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Structural and Spectroscopic Characterization of $V^{V}O$–Imidazole Complexes

The structure and spectroscopy of vanadium coordination compounds is receiving increased attention in light of the recent discoveries of vanadium-dependent enzymes.[1] To understand fully the role of vanadium in biological systems, the relationships between structure, spectroscopy, and reactivity must be elucidated. To this end we have undertaken the synthesis and complete characterization of vanadium coordination compounds which have presumed structural and/or spectroscopic similarities to naturally occurring vanadium complexes. In particular, we have focused on the active site of vanadium bromoperoxidase[1] and the role of vanadium in tunicates[1] and the mushroom *Amanita muscaria*.[1] The tunicates and *A. muscaria* are known to accumulate vanadium to high concentrations, relative to the surrounding environment, possibly utilizing siderophore type molecules which contain noninnocent ligands such as hydroxamates and/or hydroxy-DOPA. Vanadium haloperoxidases, which have been isolated from several species of marine algae and a terrestrial lichen, catalyze the reaction shown as eq 1. These haloperoxidases differ from the

$$RH + H^+ + X^- + H_2O_2 \rightarrow RX + 2H_2O \qquad (1)$$

$$X = Cl^-, Br^-, I^-$$

more widely recognized heme enzymes in three important ways: First, they use vanadium in place of iron. Second, they do not contain a prosthetic group such as a porphyrin. Third, the catalytic cycle apparently may not require metal-centered redox conversions.[2] Thus, the vanadium haloperoxidases represent a unique biological approach to the activation of halides using hydrogen peroxide. Several spectroscopic techniques have been utilized to probe the structure of the vanadium site in vanadium bromoperoxidase.[3-6] The structure that is emerging for the active site contains a mononuclear vanadium(V) that is likely found as either a monooxovanadium(V) (VO^{3+}) or a vanadate ester [$VO(OR)^{2+}$].

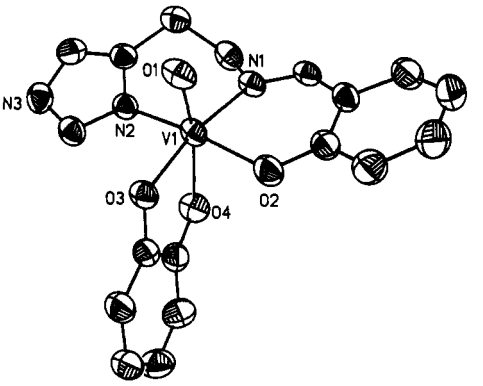

Figure 1. ORTEP diagram of **1**, showing 50% probability ellipsoids. Important bond lengths (Å) and angles (deg) are as follows: V1–O1 = 1.591 (3), V1–O2 = 1.912 (3), V1–O3 = 1.898 (2), V1–O4 = 2.193 (3), V1–N1 = 2.119 (3), V1–N2 = 2.119 (3); O1–V1–O2 = 103.1 (1), O1–V1–O3 = 96.6 (1), O1–V1–O4 = 169.7 (1), O1–V1–N1 = 95.4 (1), O1–V1–N2 = 92.8 (1), O2–V1–O3 = 88.6 (1), O2–V1–O4 = 84.9 (1), O2–V1–N1 = 86.3 (1), O2–V1–N2 = 163.1 (1), O3–V1–O4 = 76.9 (1), O3–V1–N1 = 167.8 (1), O3–V1–N2 = 95.1 (1), O4–V1–N1 = 91.5 (1), O4–V1–N2 = 80.0 (1).

Imidazole coordination has been inferred on the basis of ESEEM measurements on the reduced catalytically inactive enzyme.[7] It is probable that the balance of the coordination sphere is rich in carboxylate ligands.[6,8] Below we report the structural and spectroscopic characterization for a series of complexes which contain the $V^{V}O$–imidazole moiety and oxo, catecholato, or hydroximato ligands. The large ^{51}V NMR chemical shift range for this homologous series is unprecedented for vanadium complexes with oxygen and nitrogen donor ligands.

Although high-valent vanadium complexes containing the tris(pyrazolyl)borato ligand have appeared,[9] crystallographically characterized V(V)–*imidazole* compounds, which are not limited to the sterically constrained facial coordination, have not been reported. Such materials may provide models for both the structure and reactivity of this unique vanadoenzyme. The neutral $V^{V}O(SALIMH)(CAT)$[10] (**1**) can be prepared from $V^{IV}O(SALIMH)ACAC$[11] (**2**) by the addition of 1 equiv of catechol to an

(1) For recent reviews of biologically relevant vanadium chemistry, see: (a) *Vanadium in Biological Systems*; Chasteen, N. D., Ed.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1990. (b) Butler, A.; Carrano, C. J. *Coord. Chem. Rev.* **1991**, *109*, 61. (c) Rehder, D. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 148.
(2) Vanadium(IV) has not been observed by EPR spectroscopy during the catalytic cycle of V–BrPO; for a discussion of this point, see: Wever, R.; Krenn, B. E. In *Vanadium in Biological Systems*; Chasteen, N. D., Ed.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1990; p 81. It is important to note that this does not rule out V^{V}/V^{III} redox cycling during catalysis. A III/V cycle has been inferred for the vanadium-catalyzed air oxidation of Br^- to Br_2 (Neumann, R.; Assael, I. *J. Am. Chem. Soc.* **1989**, *111*, 8410).
(3) Arber, J. M.; de Boer, E.; Garner, C. D.; Hasnain, S. S.; Wever, R. *Biochemistry* **1989**, *28*, 7968.
(4) de Boer, E.; Boon, K.; Wever, R. *Biochemistry* **1988**, *27*, 1629.
(5) Vilter, H. *Phytochemistry* **1984**, *23*, 1387.
(6) Vilter, H.; Rehder, D. *Inorg. Chim. Acta* **1987**, *136*, L7.
(7) de Boer, E.; Keijzers, C. P.; Klaassen, A. A. K.; Reijerse, E. J.; Collison, D.; Garner, C. D.; Wever, R. *FEBS Lett.* **1988**, *235*, 93.
(8) Rehder, D.; Weidmann, C.; Duch, A.; Priebsch, W. *Inorg. Chem.* **1988**, *27*, 584.
(9) (a) Kime-Hunt, E.; Spartalian, K.; DeRusha, M.; Nunn, C. M.; Carrano, C. J. *Inorg. Chem.* **1989**, *28*, 4392. (b) Holms, S. M.; Carrano, C. J. *Inorg. Chem.* **1991**, *30*, 1231. (c) Collison, D.; Mabbs, F. E.; Passand, M. A.; Rigby, K.; Cleland, W. E. *Polyhedron* **1989**, *8*, 1827.
(10) Abbreviations used: HSALIMH = 4-(2-(salicylideneamino)ethyl)-imidazole, $CATH_2$ = catechol, HACAC = acetylacetone, $AHAH_2$ = acetohydroxamic acid, AHI = the dianion acetohydroximate, ENSAL = *N*-salicylideneethylenediamine, and H_2SHED = *N*-salicylidene-*N'*-(2-hydroxyethyl)ethylenediamine.

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acetonitrile, dichloromethane, or methanol solution of the vanadium(IV) precursor.[12] Compound **1** has been characterized by X-ray crystallography, and an ORTEP diagram is presented as Figure 1.[13] Important bond lengths and angles are provided in the figure caption and are comparable to other vanadium–catechol structures reported in the literature.[14] The vanadium to terminal oxo group (O1) distance is 1.59 Å which is slightly shorter than the V^{IV}=O bond (1.64 Å) in **2**. EXAFS results for the native enzyme[3] yield a 1.63-Å V=O distance. There is also a slight shortening of the phenolate to vanadium distance in **1** (V–O2 = 1.91 Å) versus **2** (V–O2 = 1.98 Å), consistent with metal-centered oxidation. Little change is seen with the vanadium to imidazole nitrogen ligation (**1**, V–N2 = 2.11 Å; **2**, V–N2 = 2.10 Å). The vanadium–imidazole nitrogen distance in **1** is the same as that reported for the native enzyme on the basis of EXAFS. The elongation of the V–O4 bond (trans to the terminal oxo) relative to V–O3 in the basal plane is more striking in **1** (V–O4 = 2.20 Å; V–O3 = 1.91 Å) than **2** (V–O4 = 2.20 Å; V–O3 = 1.97 Å), and as a consequence, the vanadium to imine nitrogen distance in **1** increases to 2.15 Å from 2.05 Å seen in **2**.

Reaction of **2** with acetohydroxamic acid ($AHAH_2$) in a manner similar to that described above affords $V^{V}O$(SALIMH)AHI (**3**) as a microcrystalline solid in 80% yield.[15] On the basis of the composition and spectroscopic properties, we believe **3** is structurally analogous to **1** and **2**.[16] The formation of the *cis*-dioxovanadium(V) monomer $V^{V}O_2$(SALIMH) (**4**) occurs in high yield via the reaction of an acetonitrile solution of **2** with 1 molar equiv of *tert*-butyl hydroperoxide.[17] Compound **4** is believed to be isostructural with VO_2(HSHED), which has the common *cis*-VO_2^+ unit.[18] Pyrogallol also reacts with **2** to yield a complex, **5**, with spectroscopic properties similar to those of **1**; however, this complex decomposes over time and has not been isolated.

Strong ligand to metal charge-transfer (LMCT) excitations are observed in the visible spectrum for **1** [540 nm (ϵ = 3500 cm^{-1} M^{-1}) and 926 nm (ϵ = 4140 cm^{-1} M^{-1})] and **3** [460 nm (ϵ = 2020 cm^{-1} M^{-1}) and 605 nm (ϵ = 2300 cm^{-1} M^{-1})]. In contrast, **2** has weak d–d transitions [539 nm (ϵ = 59 cm^{-1} M^{-1}) and 743 nm (ϵ = 34 cm^{-1} M^{-1})] in the visible region and **4** is transparent at wavelengths above 400 nm. Ligand to metal charge-transfer excitations have been reported for the "naked" vanadium(V) complex $KV(CAT)_3$,[14d] and strong charge-transfer excitations associated with VO^{3+}–phenolate compounds have been reported.[18,9b] Therefore, we cannot definitively assign the origin of the transitions in **1** to phenolate or catecholate moieties. The presence of these charge-transfer bands reiterates the absence of a V^{V}–(O)–phenolate (tyrosine) moiety in the native enzyme.

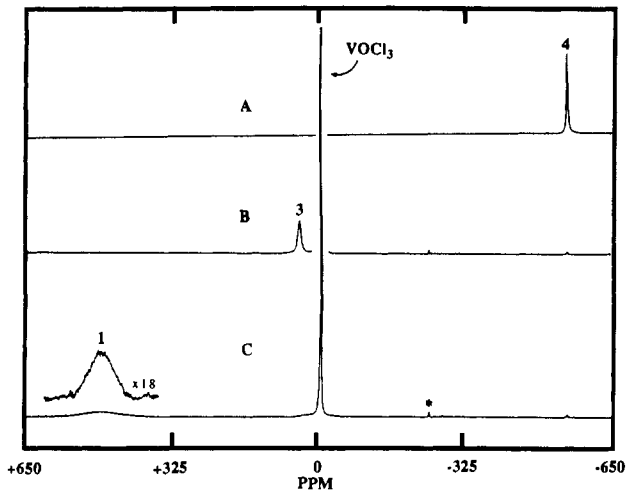

Figure 2. ^{51}V NMR spectra of acetonitrile solutions of (A) $V^{V}O_2$(SALIMH) (**4**), (B) $V^{V}O$(SALIMH)AHI (**3**), and (C) $V^{V}O$(SALIMH)CAT (**1**). All spectra were collected at 52.62 MHz and referenced to external $VOCl_3$. The sweep width was 125 000 Hz, and 8000 data points were used for the typical aquisition. Signal/noise was improved by exponential multiplication of the FID, inducing 50 Hz of line broadening. The asterisk denotes an impurity in the external $V^{V}OCl_3$ standard, which was run with every spectrum.

Rehder has presented a referencing scale based on the correlation of ^{51}V NMR shifts with the sum of the ligand electronegativities, $\sum\chi$, for a wide variety of V(V) complexes with coordination numbers 4, 5, and 6.[8] A listing of vanadium complexes containing exclusively oxygen and nitrogen ligands reveals that, with rare exception,[24] the chemical shifts are upfield of the standard, $VOCl_3$, and that the bulk of these resonances occur between −400 and −600 ppm. In the course of our work, we have found that vanadium complexes of noninnocent ligands, such as catechol and hydroxamic acid, can fall well outside this range. This finding is important since many biomolecules contain these functional groups. In particular, the vanadium-accumulating tunicates maintain a high level of hydroxy-dopa-based molecules known as tunichromes, which have recently been isolated and characterized.[19] Furthermore, the mushroom *A. muscaria* accumulates vanadium to form the η^2-hydroxyl amine complex amavadin[20] and vanadate has been shown to strongly coordinate the polyhydroxamic acid siderophore desferriferrioxamine B.[21] Butler has utilized desferriferrioxamine B to selectively extract vanadate from the phosphate binding site of an ATPase.[22]

The ^{51}V NMR chemical shift range for the complexes of $V^{V}O$(SALIMH)L, where L is a noninnocent ligand or an oxo group, extends over a remarkable 1020 ppm. The spectra of **4**, **3**, and **1** are presented in Figure 2 from top to bottom, respectively. The $(VO_2)^+$ complex, **4**, has a single resonance at −542 ppm. This shift is typical for dioxovanadium(V) complexes of oxygen/nitrogen ligands. Utilizing the Zhang formalism, one would cal-

(11) Cornman, C. R.; Kampf, J.; Lah, M. S.; Pecoraro, V. L. *Inorg. Chem.*, companion paper in this issue.

(12) Anal. Calcd for **1**, $VC_{18}H_{16}N_3O_4$: C, 55.54; H, 4.14; N, 10.79; V, 13.09. Found: C, 55.76; H, 4.32; N, 10.19; V, 13.1. Negative FAB mass spectral molecular ion: *m/e* 389.

(13) X-ray-quality crystals of **1** were obtained by slow evaporation of a acetonitrile/diethyl ether solution of the complex. X-ray parameters for V(O)(SALIMH)CAT (**1**): $C_{18}H_{16}N_3O_4V$, M_r 389.28, $P2_1/n$ (No. 14); a = 13.660 (9) Å, b = 6.483 (4) Å, c = 19.18 (1) Å, β = 96.69 (6)°; V = 1681 Å^3; Z = 4; ρ_{calc} = 1.537 g/cm^3, ρ_{obs} = 1.50 g/cm^3; λ(Mo Kα) = 0.710 73 Å; crystal dimensions 0.20 × 0.24 × 0.26 mm; largest residual +0.61/−0.42 e/Å^3. The intensity of 2966 unique reflectioins ($5 < 2\theta < 50$) were measured at ambient temperature on a Siemens R3m/v diffractometer. The structure was solved by direct methods using the SHELXTL PLUS program package. The structure was refined using the full-matrix least-squares method. Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotropically. For 2569 data with $F_o \geq 0.6\sigma(F)$, the final R = 0.0630 and R_w = 0.0586. $R = \sum(|F_o| - |F_c|)/\sum|F_o|)$, and $R_w = [\sum(w|F_o| - |F_c|)^2/\sum w(F_o)^2]^{1/2}$.

(14) (a) Kabanos, T. A.; White, A. J. P.; Williams, D. J.; Woollins, J. D. *J. Chem. Soc., Chem. Commun.* **1992**, 17. (b) Kabanos, T. A.; Slawin, A. M. Z.; Williams, D. J.; Woollins, J. D. *J. Chem. Soc., Chem. Commun.* **1990**, 193. (c) Cass, M. E.; Gordon, N. R.; Pierpont, C. G. *Inorg. Chem.* **1986**, *25*, 3962. (d) Cooper, S. R.; Koh, Y. B.; Raymond, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 5092.

(15) Anal. Calcd for V(O)(SALIMH)AHI (**3**), $VC_{14}H_{15}N_4O_4$: C, 47.47; H, 4.27; N, 15.82; V, 14.38. Found: C, 47.12; H, 4.42; N, 15.86; V, 15.0. Negative FAB mass spectral molecular ion: *m/e* 354.

(16) Raymond and co-workers have structurally characterized two vanadium(V) *hydroxamate* (monoanion of phenylhydroxamic acid) complexes (Fisher, D. C.; Barclay-Peet, S. J.; Balfe, C. A.; Raymond, K. N. *Inorg. Chem.* **1989**, *28*, 4399). We believe complex **3** is the dianionic *hydroximate* on the basis of the absence of an anion in the elemental analysis. Alternatively, the hydroxylamine nitrogen is protonated and the bound imidazole is deprotonated.

(17) Anal. Calcd for VO_2(SALIMH) (**4**), $VC_{12}H_{12}N_3O_3{\cdot}0.5H_2O$: C, 47.07; H, 4.28; N, 13.71; V, 16.64. Found: C, 47.08; H, 4.21; N, 13.36; V, 15.6. Mass spectral analysis did not yield a molecular ion peak; however, the fragmentation pattern was consistent with a dimeric formulation for **4** in the FAB matrix (3-nitrobenzyl alcohol). This is consistent with other $(V^{V}O_2)^+$ complexes. See ref 16.

(18) Li, X.; Lah, M. S.; Pecoraro, V. L. *Inorg. Chem.* **1988**, *27*, 4657.

(19) Smith, M. J.; Kim, D.; Horenstein, B.; Nakanishi, K.; Kustin, K. *Acc. Chem. Res.* **1991**, *24*, 117.

(20) de C. T. Carrondo, M. A. A. F.; Duarte, M. T. L. S.; Pessoa, J. C.; Silva, J. A. L.; Frausto da Silva; J. J. R.; Vaz, M. C. T. A.; Vilas-Boas, L. F. *J. Chem. Soc., Chem. Commun.* **1988**, 1158.

(21) Batinic-Haberle, I.; Birus, M.; Pribanic, M. *Inorg. Chem.* **1991**, *30*, 4882.

(22) Butler, A.; Parsons, S. M.; Yamagata, S. K.; De La Rosa, R. *Inorg. Chim. Acta* **1989**, *163*, 1.

culate $\sum\chi = 20.69$ for **1** and **3** and $\sum\chi = 17.05$ for **4**.[23] Upon application of the Rehder correlation, these values would predict chemical shifts in the −480 to −600 ppm region as is observed for **4**. Surprisingly, the single resonance of **3** at +45 ppm is a rare example of a VO^{3+} complex of oxygen and nitrogen donors with a shift *downfield* of $VOCl_3$.[24] Finally, the resonance of **1** has a downfield shift of +480 ppm.[25] A similar dependence of the chemical shift is observed when HSHED or ENSAL are substituted for SALIMH. The paramagnetic contribution to the shielding factor, σ^P, is almost certainly responsible for the extreme downfield shifts of **1** and **3**. According to Ramsey, σ^P is inversely proportional to the energy of the HOMO–LUMO gap and thus the low-energy LMCT is probably related to the large deshielding effect of the noninnocent ligands in **1** and **3**.[26] Apparently a new correlation may be required to describe chemical shifts of complexes with noninnocent type ligands. This may be an important consideration when NMR spectroscopy is applied to define the ligation of siderophore type ligands to V(V). We are currently evaluating in greater detail the relationship between the paramagnetic shielding factor and the structural and electronic properties of several homologous V(V) complexes to address this concern.[27]

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Supplementary Material Available: For **1**, Tables 1–6, listing crystallographic data, fractional atomic coordinates for non-hydrogen atoms, thermal parameters, fractional atomic coordinates for hydrogen atoms, a complete set of bond distances, and a complete set of bond angles, respectively, and Figure 3, showing a complete numbering scheme for all atoms (8 pages); Table 7, listing observed and calculated structure factors for **1** (11 pages). Ordering information is given on any current masthead page.

(23) Zhang, Y. *Inorg. Chem.* **1982**, *21*, 3886.
(24) A downfield shift of +780 ppm has been observed for the bare vanadium(V) complex $V^V(N_3S_2)$(dtbc)(phen) (where dtbc = di-*tert*-butylcatechol and phen is phenanthroline); see ref 14b.
(25) The line width of this resonance (ca. 4000 Hz) is considerably larger than that observed for **3** and **4** (170–440 Hz). This line width may arise from a small amount of vanadium(IV) impurity which can exchange with the vanadium(V) complex or via a large quadrupolar contribution to the relaxation time (see: Rehder, D. *Bull. Magn. Reson.* **1982**, *4*, 33). We have examined several NMR samples of **1** using EPR spectroscopy to quantify the amount of vanadium(IV) present. We found that the chemical shift and the line width of the ^{51}V resonance are invariant for samples containing 4%–15% vanadium(IV). Studies are currently in progress to address the cause of the rapid relaxation for **1**.
(26) (a) Ramsey, N. F. *Phys. Rev.* **1950**, *78*, 699. (b) Ramsey, N. F. *Phys. Rev.* **1952**, *86*, 243.
(27) Cornman, C. R.; Colpus, G. J.; Hoeschele, J. D.; Pecoraro, V. L. To be submitted for publication in *J. Am. Chem. Soc.*

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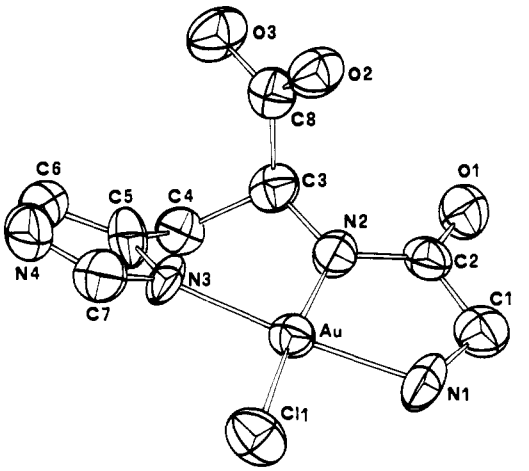

Figure 1. ORTEP drawing (50% probability thermal ellipsoids) of the cation of **1**, Au(gly-L-his)Cl^+. Selected bond lengths (Å) angles (deg) are as follows: Au–Cl1 = 2.273 (3), Au–N1 = 2.002 (9), Au–N2 = 1.94 (1), Au–N3 = 1.991 (8); Cl1–Au–N1 = 89.54, Cl1–Au–N2 = 174.5 (3), Cl1–Au–N3 = 94.9 (3), N1–Au–N2 = 84.9 (5), N1–Au–N3 = 175.5 (6), N2–Au–N3 = 90.7 (4).

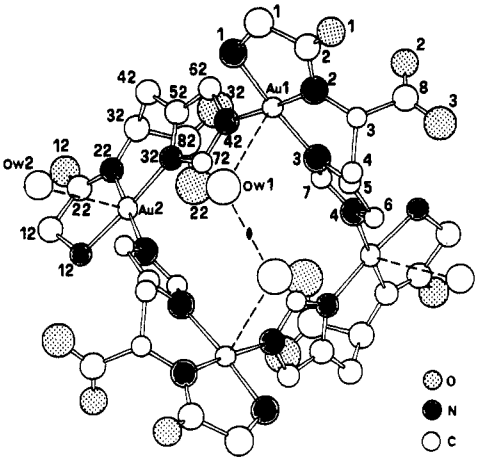

Figure 2. ORTEP drawing (50% probability thermal ellipsoids) of [Au(gly-L-his)]$_4$ (**2**) with the numbering scheme of crystallographically independent species. Coordination bond lengths (Å) are as follows: Au1–N1 = 2.018 (8), Au1–N2 = 1.993 (9), Au1–N3 = 1.981 (8), Au1–N42 = 1.987 (7), Au2–N12 = 1.993 (6), Au2–N22 = 1.999 (7), Au2–N32 = 1.985 (6), Au2–N4′ = 2.038 (8). The symbol of the crystallographic C_2 axis is also indicated.

Gold(III) Glycyl-L-histidine Dipeptide Complexes: Preparation and X-ray Structures of Monomeric and Cyclic Tetrameric Species

Metal complexes of histidine-containing peptides have been widely used as models for interactions between metal ions and proteins.[1,2] As to the simple dipeptide glycyl-L-histidine (gly-L-his), its reactivity toward Zn(II) has been studied[3] with regard to the phenomenon of increased oxygen affinity for hemoglobin on Zn(II) binding, for example.[4] Various solution studies on binary systems have favored a binding pattern in which gly-L-his acts as a tridentate chelating ligand with the metal coordinated to the amino group of glycine, the deprotonated peptide N, and the N3 site of the his-imidazole ring.[1] In the case of Cu(II), this conclusion has been confirmed by an X-ray structure determination.[5,6] As reported by Morris and Martin,[7] mononuclear gly-L-his complexes of Cu(II), Ni(II), and Pd(II) associate into

(1) Sigel, H.; Martin, R. B. *Chem. Rev.* **1982**, *82*, 385.
(2) (a) See e.g.: Laurie, S. H. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Gillard, R. D., McCleverty, J. A., Eds.; Pergamon Press: Oxford, England, 1987; Vol. 2, pp 739–776. (b) See various articles in: *Metal Ions in Biological Systems*; Sigel, H., Ed.; M. Dekker: New York, 1979; Vol. 9.
(3) Rabenstein, D. L.; Daignault, S. A.; Isab, A. A.; Arnold, A. P.; Shoukry, M. M. *J. Am. Chem. Soc.* **1985**, *107*, 6435.
(4) Rifkind, J. M. *Met. Ions Biol. Syst.* **1983**, *15*, 275.
(5) Blount, J. F.; Fraser, K. A.; Freeman, H. C.; Szymanski, J. T.; Wang, C.-H. *Acta Crystallogr.* **1967**, *22*, 396.
(6) We note that an alternative chelation via NH_2 (gly), N (peptide), and O (carboxylate of his) has been reported as well: Preut, H.; Vornefeld, M.; Huber, F. *Acta Crystallogr.* **1991**, *C47*, 264.
(7) Morris, P. J.; Martin, R. B. *J. Inorg. Nucl. Chem.* **1971**, *33*, 2913.

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