

Characterization of an Air-Stable Chromium(II) Dinicotinate Complex: *trans*-[Cr^{II}(nic-N)₂(H₂O)₄]

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The synthesis and structural characterization of *trans*-[Cr^{II}(nic-N)₂(H₂O)₄] and *trans*-[Zn^{II}(nic-N)₂(H₂O)₄] are reported. The chromium(II) complex was isolated as an air-stable, high-spin, monomeric solid. [Cr^{II}(nic-N)₂(H₂O)₄] crystallized in the space group *P*1̄ with *Z* = 1, *a* = 7.010 (2) Å, *b* = 7.223 (1) Å, *c* = 8.851 (2) Å, α = 68.08 (1)°, β = 68.76 (2)°, and γ = 63.07 (1)°. The structure was refined to *R* = 0.026 and *R*_w = 0.034. The chromium(II) complex is found as discrete zwitterions with the nicotinate coordinated to the metal center through the pyridyl nitrogen in a *trans* configuration. The complex is found in a distorted octahedral arrangement as evidenced by the elongated Cr-O(1) and Cr-O(1a) bonds, 2.471 (3) Å. [Zn^{II}(nic-N)₂(H₂O)₄] crystallized in the space group *C*2 with *Z* = 2, *a* = 14.195 (2) Å, *b* = 6.900 (1) Å, *c* = 8.482 (1) Å, β = 118.19 (1)° and the final agreement factors of *R* = 0.029 and *R*_w = 0.048. The Zn complex has a configuration similar to that of the Cr complex with the nicotinate arranged in a *trans* fashion. The Cr(II) complex was also found to cocrystallize with the Zn(II) complex, adopting the nondistorted (no tetragonal elongation) structure of the Zn(II) complex (*C*₂ symmetry).

Introduction

We have been investigating the coordination chemistry of cobalt(III) and chromium(III) nicotinic acid complexes.^{1,2} Our interest in these systems stems from the role of chromium(III) in the maintenance of normal glucose metabolism.³⁻⁷ The biologically active form of chromium has been termed the glucose tolerance factor (GTF). The structure of GTF has not been determined but has been proposed to contain, minimally, chromium(III) in conjunction with nicotinic acid.³ There has also been considerable interest in transition-metal complexes of nitrogen heterocycles, such as nicotinic acid, which function as electron-transfer mediators or bridging ligands in oxidation-reduction reactions between two metal centers.⁸⁻¹¹

We have recently made use of the reducibility of nicotinic acid by aqueous chromium(II) to produce stable, pyridyl-nitrogen-coordinated nicotinic acid chromium(III) complexes.¹ The complexes *cis*- and *trans*-H[Cr(mal)₂(nic-N)₂] (mal = malonate; nic-N = *N*-coordinated nicotinate) were synthesized directly simply by addition of aqueous chromium(II) to a deoxygenated, pH 6 solution of malonate and nicotinate.¹ Apparently, the chromous ion coordinates malonate and nicotinate and then intramolecularly reduces one of the nicotinate ligands to produce a chromium(III) ligand radical intermediate, which most likely disproportionates to the Cr(III)-nicotinate species and a dihydro-nicotinate complex. (This mechanism is currently under investigation.)

Because of these findings we were very interested in the recent report by Cooper et al. of the synthesis and characterization, including a single-crystal X-ray analysis, of *trans*-[Cr^{II}(nic-N)₂(H₂O)₄].¹² Some unusual properties were described for this complex, including the discrete nonclassical zwitterion nature of the complex in the solid state, the air stability of the solid, and a low-spin electronic configuration for the chromium(II) metal center. Our investigations of this system have revealed that the chromium(II) nicotinate complex reported by Cooper et al. is,

in fact, an isomorphous mixture of high-spin [Cr^{II}(nic-N)₂(H₂O)₄] and [Zn^{II}(nic-N)₂(H₂O)₄].

We report here the synthesis and characterization, including a crystallographic study, of *trans*-[Cr^{II}(nic-N)₂(H₂O)₄] and *trans*-[Zn(nic-N)₂(H₂O)₄] in addition to the correct characterization of the complex reported by Cooper et al. as *trans*-[Cr^{II}_{0.42}Zn^{II}_{0.58}(nic-N)₂(H₂O)₄].

Experimental Section

Materials. All chemicals were reagent grade and were used as received. Standard Schlenkware and syringe techniques were used to handle chromium(II) solutions, which were made from electrolytically pure chromium metal (Gallard Schlesinger) as previously described.¹

Synthesis. *trans*-[Cr(nic-N)₂(H₂O)₄]. This complex was synthesized by a method similar to that reported by Cooper et al.¹² An aliquot of a stock chromium(II) chloride solution (0.004 mol) was added to a deoxygenated, stirred solution of nicotinic acid (0.98 g, 0.008 mol) that had been adjusted to pH 6.5 with 20% KOH. A red-pink precipitate formed, which changed to a yellow-green, microcrystalline compound in ca. 10 min. The solution was stirred for 15 min, filtered (aerobically), and washed with water, ethanol, and acetone; yield 1.1 g (75%). Crystals suitable for single-crystal X-ray analysis were obtained by the same procedure as above, except that β-alanine (0.71 g) was added as a buffer to the nicotinic acid solution at pH 6, and the solution was stirred only during the chromous addition. After ca. 24 h, the lime-green plates that had formed were harvested by decanting off the remaining solution, rinsing with water (50 mL) three times, and filtering. The plates were washed with water and methanol and air-dried. Anal. Calcd for *trans*-Cr(nic-N)₂(H₂O)₄: C, 39.1; H, 4.38; N, 7.61; Cr, 14.1. Found: C, 38.7; H, 4.32; N, 7.67; Cr, 13.9.

trans-[Cr^{II}_{0.58}Zn^{II}_{0.42}(nic-N)₂(H₂O)₄]. This compound was prepared by the same method as used for *trans*-[Cr(nic-N)₂(H₂O)₄] except ZnSO₄·7H₂O (0.58 g, 0.002 mol) was dissolved in the chromium(II) aliquot before it was added to the nicotinate solution. A dull yellow, microcrystalline solid was isolated; yield 1.3 g. Chromium analysis: 8.13% Cr, which corresponds to 58.3 mol% Cr and 41.7 mol% Zn. This corresponds to a calculated molecular weight of 374. Anal. Calcd for Cr_{0.583}Zn_{0.417}(nic)₂(H₂O)₄: C, 38.5; H, 4.31; N, 7.49. Found: C, 38.3; H, 4.21; N, 7.35.

trans-[Zn(nic-N)₂(H₂O)₄]. This compound was prepared by a method similar to that used for the synthesis of the cobalt(II) and nickel(II) analogues.¹³ Nicotinic acid (6.15 g, 0.05 mol) was dissolved in 100 mL of water, and the pH was adjusted to 6.0 with 20% KOH. ZnSO₄·7H₂O (7.19 g, 0.025 mol), in 100 mL of water, was added, and a white powder precipitated out of solution on stirring. The solid was filtered and washed with water, ethanol, and acetone; yield 8.7 g (91%). Colorless plates were obtained by warming the solutions to 60 °C prior to mixing and allowing the solution to cool slowly without stirring. Anal. Calcd for Zn(nic-N)₂(H₂O)₄: C, 37.8; H, 4.23; N, 7.34. Found: C, 37.5; H, 4.31; N, 7.25.

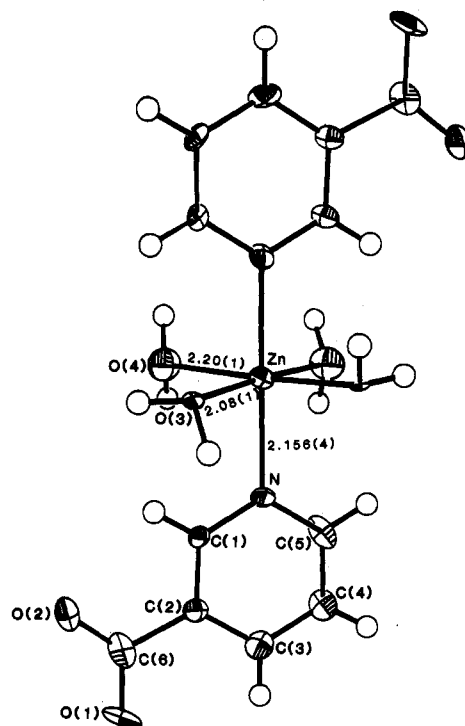
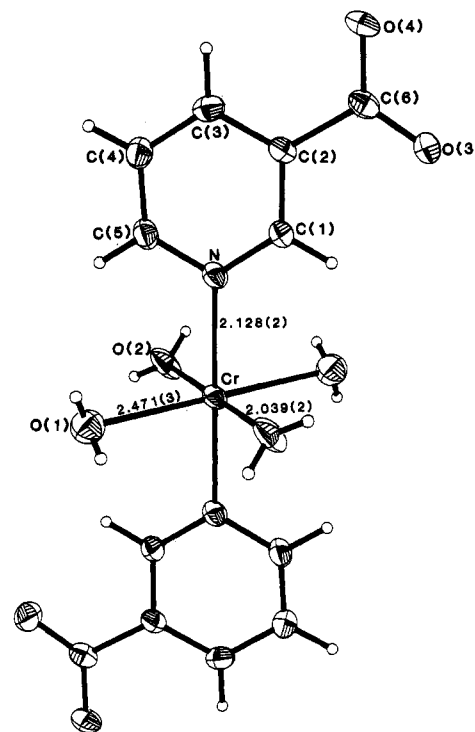
Physical Measurements. Analysis. Elemental analyses (C, H, N) were obtained from Galbraith Laboratories, Inc., Knoxville, TN. Chromium

- Broderick, W. E.; Legg, J. I. *Inorg. Chem.* **1985**, *24*, 3724.
- (a) Wierenga, T. J.; Legg, J. I. *Inorg. Chem.* **1982**, *21*, 2881. (b) Green, C. A.; Bianchini, R. J.; Legg, J. I. *Inorg. Chem.* **1984**, *23*, 2713.
- Barret, J.; O'Brien, P.; Pedrosa DeJesus, J. *Polyhedron* **1985**, *4*, 1.
- Mertz, W.; Schwarz, K. *Arch. Biochem. Biophys.* **1957**, *72*, 515.
- Mertz, W. *Physiol. Rev.* **1969**, *49*, 163.
- (a) Anderson, R. A.; Mertz, W. *Trends Biochem. Sci. (Ref. Ed.)* **1977**, *2*, 277. (b) Anderson, R. A. *Sci. Total Environ.* **1981**, *17*, 13.
- Mertz, W.; Toepfer, E. W.; Roginski, E. E.; Polanski, M. M. *Fed. Proc., Fed. Am. Soc. Exp. Biol.* **1974**, *33*, 2275.
- Gould, E. S.; Taube, H. *J. Am. Chem. Soc.* **1964**, *86*, 1318.
- Taube, H.; Gould, E. S. *Acc. Chem. Res.* **1969**, *2*, 321.
- Haim, A. *Acc. Chem. Res.* **1975**, *8*, 264.
- Gould, E. S. *Acc. Chem. Res.* **1985**, *18*, 22.
- Cooper, J. A.; Anderson, B. F.; Buckley, P. D.; Blackwell, L. F. *Inorg. Chim. Acta* **1984**, *91*, 1.

- Anagnostopoulos, A.; Matthews, R. W.; Walton, R. A. *Can. J. Chem.* **1972**, *50*, 1307.

Table I. Crystal Data for trans-[Zn^{II}(nic-N)₂(H₂O)₄] and trans-[Cr^{II}(nic-N)₂(H₂O)₄]

formula	ZnC ₁₂ H ₁₆ N ₂ O ₈	CrC ₁₂ H ₁₆ N ₂ O ₈
<i>M_r</i>	381.64	368.27
space group	C2	P1
cell dimens		
<i>a</i> , Å	14.195 (2)	7.010 (2)
<i>b</i> , Å	6.900 (1)	7.223 (1)
<i>c</i> , Å	8.482 (1)	8.851 (2)
<i>α</i> , deg	90	68.08 (1)
<i>β</i> , deg	118.192 (9)	68.76 (2)
<i>γ</i> , deg	90	63.07 (1)
<i>V</i> , Å ³	732.3 (1)	360.4 (1)
<i>Z</i>	2	1
<i>D</i> (calcd), g/cm ³	1.73	1.70
radiation, Å	0.710 69 (Mo Kα)	0.710 69 (Mo Kα)
data collcn	<i>θ</i> -2 <i>θ</i>	<i>ω</i>
cryst dimens, mm	0.12 × 0.34 × 0.4	0.1 × 0.3 × 0.3
abs coeff (μ), cm ⁻¹	17.57	8.17
abs range <i>T</i> _{max}	0.751	1.000
abs range <i>T</i> _{min}	0.622	0.949
2 <i>θ</i> range, deg	3 < 2 <i>θ</i> < 45	3 <i>θ</i> 2 <i>θ</i> < 45
no. of data measd (total)	682	942
no. of indep data (total)	532	875
no. of indep data [<i>I</i> > 3σ(<i>I</i>)]	523	815
refin <i>R</i> ¹⁷	0.0294	0.0264
refin <i>R_w</i> ¹⁷	0.0483	0.0341
goodness of fit	1.618	1.362
largest peak on final difference map, e/Å ³	0.30 (near O(3))	0.22 (between C(2) and C(6))

**Figure 1.** ORTEP drawing and labeling scheme for trans-[Zn^{II}(nic-N)₂(H₂O)₄].**Figure 2.** ORTEP drawing and labeling scheme for trans-[Cr^{II}(nic-N)₂(H₂O)₄].

was determined by spectrophotometric analysis of CrO₄²⁻ at 372 nm after oxidation of the complexes with hot alkaline hydrogen peroxide.¹⁴

UV-Visible Spectra. Since the complexes were not appreciably soluble in common polar or nonpolar solvents, UV-visible spectra were obtained by the diffuse reflectance technique using a Perkin-Elmer 320 spectrophotometer.

Magnetic Measurements. Magnetic susceptibility measurements were made on a PAR vibrating-sample magnetometer equipped with a Janis cryostat. The thermometry was calibrated with KCr(SO₄)₂·6H₂O and HgCo(CN)₄. Diamagnetic and TIP corrections were made.

X-ray Powder Patterns. The X-ray powder patterns were determined by use of a conventional film powder camera with nickel-filtered Cu Kα₁ radiation.

Crystal Structure Determinations. The clear plates of [Zn(nic-N)₂(H₂O)₄] obtained as described above were ground to approximate ellipsoids prior to crystallographic analysis. Suitable crystals of [Cr^{II}(nic-N)₂(H₂O)₄] and [Zn^{II}(nic-N)₂(H₂O)₄] were attached to glass fibers and mounted on a Nicolet R3m/E four-circle diffractometer equipped with a Mo Kα X-ray source (graphite monochromator for the Cr complex, Zr-filtered for the Zn complex). Twenty-five well-dispersed high-angle reflections were accurately centered, and the lattice parameters as well as crystal orientation were optimized by a least-squares procedure. Data collection parameters¹⁵ and details of the crystallographic analysis for both compounds are summarized in Table I. Three strong, well-separated reflections were measured every 50 reflections to check for crystal movement or decomposition. Absorption (based on *ψ*-scan data; [Cr^{II}(nic-N)₂(H₂O)₄], lamellar; [Zn^{II}(nic-N)₂(H₂O)₄], ellipsoidal), Lorentz, and polarization corrections were applied in the usual manner.

The structure of [Cr^{II}(nic-N)₂(H₂O)₄] was solved by direct methods by using the SHELXTL-84 program.¹⁶ The refined atom parameters from the Cr/Zn nicotinate structure reported by Cooper et al.¹² were entered as initial positions for Zn, N, C(1)–C(6), and O(1)–O(4) in the [Zn^{II}(nic-N)₂(H₂O)₄] structure solution before the least-squares refinement. All non-hydrogen atoms were assigned anisotropic thermal parameters, and these as well as positional parameters were refined by least squares. A full-matrix least-squares refinement minimizing $\sum w(|F_o| - |F_c|)^2$ was used. All hydrogen atoms were located on a ΔF map. They were included with isotropic thermal parameters set at approximately 20% larger than the corresponding heavy atom, and all parameters were refined until

Table II. Electronic Spectral Data^a

complex	λ_{\max} , nm
trans-[Cr ^{II} (nic-N) ₂ (H ₂ O) ₄]	267, 340 (sh), 380 (sh), 585 (broad)
trans-[Cr ^{II} _{0.58} Zn ^{II} _{0.42} (nic-N) ₂ (H ₂ O) ₄]	267, 340 (sh), 380 (sh), 580 (broad sh)
trans-[Zn ^{II} (nic-N) ₂ (H ₂ O) ₄]	265

^a Recorded by the diffuse reflectance technique.

(14) (a) Haupt, G. W. *J. Res. Natl. Bur. Stand.* **1952**, *40*, 2331. (b) Deutsch, E.; Taube, H. *Inorg. Chem.* **1968**, *7*, 1532.

(15) Campana, C. F.; Sheperd, D. F.; Litchman, W. N. *Inorg. Chem.* **1980**, *20*, 4039.

(16) Sheldrick, G. *SHELXTL*; Nicolet Analytical Instruments: Madison, WI, 1984.

the agreement factors *R* and *R_w*¹⁷ had the final values shown in Table I. ORTEP views of trans-[Zn^{II}(nic-N)₂(H₂O)₄] and trans-[Cr^{II}(nic-N)₂(H₂O)₄].

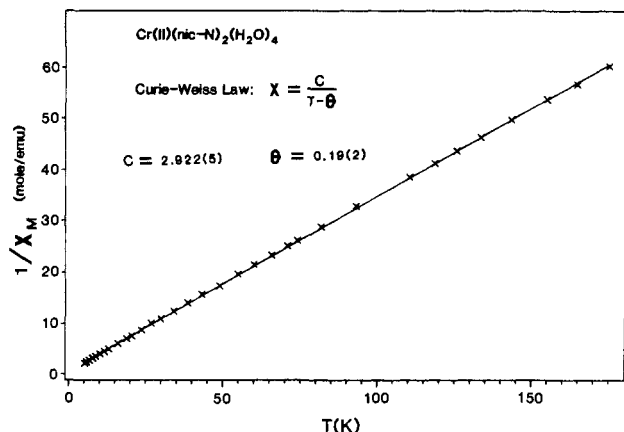


Figure 3. Curie-Weiss plot of the magnetic susceptibility data for $\text{Cr}^{\text{II}}(\text{nic})_2(\text{H}_2\text{O})_4$.

$(\text{H}_2\text{O})_4$] are shown in Figures 1 and 2, respectively.

Results

Attempts to synthesize the chromium(II) dinicotinate compound reported by Cooper et al.¹² resulted in a yellow-green solid, not the dull yellow colored solid reported. The yellow-green solid was obtained under conditions identical with those reported,¹² except that a zinc-free chromous solution was used in the synthesis. The lime-green solid yielded an excellent chemical analysis for C, H, N, and Cr for the formula $\text{Cr}(\text{nic-N})_2(\text{H}_2\text{O})_4$. The features of the ultraviolet-visible diffuse reflectance spectrum for this compound, summarized in Table II, are also consistent with the maxima previously reported by Cooper et al. for this compound.¹² The marked difference in color for the compound we obtained was perplexing; thus, it was further characterized.

A temperature profile of the magnetic susceptibility for this compound, shown in Figure 3, obeyed the Curie-Weiss law over the temperature range 6–175 K. The Curie constant obtained results in an effective magnetic moment of $4.83 \mu_{\text{B}}$ which agrees very well with the spin-only value expected for high-spin chromium(II), $4.90 \mu_{\text{B}}$. This result is consistent with the ligand field present (four aquo ligands and two pyridyl nitrogen ligands) since, generally, only chromium(II) complexes with very strong ligand fields, such as $[\text{Cr}(\text{CN})_6]^{4-}$, $[\text{Cr}(\text{bpy})_3]^{2+}$, $[\text{Cr}(\text{phen})_3]^{2+}$, or $[\text{Cr}(\text{TPP})(\text{py})_2]$, exhibit low-spin electronic configurations.¹⁸ The low magnetic moment reported previously for this compound,¹² $3.18 \mu_{\text{B}}$, suggested that the compound was magnetically diluted by isomorphous substitution of zinc(II). (The zinc(II) was introduced to the reaction mixture because of the use of zinc amalgam to generate chromium(II) from chromium(III)).

In order to test this hypothesis, we added a 0.5 equiv of zinc(II) to our (zinc-free) chromium(II) stock solution and used this in the synthesis of the chromium(II) nicotinic acid compound. A dull yellow solid was obtained that contained only 8.13% weight Cr. This corresponds to 58.4 mol% Cr and 41.7 mol% Zn, by difference. The chemical analysis for C, H, and N that was obtained agreed well with calculated percentages based on the molecular weight for $[\text{Cr}_{0.58}\text{Zn}_{0.42}(\text{nic-N})_2(\text{H}_2\text{O})_4]$. The ultraviolet-visible diffuse reflectance spectrum for this compound was the same as that reported by Cooper et al.¹² and very similar to that we obtained for the pure chromium(II) compound except that no minimum was observed at 525 nm (Table II). This may account for the yellow color of the mixed Cr-Zn solid. The room-temperature magnetic moment for our mixed chromium-zinc compound was determined to be $3.53 \mu_{\text{B}}$, which corresponds to 53 mol% Cr(II). This value is close to the chromium analysis for this compound (58.4 mol% Cr(II)).

Table III. X-ray Diffraction Powder Patterns

$\text{Zn}(\text{nic-N})_2(\text{H}_2\text{O})_4$		$\text{Cr}_{0.58}\text{Zn}_{0.42}(\text{nic-N})_2(\text{H}_2\text{O})_4$		$\text{Cr}(\text{nic-N})_2(\text{H}_2\text{O})_4$	
<i>d</i> , Å	rel intens ^a	<i>d</i> , Å	rel intens	<i>d</i> , Å	rel intens
7.47	w	7.48	w	7.97	vw
6.55	s	6.56	s	6.53	m
6.05	s	6.05	s	6.07	s
5.34	vw	5.34	vw	5.83	w
4.25	m	4.23	m	5.41	w
3.96	m	3.93	m	4.34	m
3.89	w			4.17	w
3.55	vw	3.57	vw	3.73	w
3.45	s	3.45	s	3.59	m
3.34	m-w	3.34	m-w	3.25	m
3.05	w	3.06	w	3.18	m
3.02	w	3.02	w	3.11	m

^a s = strong; m = medium; w = weak.

In order to determine independently whether zinc(II) forms a dinicotinate complex, zinc(II) was added to 2 equiv of nicotinate at pH 6 as described in the Experimental Section. The clear plates obtained were analyzed for C, H, and N; the results were consistent with the $[\text{Zn}^{\text{II}}(\text{nic-N})_2(\text{H}_2\text{O})_4]$ formulation.

The results of the crystal structure analysis on the pure Zn(II) compound confirm this formulation (Figure 1). Indeed, the zinc(II)-dinicotinate compound is isomorphous with the structure of the (presumably) mixed Cr(II)/Zn(II)-dinicotinate compound reported by Cooper et al.,¹² and in most respects the two structures are virtually identical. The Zn(II) structure consists of discrete nonclassical zwitterions of *trans*- $[\text{Zn}(\text{nic-N})_2(\text{H}_2\text{O})_4]$ that crystallize in the C_2 space group (Figure 1). This is manifested in the C_2 rotation axis that bisects the O(3)-Cr-O(3a) bond angle. This structure is almost isomorphous with the structure reported by Anagnostopoulos et al.¹⁹ for *trans*- $[\text{Co}^{\text{II}}(\text{nic-N})_2(\text{H}_2\text{O})_4]$ except that the Co structure is confined to the $C2/m$ space group. A comparison of X-ray powder diffraction data for *trans*- $[\text{Zn}(\text{nic-N})_2(\text{H}_2\text{O})_4]$ (Table III) and $[\text{Ni}^{\text{II}}(\text{nic-N})_2(\text{H}_2\text{O})_4]$ ¹³ suggests that the nickel dinicotinate is isomorphous to the zinc dinicotinate.

The M-N distance reported here for the pure Zn compound (2.156 (4) Å) is slightly longer than that for the mixed Cr(II)/Zn(II) structure (2.135 (8) Å).¹² There are also small differences in the M-OH₂ distances: 2.08 (1) and 2.20 (1) Å reported here for the Zn(II) structure compared to 2.10 (2) and 2.16 (2) Å for the Zn(II)/Cr(II) structure.¹² The estimated standard deviation for all bond distances is ≤ 0.01 Å. All hydrogen positions are reasonable. Angles formed by the ligated atoms around the zinc atom range from 87.1 (4) to 92.3 (4)°. The zinc atom is thus found in a slightly distorted octahedral environment. Hydrogen bonding within the crystal lattice of $[\text{Zn}^{\text{II}}(\text{nic-N})_2(\text{H}_2\text{O})_4]$ is similar to that reported for the mixed Zn(II)-Cr(II) structure.¹² Carboxyl oxygen O(2) is hydrogen-bonded to water oxygen O(4) (2.71 Å) on the adjacent molecule at 0, 0, 1 - z. Carboxyl oxygen O(1) is hydrogen-bonded to O(3) (2.79 Å) at 0.5 - x, 0.5 - y, 2.0 - z and O(4) (2.59 Å) at x - 0.5, y - 0.5, 1.0 + z. Water oxygen O(3) is also intramolecularly hydrogen-bonded to O(2) (2.71 Å).

The pure zinc(II) nicotinic acid compound and the mixed chromium(II)/zinc(II) nicotinic acid compound prepared in this laboratory were found to be isomorphous by comparing X-ray powder diffraction data (Table III). Comparison of the *d* spacings and intensities suggests the complexes are isostructural. In contrast, the X-ray powder data for $[\text{Cr}^{\text{II}}(\text{nic-N})_2(\text{H}_2\text{O})_4]$ (Table III) indicate this latter compound is not isomorphous to $[\text{Zn}^{\text{II}}(\text{nic-N})_2(\text{H}_2\text{O})_4]$ and $[\text{Cr}^{\text{II}}_{0.58}\text{Zn}^{\text{II}}_{0.42}(\text{nic-N})_2(\text{H}_2\text{O})_4]$.

Chromium(II) dinicotinate tetrahydrate was successfully crystallized, and the results of a single-crystal X-ray structural analysis confirm that it is found as discrete molecules of $[\text{Cr}^{\text{II}}(\text{nic-N})_2(\text{H}_2\text{O})_4]$ with the two nicotinate rings bound to the chromium in a *trans* arrangement through the nitrogen atoms

(17) $R = \sum ||F_o| - |F_c|| / \sum |F_o|$; $R_w = [\sum w(|F_o| - |F_c|)^2 / \sum w|F_o|^2]^{1/2}$.

(18) (a) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*, 4th ed.; Wiley: New York, 1980; p 724 and references therein. (b) Scheidt, W. R.; Brinegar, A. C.; Kirner, J. F.; Reed, C. A. *Inorg. Chem.* **1979**, *18*, 3610.

(19) Anagnostopoulos, A.; Drew, M. G. B.; Walton, R. A. *Chem. Commun.* **1969**, 1241.

Table IV. Interatomic Bond Distances and Angles in trans-[Zn^{II}(nic-N)₂(H₂O)₄]

bond	d, Å	angle	deg	angle	deg
Zn-N	2.156 (4)	N-Zn-N(a)	177.2 (9)	N-C(5)-C(4)	122.9 (6)
Zn-O(3)	2.08 (1)	N-Zn-O(3)	87.1 (4)	C(1)-C(2)-C(3)	118.5 (6)
Zn-O(4)	2.20 (1)	N-Zn-O(3a)	90.9 (4)	C(1)-C(2)-C(6)	118.6 (6)
N-C(1)	1.35 (1)	N-Zn-O(4)	92.3 (4)	C(2)-C(3)-C(4)	118.6 (4)
N-C(5)	1.33 (1)	N-Zn-O(4a)	89.7 (4)	C(3)-C(2)-C(6)	122.7 (4)
C(1)-C(2)	1.386 (6)	O(4)-Zn-O(3)	90.6 (4)	C(3)-C(4)-C(5)	119.0 (6)
C(2)-C(3)	1.38 (1)	O(4)-Zn-O(3a)	176.7 (3)	C(2)-C(6)-O(1)	117.5 (6)
C(2)-C(6)	1.51 (1)	O(4)-Zn-O(4a)	90.4 (6)	C(2)-C(6)-O(2)	116.9 (5)
C(3)-C(4)	1.38 (1)	Zn-N-C(1)	120.0 (4)	O(1)-C(6)-O(2)	125.4 (7)
C(4)-C(5)	1.386 (6)	Zn-N-C(5)	122.2 (4)		
C(6)-O(1)	1.270 (6)	C(1)-N-C(5)	117.6 (4)		
C(6)-O(2)	1.24 (1)	N-C(1)-C(2)	123.1 (6)		

Table V. Interatomic Bond Distances and Angles in trans-[Cr^{II}(nic-N)₂(H₂O)₄]

bond	d, Å	angle	deg	angle	deg
Cr-N	2.128 (2)	N-Cr-N(a)	180.0 (1)	N-C(1)-C(2)	123.2 (3)
Cr-O(1)	2.471 (3)	N-Cr-O(1)	92.7 (1)	N-C(5)-C(4)	123.3 (2)
Cr-O(2)	2.039 (2)	N-Cr-O(1a)	87.3 (1)	C(1)-C(2)-C(3)	118.1 (2)
N-C(1)	1.341 (3)	N-Cr-O(2)	87.8 (1)	C(1)-C(2)-C(6)	119.9 (3)
N-C(5)	1.350 (4)	N-Cr-O(2a)	92.2 (1)	C(2)-C(3)-C(4)	119.3 (3)
C(1)-C(2)	1.381 (4)	O(1)-Cr-O(2)	95.6 (1)	C(3)-C(2)-C(6)	122.0 (2)
C(2)-C(3)	1.382 (4)	O(1)-Cr-O(2a)	84.4 (1)	C(3)-C(4)-C(5)	118.9 (3)
C(2)-C(6)	1.515 (3)	O(1)-Cr-O(1a)	180.0 (1)	C(2)-C(6)-O(3)	117.5 (2)
C(3)-C(4)	1.384 (3)	O(2)-Cr-O(2a)	180.0 (1)	C(2)-C(6)-O(4)	117.1 (3)
C(4)-C(5)	1.358 (4)	Cr-N-C(1)	123.4 (2)	O(3)-C(6)-O(4)	125.3 (2)
C(6)-O(3)	1.238 (4)	Cr-N-C(5)	119.4 (2)		
C(6)-O(4)	1.261 (3)	C(1)-N-C(5)	117.3 (2)		

Table VI. Positional and Equivalent Isotropic Thermal Parameters of trans-[Zn^{II}(nic-N)₂(H₂O)₄]

atom	x/a	y/b	z/c	1000U _{eq} ^a , Å ²
Zn	0	0	0	21 (1)
N	0.1488 (3)	0.008 (2)	0.246 (1)	22 (2)
C(1)	0.1483 (4)	0.004 (3)	0.404 (1)	21 (1)
C(2)	0.2408 (4)	-0.003 (3)	0.567 (1)	20 (2)
C(3)	0.3380 (4)	0.004 (4)	0.567 (1)	28 (2)
C(4)	0.3392 (4)	0.001 (3)	0.405 (1)	30 (2)
C(5)	0.2430 (5)	0.001 (3)	0.248 (1)	27 (2)
C(6)	0.2310 (5)	-0.0005 (3)	0.737 (1)	27 (2)
O(1)	0.3168 (3)	0.008 (2)	0.884 (1)	35 (2)
O(2)	0.1391 (3)	0.006 (3)	0.720 (1)	40 (2)
O(3)	0.0538 (6)	0.216 (1)	0.891 (1)	14 (3)
O(4)	-0.0663 (7)	-0.225 (2)	0.104 (1)	38 (3)
H(1)	0.0807	0.0037	0.4041	29 ^b
H(3)	0.4036	0.0080	0.6779	37
H(4)	0.4058	-0.0007	0.4015	41
H(5)	0.2444	-0.0022	0.1362	33
H(31)	-0.0066	0.2984	0.8128	14
H(32)	0.0846	0.1567	0.8202	14
H(41)	-0.0094	-0.3138	0.1810	55
H(42)	-0.1218	-0.2969	0.0032	55

^a Equivalent isotropic U defined as one-third of the trace of the orthogonalized U_{ij} tensor. ^b U_{eq} for all hydrogens are $1.2U_{eq}$ of the attached atom.

(Figure 2). The complex crystallizes in the $P\bar{1}$ space group where one molecule comprises the unit cell contents and an inversion center is located at the chromium atom. Bond distances and angles for trans-[Cr^{II}(nic-N)₂(H₂O)₄] are found in Table V while positional and equivalent isotropic thermal parameters appear in Table VII.

A salient feature of the structure is the elongated Cr-O(1) bond, 2.471 (3) Å, as compared to the Cr-O(2) bond, 2.039 (2) Å, and the Cr-N bond, 2.128 (2) Å. This elongated tetragonal arrangement is commonly observed for Jahn-Teller-"active" high-spin chromium(II).^{18a} The Cr-N distance (2.128 (2) Å) is similar to the values found for low-spin-Cr(II)-pyridine bonds (2.141 (8) and 2.121 (8) Å)^{18b} and high-spin-Cr(II)-2,6-dimethylpyridine bonds (2.111 (3) Å).²⁰ Estimated standard deviations (esd) for

Table VII. Positional and Equivalent Isotropic Thermal Parameters of trans-[Cr^{II}(nic-N)₂(H₂O)₄]

atom	x/a	y/b	z/c	1000U _{eq} ^a , Å ²
Cr	0	0	0	21 (1)
O(1)	0.2021 (3)	0.2421 (3)	-0.0871 (3)	35 (1)
O(2)	0.2682 (3)	-0.2558 (3)	0.0665 (2)	36 (1)
N	0.0601 (3)	-0.1260 (3)	0.2444 (3)	22 (1)
C(1)	-0.0905 (4)	-0.1691 (4)	0.3836 (3)	21 (1)
C(2)	-0.0484 (4)	-0.2575 (4)	0.5414 (3)	20 (1)
C(3)	0.1559 (4)	-0.2940 (4)	0.5567 (3)	25 (1)
C(4)	0.3121 (4)	-0.2481 (4)	0.4143 (3)	28 (1)
C(5)	0.2594 (4)	-0.1669 (4)	0.2632 (3)	25 (1)
C(6)	-0.2264 (4)	-0.3056 (4)	0.6920 (3)	23 (1)
O(3)	-0.4103 (3)	-0.2509 (3)	0.6684 (2)	38 (1)
O(4)	-0.1741 (3)	-0.4007 (3)	0.8311 (2)	31 (1)
H(1)	-0.2345	-0.1370	0.3730	21 ^b
H(3)	0.1890	-0.3504	0.6650	25
H(4)	0.4553	-0.2732	0.4222	28
H(5)	0.3692	-0.1371	0.1649	26
H(21)	0.2682	-0.3656	-0.0050	31
H(22)	0.3637	-0.2623	-0.1354	31
H(11)	0.2107	0.2661	-0.0141	31
H(12)	0.1165	0.3384	-0.1084	31

^a Equivalent isotropic U defined as one-third of the trace of the orthogonalized U_{ij} tensor. ^b U_{eq} for all hydrogens were set at the indicated values.

all interatomic bond distances are ≤ 0.004 Å, while esd's for all bond angles are $\leq 0.3^\circ$. Interbond angles around the tetragonally distorted chromium(II) center vary from 84.4 (1) $^\circ$ for the angle O(1)-Cr-O(2a) to 95.6 (1) $^\circ$ for the angle O(1)-Cr-O(2).

Discussion

The lime green crystalline solid that forms after addition of aqueous chromous chloride to a solution of nicotinate at pH 6 is shown by X-ray crystallography to consist of discrete molecules of [Cr^{II}(nic)₂(H₂O)₄] where the nicotinate ligands are coordinated in a trans configuration through the pyridyl nitrogen and the water molecules occupy the equatorial sites. The molecule is best described as a nonclassical zwitterion.¹⁹

The results of the magnetic susceptibility temperature profile for trans-[Cr^{II}(nic-N)₂(H₂O)₄] (Figure 3) indicate the molecule contains four unpaired electrons, which is expected for a high-spin chromium(II) (d^4) species. However, the unusual electronic spectrum for this molecule raised the question as to whether

(20) Eremenko, I. L.; Pasynskii, A. A.; Kalinnikov, V. T.; Aleksandrov, G. G.; Struchkov, Yu. T. *Inorg. Chim. Acta* 1981, 54, L85.

[Cr(nic-*N*)₂(H₂O)₄] might best be described as a chromium(III) nicotinate-radical species. In the case of strong ferromagnetic coupling, the Cr(III)–nic[•] arrangement would also give the observed magnetic susceptibility results. The single-crystal X-ray analysis confirms the high-spin chromium(II) electronic configuration because of the observed (pseudo) Jahn–Teller distortion, which is expected for high-spin Cr(II) but not for Cr(III). The Jahn–Teller distortion is manifested as a tetragonal elongation along the O(1)–Cr–O(1a) axis (Figure 2).

An interesting property of this chromous dinicotinate complex is its remarkable stability in air. A few air-stable dinuclear chromium(II) complexes have been reported recently. Cotton and co-workers^{21,22} demonstrated that Cr₂(mhp)₄ (where mhp = 2-hydroxy-6-methylpyridinate) is stable in dry air indefinitely and in moist air for ca. 10 days. Subsequently, Ardon et al. reported that the binuclear chromous glycine complexes [Cr₂(gly)₄X₂]X₂ (where gly = zwitterionic glycine and X = Br[−] or Cl[−]), are *indefinitely* stable toward atmospheric oxidation in the solid state.²³ The mononuclear chromous dinicotinate complex reported here is also *indefinitely* stable in air. The air stability of the zwitterionic chromous glycine complexes was attributed to tight hydrogen bonding within the crystal lattice.²³ We believe the air stability of *trans*-[Cr^{II}(nic-*N*)₂(H₂O)₄] is also due, in part, to the extensive hydrogen bonding present in the crystal lattice (*vide supra*).

The air stability of *trans*-[Cr^{II}(nic-*N*)₂(H₂O)₄] may also be due in part to the strong metal–ligand interaction present as evidenced by the relatively strong absorption band(s) present between ca. 290 and 500 nm (Table II). Due to the reducing nature of the chromium(II) metal center, they are probably metal to ligand charge-transfer (MLCT) transitions. The very broad, relatively weak absorption band centered at 585 nm present in the ultraviolet–visible diffuse reflectance spectrum of *trans*-[Cr^{II}(nic-*N*)₂(H₂O)₄] is most likely d–d in origin. If the complex is approximated as having D_{4h} symmetry, this band can be assigned to the superimposed transitions ⁵B_{1g} → ⁵B_{2g} and ⁵B_{1g} → ⁵E_g.²⁴ This assignment is tentative due to the nature of the diffuse reflectance technique.

The structural results for [Zn^{II}(nic-*N*)₂(H₂O)₄] show that this complex also consists of discrete zwitterions with the nicotinate ligands arranged in a *trans* fashion. It is interesting that the mixed [Cr^{II}/Zn^{II}(nic-*N*)₂(H₂O)₄] structure reported by Cooper et al. (as [Cr^{II}(nic-*N*)₂(H₂O)₄]) is isomorphous to the pure zinc compound reported here. Considering the effective magnetic moment reported by Cooper et al.,¹² 3.18 μ_B, the compound is best described as *trans*-[(Cr_{0.42}Zn_{0.58})(nic-*N*)₂(H₂O)₄]. The structural results reported for the mixed-metal complex¹² do not indicate that the chromium(II) exhibits a (pseudo-) Jahn–Teller distortion (tetragonal elongation) as expected for high-spin chromium(II). This suggests that the mixed-metal structure is a superposition of the *trans*-[Zn^{II}(nic-*N*)₂(H₂O)₄] structure and either a dynamically distorted Cr(II) structure or a disordered statically distorted Cr(II) structure.

The crystallization of *trans*-[Cr^{II}(nic-*N*)₂(H₂O)₄] from aqueous solution proceeds via an intermediate, a red–pink precipitate that forms immediately after addition of chromium(II) to the nicotinate solution. The insolubility and color of the precipitate suggest it may be the carboxyl-bridged chromium(II) dinuclear compound of nicotinate. (This is supported by the observation that no red–pink precipitate forms when nicotinamide or methyl nicotinate is substituted for nicotinic acid.) That the monomeric Cr(II) nicotinate species is favored over the carboxyl-bridged dimeric compound is a surprising observation, given the numerous carboxylato-bridged chromium(II) dinuclear compounds known and

the propensity of chromium(II) to form these Cr–Cr quadruply bonded species.²² However, this may be merely a reflection of the stability of the zwitterionic compound in the crystal lattice. Thus, it is not surprising that practically the entire first-row transition series divalent metal ions have been shown to adopt this general structure with nicotinate; the list includes Co(II),²⁰ Ni(II),¹³ Mn(II),¹² Cu(II),²⁵ Fe(II),²⁵ and of course Cr(II) and Zn(II). Another point to be made is that the Cr–Cr bond is very sensitive to the nature of the bridging and axial ligands, due to the shallow potential energy curve for this bond.^{22,23} As dem-

onstrated for [Cr₂(O₂CCH₂NH₃)₄Br₂·4H₂O],²³ the Cr–Cr bond can undergo facile scission in solution, unlike analogous Mo₂⁴⁺ complexes, which remain intact in solution. Thus, conversion of the proposed dichromium tetraniocinate dinuclear intermediate to the observed mononuclear chromous dinicotinate is supported by known dinuclear chromium(II)–carboxylate chemistry.

It is interesting to note that under the conditions present for the synthesis of *trans*-[Cr^{II}(nic-*N*)₂(H₂O)₄], reduction of nicotinate by aqueous chromium(II) is not observed. Our recent report¹ on the synthesis of *cis*- and *trans*-H[Cr^{III}(mal)₂(nic-*N*)₂] demonstrated that chromium(II) does reduce nicotinate under conditions similar to those reported here except that 2 equiv of malonate was present. These complexes were formed directly via ligand reduction “redox trapping”.¹ In one of the classic studies on bridging ligand electron transfer, Gould and Taube⁸ indicated that, in acid, aqueous chromium(II) reduces free nicotinic acid to a small extent (20% Cr(II) consumed after 40 min). Subsequently, a study on the reduction of pyridinecarboxylic acids with Eu(II) (aq), Cr(II) (aq), or V(II) (aq) indicated that nicotinic acid was not reduced by Cr(II) (aq) in acid.²⁶ The one-electron-reduction potentials of nicotinic acid and the closely related nicotinamide are −1.26 V (pH 7, 25 °C) and −1.20 V (pH 7, 25 °C), respectively.^{10,27,28} On the basis of these reduction potentials, it is not expected that Cr(II) (aq) would reduce nicotinic acid (Cr^{III/II} E° = −0.41 V). But, when the pyridyl nitrogen is “blocked”, these species are more easily reduced (more positive reduction potential). For example, the one-electron-reduction potential for *N*-methylnicotinamide²⁷ is E° = −0.42 V (pH 7, 25 °C). On the basis of the similarity of the reduction potentials for nicotinamide and nicotinic acid, the reduction potential of *N*-methylnicotinic acid should be similar to that for *N*-methylnicotinamide, if not slightly more negative. A similar reduction potential for nicotinic acid might be expected when a metal ion, such as Cr(II) (aq), is coordinated by (“blocks”) the pyridyl nitrogen. Thus, coordination of nicotinic acid to Cr(II) (aq) through the pyridyl nitrogen results in a system that is “poised” toward the intramolecular electron transfer to give a chromium(III) ion radical species, but apparently not enough driving force is present. The observance of MLCT bands in high-spin *trans*-[Cr^{II}(nic-*N*)₂(H₂O)₄] supports this hypothesis. This is also in accord with the observance by Gould and Taube⁸ of no radical cation or chemical mechanism^{9,11} in the reduction of nicotinoylpentaaminecobalt(III) by Cr(II) (aq).⁸ Addition of malonate to Cr(II) (aq) apparently provides the driving force for reduction of nicotinic acid by chelating Cr(II) and raising the oxidation potential of Cr(II) (E° for Cr^{III/II} is more negative).

Although Cr(III) and nicotinic acid have been implicated in glucose metabolism, there has been no rationale for their coexistence.³ A redox mode of action for GTF has generally not been considered,³ especially since nicotinic acid is not thought to act as a bridging ligand in inner-sphere electron-transfer reactions.⁸ But our observance of a poised redox couple for Cr(II/III)–nic-*N*/nic-*N*[•] suggests the possibility of a redox role for Cr–nicotinic acid in glucose metabolism.

(21) Cotton, F. A.; Fanwick, P. E.; Niswander, R. H.; Sekutowski, J. C. *J. Am. Chem. Soc.* **1978**, *100*, 4725.

(22) Cotton, F. A.; Walton, R. A. *Multiple Bonds Between Metal Atoms*; Wiley: New York, 1982.

(23) Ardon, M.; Bino, A.; Cohen, S.; Felthouse, T. R. *Inorg. Chem.* **1984**, *23*, 3450. Kok, R. A.; Hall, M. B. *Inorg. Chem.* **1985**, *24*, 1542.

(24) (a) Holmes, O. G.; McClure, D. S. *J. Chem. Phys.* **1957**, *26*, 1686. (b) Larkworthy, L. F.; Tabatabai, J. M. *J. Chem. Soc., Dalton Trans.* **1976**, 814.

(25) Unpublished results. The Cu(II) dinicotinate was recently shown by single-crystal X-ray crystallography to be isomorphous to the Cr(II) dinicotinate structure reported here.

(26) Vachnon-Astra, E.; Katakis, D. *J. Am. Chem. Soc.* **1973**, *95*, 3814.

(27) Brühlmann, U.; Hayon, E. *J. Am. Chem. Soc.* **1974**, *96*, 6169.

(28) Kolthoff, I. M.; Lingane, J. J. *Polarography*; Interscience: New York, 1946; p 421.

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Registry No. *trans*-[Cr^{II}(nic-*N*)₂(H₂O)₄], 89230-21-7; *trans*-[Zn^{II}(nic-*N*)₂(H₂O)₄], 34383-87-4.

Supplementary Material Available: Listings of anisotropic parameters for *trans*-[Cr^{II}(nic-*N*)₂(H₂O)₄] and *trans*-[Zn^{II}(nic-*N*)₂(H₂O)₄] (2 pages). Ordering information is given on any current masthead page.

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

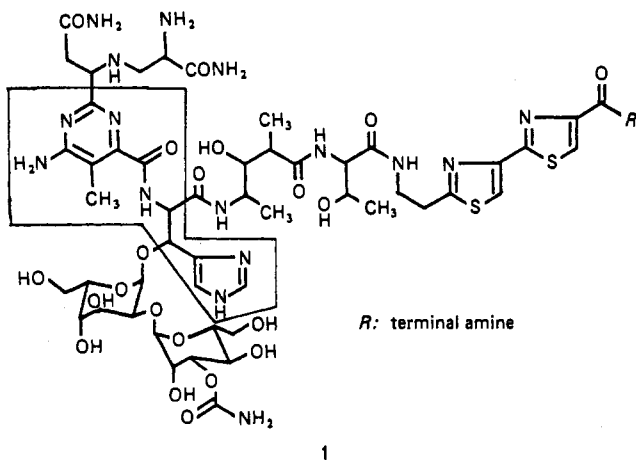
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As part of a synthetic analogue approach to metallobleomycins, copper complexes of two peptides, PypepH and PmppepH, resembling fragments of the metal-chelating section of bleomycins (BLM) have been isolated. The structures of two synthetic analogues have been determined by X-ray crystallography. [Cu(Pypep)(CH₃COO)]₂·1.46H₂O (**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) Å³, and *Z* = 4. The structure of **4** was refined to *R* = 5.15% on the basis of 1594 unique data (*F*_o² > 3σ(*F*_o²)). 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(Pmppep)(CH₃COO)(H₂O)] (**5**) crystallizes in the space group P2₁/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) Å³, 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 PmppepH 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*_{||} 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 Fe²⁺ and Cu²⁺ 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



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 ab-

sorption 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 CH₃ 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 restricted 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

- (1) (a) Dabrowiak, J. C. *Adv. Inorg. Biochem.* **1983**, *4*, 69. (b) Dabrowiak, J. C. *Met. Ions Biol. Syst.* **1980**, *11*, 305.
- (2) Umezawa, H.; Takita, T. *Struct. Bonding (Berlin)* **1980**, *40*, 73.
- (3) *Bleomycin: Chemical, Biochemical and Biological Aspects*; Hecht, S. M., Ed.; Springer-Verlag: New York, 1979.
- (4) *Bleomycin: Current Status and New Developments*; Carter, S. K., Crooke, S. T., Umezawa, H., Eds.; Academic: New York, 1978.
- (5) Horwitz, S. B.; Sausville, E. A.; Peisach, J. In ref 3, p 170, and references cited therein.
- (6) (a) Dabrowiak, J. C.; Tsukayama, M. *J. Am. Chem. Soc.* **1981**, *103*, 7543. (b) Dabrowiak, J. C. *J. Inorg. Biochem.* **1980**, *13*, 317. (c) Dabrowiak, J. C.; Greenaway, F. T.; Santillo, F. S. In ref 3, p 137, and references cited therein. (d) Sugiura, Y.; Takita, T.; Umezawa, H. *Met. Ions Biol. Syst.* **1985**, *19*, 81. (e) Sugiura, Y. *J. Am. Chem. Soc.* **1980**, *102*, 5208, 5216.
- (7) (a) Hori, M. In ref 3, p 195, and references cited therein. (b) Takeshita, M.; Grollman, A. P. In ref 3, p 207, and references cited therein.
- (8) Itaka, Y.; Nakamura, H.; Nakatani, T.; Muraoka, Y.; Fuji, A.; Takita, T.; Umezawa, H. *J. Antibiot.* **1978**, *31*, 1070.
- (9) (a) Umezawa, H.; Takita, T.; Sugiura, Y.; Otsuka, M.; Kobayashi, S.; Ohno, M. *Tetrahedron* **1984**, *40*, 501. (b) Sugiura, Y.; Suzuki, T.; Otsuka, M.; Kobayashi, S.; Ohno, M.; Takita, T.; Umezawa, H. *J. Biol. Chem.* **1983**, *258*, 1328.
- (10) Otsuka, M.; Yoshida, M.; Kobayashi, S.; Ohno, S.; Sugiura, Y.; Takita, T.; Umezawa, H. *J. Am. Chem. Soc.* **1981**, *103*, 6986.
- (11) (a) Henichart, J.; Bernier, J.; Houssin, R.; Lohez, M.; Kenani, A.; Catteau, J. *Biochem. Biophys. Res. Commun.* **1985**, *126*, 1036. (b) Henichart, J.; Houssin, R.; Bernier, J.; Catteau, J. *J. Chem. Soc., Chem. Commun.* **1982**, 1295.

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