible region, a feature characteristic of many Cu(II) systems. The most significant difference is the red shift (ca. 60 nm) of the λ_{max} value observed for **5**, in which a pyrimidine ring replaces the pyridine ring in the equatorial plane of the Cu atom in **4**. Evidently the pyrimidine N provides a weaker ligand field in the basal plane of Cu(II) chromophore. Another obvious difference is the intensity of the d–d band. The enhanced intensity in the case of **5** is suggestive of distortion from the tetragonal stereochemistry apparently caused by steric constraints. Similar enhancement of intensity due to distortion has been reported for a variety of copper complexes of aza macrocycles.[31]

Table V exhibits a blue shift of the visible band maximum for **4** and **5** as the solvent is changed from water to methanol and from methanol to DMF. This shift is indicative of axial coordination by solvent molecules. The λ_{max} value for the d–d band in such cases should shift to higher energy with decrease in the axial ligand

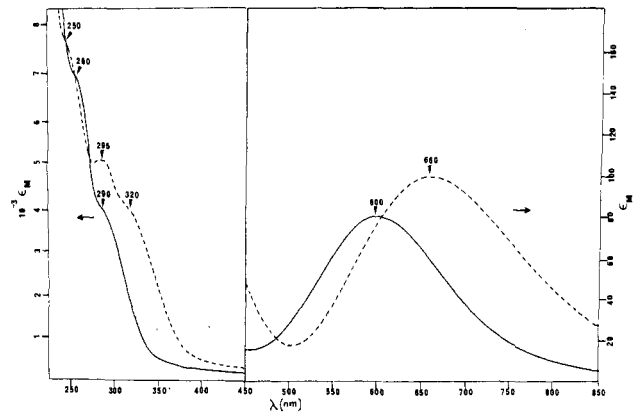

Figure 4. Absorption spectra of **4** (solid line) and **5** (broken line) in methanol solutions.

basicity,[35] and this is the trend observed in the present study. Weakening of the ligand field strength in the basal plane of copper due to hydrogen bonding between the peptide oxygen (and/or imidazole nitrogen) and solvent is also expected to contribute to the observed shift of λ_{max} with solvent.

The features in the 300–250-nm range of the electronic spectra of **4** and **5** arise from absorption by the organic chromophores of the peptide ligands. The ~260-nm band maxima of the free ligands shift to lower energy (~290 nm) on coordination to copper. Similar behavior has been observed with BLM.[36] The shoulder at 327 nm on the bithiazole peak has previously been assigned as a $d\pi \rightarrow \pi^*$, metal-to-ligand charge-transfer transition involving the 4-aminopyrimidine moiety.[33] The additional shoulder at 320 nm in the case of **5** (Figure 4) confirms this assignment. Indeed, the absorption features of **5** in the 350–250-nm range closely resemble the spectrum of Cu(II)–BLM except for the bithiazole absorption.

It is interesting to note that the visible absorption spectrum of **4** but not **5** resembles that reported for Cu(II)–BLM even though in both **4** and **5** the copper center is expected to have three N and possibly three O (one or two from solvent) atoms in the first coordination sphere. This observation is somewhat surprising since **5** was supposed to mimic Cu(II)–BLM more closely due to the presence of the pyrimidine ring.[37] It is thus evident that two structurally similar species might exhibit different spectroscopic behavior depending on finer structural detail. The absorption spectrum of **4** also suggests that a planar N_3O or tetragonal N_3O_3 coordination can give rise to a visible absorption spectrum similar to that of Cu(II)–BLM, in which a N_5 coordination around copper has been proposed. Therefore, the alternative suggestion of N_3O coordination in the basal plane of copper in Cu(II)–BLM cannot be ruled out on the basis of absorption and EPR spectroscopic data.

Electrochemical Data. The redox properties of **4** and **5** in methanol and DMF have been studied by cyclic voltammetry. Both complexes undergo irreversible reduction on platinum and glassy-carbon electrodes. In methanol, **4** and **5** are reduced at $E_p = -0.46$ and -0.22 V (vs. SCE), respectively. The reduced species appear to undergo decomposition or some other subsequent reaction around the working electrode since no appreciable anodic current is detected in the reverse scan. Introduction of a pyrimidine ring in the coordination sphere of copper lowers the reduction potential, indicating contribution of pyrimidine in the molecular orbitals involved in the redox process. The reduction potential of **4** is close to the value reported for a pyridine-based

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(37) Preliminary studies have shown that addition of N donors like ethylenediamine to **5** in methanol shifts the visible band maximum to 600 nm. The stronger ligand field provided by the N (as compared to O) atoms around copper is expected to be responsible for the blue shift. Thus it appears that replacement of the acetate group by N donors in **5** will result in a close match of the absorption spectra. Such studies are in progress.

analogue of BLM[9] but less negative than that of Cu(II)-BLM.

Summary. The following are the principal results and conclusions of this investigation.

(1) As part of a synthetic analogue approach to metallobleomycins, copper complexes (**4** and **5**) of two peptides (PypepH and PmpepH) resembling portions of the metal-chelating section of BLM have been isolated and structurally characterized. Prior to this report, no synthetic analogue has been isolated in crystalline form.

(2) In **5**, three of the five proposed BLM donor centers, namely a pyrimidine N, a peptide N, and an imidazole N, are coordinated to copper. A pyridine N replaces the pyrimidine N in the coordination sphere of copper in **4**. The remaining coordination sites around copper in both these complexes are filled by acetate ion and water. The presence of bulky groups on the pyrimidine ring in PmpepH leads to a monomeric copper complex whereas PypepH gives rise to an acetate-bridged dimer. Two distinctly different kinds of acetate coordination are observed in these two complexes. The coordination geometries of copper in **4** and **5** are square pyramidal and distorted octahedral, respectively.

(3) Apart from important structural data pertinent to the proposed structure of Cu(II)-BLM, **4** and **5** provide opportunities of correlating spectroscopic properties of synthetic analogues to their structures. Results from such attempts have raised questions regarding the proposed structure of Cu(II)-BLM based on the crystallographic data for Cu(II)-P-3A. The absorption and EPR spectra of **4** are remarkably similar to those of Cu(II)-BLM. This observation points out the possibility of a N_3O coordination in the basal plane of copper in Cu(II)-BLM. The spectral characteristics of **4** and **5** also suggest that a "typical" Cu(II)-BLM spectrum can arise from a few alternative structures where a N_5 coordination might not necessarily be present. Thus the apparent match in spectroscopic properties of synthetic analogues generated in situ and Cu(II)-BLM, reported in previous accounts, should not be taken as conclusive proof of the proposed structures.

Structural characterization of the copper complex of a synthetic fragment containing all the five proposed donor centers of BLM is in progress.

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Registry No. **1**, 11056-06-7; **2**, 103692-68-8; **3**, 103692-69-9; **4**, 103671-02-9; **5**, 103671-03-0; $[Cu(Pypep)(Cl)(H_2O)]_2$, 103671-04-1; $[Cu(Pmpep)(Br)]_2$, 103671-05-2; ethyl picolinate, 2524-52-9; histamine, 51-45-6; ethyl 2-methyl-5-bromopyrimidinecarboxylate, 83410-38-2.

Supplementary Material Available: Thermal parameters for non-hydrogen atoms (Table S1) and positional and thermal parameters for hydrogen atoms (Table S2) for $[Cu(Pypep)(CH_3COO)]_2 \cdot 1.46H_2O$ (**4**) and $[Cu(Pmpep)(CH_3COO)(H_2O)]$ (**5**) (2 pages). Ordering information is given on any current masthead page.

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Diplatinum(III) Complexes with Bridging 1-Methyluracil Ligands in Head-Tail Arrangement: Synthesis, Structures, and Solution Behavior

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The preparation, composition, and the solution behavior of a series of diplatinum(III) complexes of general formula $[X(NH_3)_2PtL_2Pt(NH_3)_2Y]Z_n \cdot mH_2O$ (L = 1-methyluracil anion, $C_5H_5N_2O_2$, or 5-chloro-1-methyluracil anion, $C_5H_4N_2O_2Cl$; X, Y = NO_2^-, NO_3^-, Cl^-, Br^-, H_2O, or combinations thereof; Z = NO_3^-, Cl^-, Br^-; n = 2, 3) are reported. The compounds are obtained by chemical oxidation (HNO_3, HNO_2, Cl_2) of the head-tail Pt(II) dimer *cis*-$[(NH_3)_2Pt(C_2H_5N_2O_2)]_2(NO_3)_2$ or via ligand exchange reactions of the Pt(III) dimers, respectively. The crystal structures of two modifications of $[(ONO_2)(NH_3)_2Pt(C_5H_5N_2O_2)_2Pt(NH_3)_2(OH_2)](NO_3)_3 \cdot mH_2O$ with m = 3 (**4**) and 2 (**5**) have been determined. **4** is triclinic, space group $P\bar{1}$, a = 9.742 (1) Å, b = 12.436 (2) Å, c = 14.019 (2) Å, α = 123.06 (1)°, β = 96.51 (1)°, γ = 93.66 (1)°, V = 1398.0 Å^3, Z = 2; **5** is monoclinic, space group $P2_1/c$, a = 14.202 (2) Å, b = 20.571 (2) Å, c = 9.760 (1) Å, β = 95.87 (2)°, V = 2836.4 Å^3, Z = 4. As expected, the cations of both compounds are similar: Pt-Pt = 2.556 (1) Å (**4**), 2.560 (1) Å (**5**); Pt-OH_2 = 2.18 (1) Å (4), 2.17 (1) Å (**5**); Pt-ONO_2 = 2.14 (1) Å (**4**), 2.12 (1) Å (**5**). The structures are compared with the previously reported analogue with X = NO_2^- and Y = OH_2. In aqueous solution, axial X and Y ligands such as Cl^-, ONO_2^-, and NO_2^- readily undergo solvolysis with formation of the diaqua complex $[(OH_2)(NH_3)_2PtL_2Pt(NH_3)_2(OH_2)]^{4+}$. pK_a values of this complex have been determined as 3.5 and 6.7. At pH >2, diplatinum(III) complexes containing nitro ligands are spontaneously reduced to the diplatinum(II) starting compound. In a secondary reaction, evolution of N_2 is observed, presumably formed between NH_3 and NO_2^-. Diplatinum(III) complexes obtained through Cl_2 oxidation are special in that Cl_2 also attacks the uracil ring with substitution of H5 by Cl. Iodine has been found not to oxidize the diplatinum(II) precursor to the diplatinum(III) complex.

Introduction

Dinuclear complexes of platinum in its unusual +3 oxidation state represent a relatively new class of coordination compounds. At present, two types of diplatinum(III) complexes are known, those with four bridging ligands, e.g. SO_4^{2-},[2] HPO_4^{2-} or $H_2PO_4^-$,[3] $H_2P_2O_5^{2-}$,[4] dithioacetate,[5] acetamide,[6] and pyrimidine-2-thione,[7] and those with two bridging ligands, e.g. acetate or derivatives,[8] pyrimidin-2-one,[9] 1-methyluracil,[10,11] and 1-methylcytosine.[12] Among the latter and with unsymmetrical ligands such as hydroxopyridine and pyrimidine derivatives, the two bridges may be oriented in a head-head or head-tail fashion. At least with 1-methyluracil ligands, these two types of complexes exhibit distinct differences in stability: while the head-tail dimers described subsequently are relatively stable in solution, the corre-

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