shifted toward wavelengths longer than 700 nm by both the reduction and oxidation of the high-spin iron ions and low-spin iron ions, respectively. This result can possibly predict that the crystal destabilization energy, $E_{cryst}$, should be decreased by the reduction and oxidation of the iron ions in the film. The calculation of $E_{cryst}$ for the partially oxidized and reduced forms of PB would be of special interest. This electrostatic (Coulombic) energy seems to be more acceptable for the explanation of the band shift than the mixed-valence delocalization energies proposed by Mortimer and Rosseinsky.[4d] Finally, it is noteworthy that the peak positions of the intervalence charge transfer bands for the iron ruthenium cyanide, $Fe^{3+}_4[Ru^{II}(CN)_6]_3$,[3a] and the iron osmium cyanide, $Fe^{3+}_4[Os^{II}(CN)_6]_3$,[3b] are also considerably shifted to longer wavelengths. This behavior is basically the same as observed in the PB films.

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**Registry No.** PB, 12240-15-2; $SnO_2$, 18282-10-5.

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## Reactions of Metal Complexes with Carbohydrates: Nickel(II) Complexes Containing *N*-Glycosides Derived from a Sugar and β-Alanine

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It is an interesting subject to clarify the interactions between the transition-metal complexes of amino acids and sugars in coordination chemistry and in bioinorganic chemistry. Recently we have studied the nickel(II) complexes containing the *N*-glycosides derived from the reaction of a diamine and a monosaccharide, including X-ray crystallography.[1-5] It is well-known that sugars react with an amine center of amino acids as well as amines to yield *N*-glycosides.[6] Accordingly, the coordination behavior of the *N*-glycosides derived from aldoses and amino acids are expected to be similar to that of *N*-glycosides from diamines and aldoses. Weitzel et al. reported in 1957 that they isolated several metal complexes of the *N*-glycosides derived from an aldose and an amino acid.[7] They confirmed the composition of the compounds by elemental analyses, but made no comment upon the spectral and stereochemical features. We reinvestigated to obtain such complexes according to their methods. However it was difficult to isolate analytically pure metal complexes containing a series of monosaccharides.[8]

We found that the metal complexes having sugar and amino acid residues can be easily obtained from the reaction of aldoses with $[Ni(\beta\text{-ala})_2(H_2O)_2]$, which is unusually soluble in methanol for bis(amino acidato)nickel(II) complexes, where β-ala is β-alaninato. The structures of these complexes were assigned by using several analogous of D-glucose in relation to their spectral features.

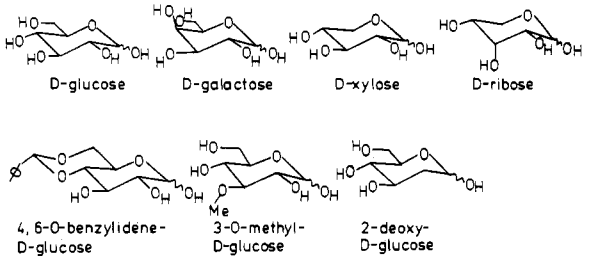


**Figure 1.** Structures of starting sugars.

### Experimental Section

**Preparation of $[Ni(\beta\text{-ala})_2(H_2O)_2]$.** A 0.05-mol sample of $NiCl_2 \cdot 6H_2O$ followed by 0.1 mol of β-alanine was dissolved in 150 mL of water. To this solution was added an aqueous solution of NaOH (0.1 mol in 50 mL) gradually. The blue precipitates formed were collected and washed with cold water and dried. Analytical data of this complex agreed with the proposed formula (C, H, N); the IR spectral data correspond to the reported value[9] in the range 4000–200 $cm^{-1}$.

**Reaction of Monosaccharides with $[Ni(\beta\text{-ala})_2(H_2O)_2]$.** The following monosaccharides (Figure 1) were used in this study; D-glucose (D-Glc), D-galactose (D-Gal), D-xylose (D-Xyl), D-ribose (D-Rib), 4,6-*O*-benzylidene-D-glucose (4,6-Bn-D-Glc),[10] 3-*O*-methyl-D-glucose (3-Me-D-Glc), and 2-deoxy-D-glucose (2-De-D-Glc). Methanol was dried over 3-Å molecular sieves before use. A 10-mmol sample of monosaccharide was added to a solution of $[Ni(\beta\text{-ala})_2(H_2O)_2]$ (5 mmol) in 60 mL of warm methanol (to dissolve D-Gal, 120 mL of methanol was used) and then heated to reflux. Blue precipitates were formed in the midst of refluxing in the cases of D-Gal and D-Rib. For the case of D-Glc, the solution was refluxed for 1 h and allowed to stand at room temperature; then a green complex crystallized. The blue compounds containing D-Xyl, 4,6-Bn-D-Glc, and 3-Me-D-Glc were formed when the solution was refluxed for 1 h and concentrated to about 30 mL. Of these complexes, the D-Gal, 3-*O*-Me-D-Glc, and 4,6-*O*-Bn-D-Glc complexes were obtained as gel-like solids. The aldose residues contained in these complexes were analyzed as follows. The complexes were dissolved in water, and then the solution was passed through ion-exchange resins (Dowex 50W, $H^+$ form, and Dowex 2, $HCO_3^-$ form). By this process, the complexes were hydrolyzed and the free aldoses were separated. The aldoses in this solution were analyzed by HPLC system.[11]

**Measurements.** Visible and near-infrared absorption spectra, diffusion reflectance spectra, circular dichroism spectra, and magnetic susceptibility were measured as previously described.[4b]

### Results and Discussion

Blue or green compounds were obtained from the reaction between $[Ni(\beta\text{-ala})_2(H_2O)_2]$ and aldoses except in the case of 2-De-D-Glc. They are scarcely soluble in methanol except for the 3-Me-D-Glc complex. Analytical data indicated that they have two *N*-glycoside ligands, which are made from a β-alanine and an aldose, except for the 3-Me-D-Glc complex (Table I).[12] The 3-Me-D-Glc complex was found to have an *N*-glycoside ligand, a β-ala ligand, an aqua ligand, and a solvated methanol. HPLC analysis indicated that all these complexes contain the starting aldose residue. All these compound are hydrolyzed gradually in water.

The effective magnetic moments of the isolated complexes are also listed in table I, and the near-infrared and visible absorption spectra and the CD spectra of these complexes are shown in Figure

(1) (a) Takizawa, S.; Sugita, H.; Yano, S.; Yoshikawa, S. *J. Am. Chem. Soc.* **1980**, *102*, 7969–7971. (b) Yano, S.; Takizawa, S.; Sugita, H.; Takahashi, K.; Tsubomura, T.; Shioi, H.; Yoshikawa, S. *Carbohydr. Res.* **1985**, *142*, 179–193.
(2) Shioi, H.; Yano, S.; Toriumi, K.; Ito, T.; Yoshikawa, S. *J. Chem. Soc., Chem. Commun.* **1983**, 201–202.
(3) Yano, S.; Sakai, Y.; Toriumi, K.; Ito, T.; Yoshikawa, S. *Inorg. Chem.* **1985**, *24*, 498–504.
(4) (a) Tsubomura, T.; Yano, S.; Toriumi, K.; Ito, T.; Yoshikawa, S. *Polyhedron* **1983**, *2*, 123–124. (b) Tsubomura, T.; Yano, S.; Toriumi, K.; Ito, T.; Yoshikawa, S. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 1833–1838.
(5) Tsubomura, T.; Yano, S.; Toriumi, K.; Ito, T.; Yoshikawa, S. *Inorg. Chem.* **1985**, *24*, 3218–3223.
(6) "The Carbohydrates. Chemistry and Biochemistry"; Pigman, W., Horton, D., Eds.; Academic Press: New York, 1980; Vol. IB, pp 883.
(7) Weitzel, G.; Geyer, H.-U.; Fretzdorff, A.-M. *Chem. Ber.* **1957**, *90*, 1153–1161.
(8) Most bis(α-amino acidato)nickel(II) complexes are sparingly soluble in methanol as well as the sugar–amino acid complexes, so that bis(amino acidato)metal complexes precipitate with the objective sugar complexes.
(9) Percy, G. C.; Stenton, H. S. *J. Chem. Soc., Dalton Trans.* **1976**, 2429–2433.
(10) Wood, H. B., Jr.; Diehl, H. W.; Fletcher, H. G., Jr. *J. Am. Chem. Soc.* **1957**, *79*, 1986–1988.
(11) Honda, S.; Matsuda, Y.; Takahashi, M.; Kakehi, K.; Ganno, S. *Anal. Chem.* **1980**, *52*, 1979–1082.
(12) The following abbreviations are used: *N*-D-glucosyl-3-aminopropionate anion, D-Glc-β-ala; *N*-D-galactosyl-3-aminopropionate anion, D-Gal-β-ala; *N*-D-xylosyl-3-aminopropionate anion, D-Xyl-β-ala; *N*-D-ribosyl-3-aminopropionate anion, D-Rib-β-ala; *N*-(4,6-*O*-benzylidene-D-glucosyl)-3-aminopropionate anion, 4,6-Bn-D-Glc-β-ala; *N*-(3-*O*-methyl-D-glucosyl)-3-aminopropionate anion, 3-Me-D-Glc-β-ala.

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**Table I.** Analytical Data, Yield, and Effective Magnetic Moment of Complexes

| | analytical data[a] | | | | | |
|---|---|---|---|---|---|---|
| | Ni | C | H | N | yield, % | $\mu_{eff}$, $\mu_B$ |
| $[Ni(D\text{-Glc-}\beta\text{-ala})_2]\cdot H_2O$ | 10.0 (10.2) | 37.67 (37.45) | 5.92 (5.94) | 4.85 (4.85) | 31 | 3.27 |
| $[Ni(D\text{-Gal-}\beta\text{-ala})_2]\cdot CH_3OH\cdot{}^1/_2H_2O$ | 9.0 (9.8) | 38.03 (38.02) | 6.25 (6.26) | 4.57 (4.66) | 52 | 3.13 |
| $[Ni(D\text{-Xyl-}\beta\text{-ala})_2]\cdot 2H_2O$ | 10.7 (10.9) | 35.31 (35.91) | 5.63 (6.03) | 5.43 (5.23) | 37 | 3.30 |
| $[Ni(D\text{-Rib-}\beta\text{-ala})_2]\cdot H_2O$ | 11.5 (11.4) | 37.17 (37.16) | 5.94 (5.84) | 5.60 (5.41) | 69 | 3.22 |
| $[Ni(4,6\text{-Bn-}D\text{-Glc-}\beta\text{-ala})_2]\cdot 2H_2O$ | 7.2 (7.6) | 49.49 (49.82) | 5.85 (5.74) | 3.62 (3.63) | 26 | 3.16 |
| $[Ni(\beta\text{-ala})(H_2O)(3\text{-Me-}D\text{-Glc-}\beta\text{-ala})]\cdot CH_3OH$ | 13.1 (12.7) | 36.62 (36.47) | 6.71 (6.56) | 6.52 (6.07) | 30 | 3.18 |

[a] Calculated values are given in parentheses.

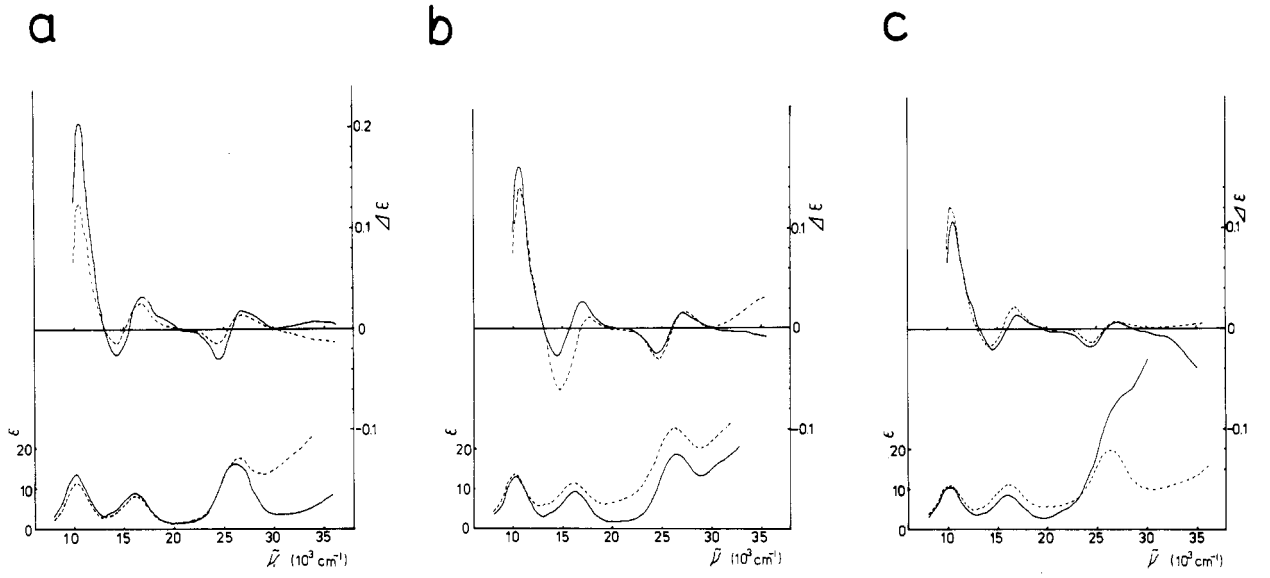


**Figure 2.** Absorption spectra (lower) and circular dichroism spectra (upper): (a) $[Ni(D\text{-Glc-}\beta\text{-ala})_2]\cdot H_2O$ (–), $[Ni(D\text{-Gal-}\beta\text{-ala})_2]\cdot CH_3OH\cdot{}^1/_2H_2O$ (--); (b) $[Ni(D\text{-Xyl-}\beta\text{-ala})_2]\cdot 2H_2O$ (–), $[Ni(D\text{-Rib-}\beta\text{-ala})_2]\cdot H_2O$ (--) (c) $[Ni(4,6\text{-Bn-}D\text{-Glc-}\beta\text{-al})_2]\cdot 2H_2O$ (–), $[Ni(\beta\text{-ala})(H_2O)(3\text{-Me-}D\text{-Glc-}\beta\text{-ala})]\cdot CH_3OH$ (--).

2.[13] All the absorption spectra show three peaks in the d–d transition region. The magnetic moments and the absorption spectra indicate that all these complexes have an essentially octahedral stereochemistry.[14] Although some differences of wavenumber of peaks between the absorption spectra in the solution and the diffusion reflectance spectra in the solid state (within 500 $cm^{-1}$) are observed, they can be regarded as a similar pattern for all complexes. Accordingly these complexes seem to have similar coordination structures both in the solid state and in the solution state.

It was found that D-Glc, D-Gal, D-Xyl, D-Rib, 4,6-Bn-D-Glc, and 3-Me-D-Glc reacted with the nickel $\beta$-ala complex to yield the nickel complexes containing the *N*-glycosides in this study. The CD intensity of these complexes in the d–d transition regions are comparable to (or stronger than) the previously studied nickel sugar complexes,[2-5] so that it is supposed that the sugar moiety forms a chiral chelate ring to the nickel atom and that this makes a significant contribution to the circular dichroism. Even if the hydroxyl group(s) on the C(3), C(4), or C(6) atoms were protected, *N*-glycoside complexes could be obtained. On the other hand, no sugar complex was obtained by using 2-De-D-glc. The two crystal structures of $[Ni(D\text{-}N\text{-Glc-en})_2]Br_2\cdot 4H_2O$[3] and $[Ni(L\text{-Rha-tn})_2]Br_2\cdot 2H_2O\cdot CH_3OH$[2] (*N*-Glc = glucosamine and Rha = rhamnose) confirmed that the *N*-glycosides coordinate to nickel atom at three points by two amino groups of the diamine residue

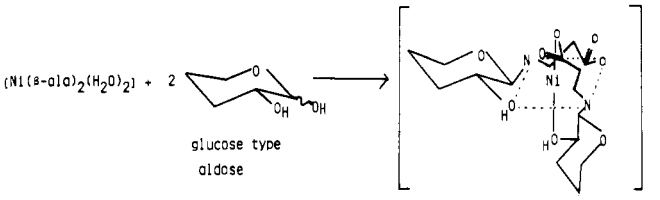


**Figure 3.** Proposed structure of the glucose type sugar–$\beta$-ala complex.

and a hydroxyl group on C(2) of the aldose residue. It can be expected that the hydroxyl group on C(2) also coordinates to the nickel atom in these *N*-glycosides derived from an aldose and an amino acid. From all considerations, these *N*-glycoside ligands are supposed to be tridentate ligands with coordination through the oxygen atom of the carboxylate of the $\beta$-ala moiety, through the oxygen atom of the hydroxyl group on the C(2) atom of the aldose residue, and through the nitrogen atom of $\beta$-ala (Figure 3).

Since all the aldoses used (glucose type aldoses) have the same (*R*) configuration of the C(2) atom and the hydroxyl group on this C(2) atom takes the equatorial orientation to the pyranose ring, the coordination geometries of all these *N*-glycosides derived from these aldoses and $\beta$-ala were inferred to be similar. These structural features are clearly supported by the circular dichroism spectra. All the CD curves of these complexes show similar patterns (Figure 2). The formation of the five-membered chelate ring of the aldose residue as well as the six-membered chelate ring of the $\beta$-ala residue may stabilize the *N*-glycoside, which is not stable in itself (see below).

(13) Since these complexes are sparingly soluble in methanol, the spectra were measured in a methanol–water (8:2) mixture soon after dissolution.
(14) Sacconi, L. *Transition Met. Chem. (N.Y.)* **1968**, *4*, 199–296.

The results obtained in this work revealed that the glucose type aldoses react with $[Ni(\beta\text{-ala})_2(H_2O)_2]$ to yield the novel nickel(II) complexes containing the *N*-glycosides, which are the products of the first step of the "Maillard reaction".[15] Since the Amadori rearrangement occurs immediately after the formation of the *N*-glycosides of amino acids as the second step of the Maillard reaction and forms ketose-amino acids,[6] it is difficult to stop the Maillard reaction at the first step and to isolate such *N*-glycosides. Therefore it is an important fact that the Maillard reaction stopped at the first step and that the *N*-glycosides derived from amino acids and sugars can be obtained very easily by using nickel β-alaninato complex.

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**Registry No.** Ni(D-Glc-β-ala)$_2$, 99656-37-8; Ni(D-Gal-β-ala)$_2$, 99685-50-4; Ni(D-Xyl-β-ala)$_2$, 99656-38-9; Ni(D-Ribo-β-ala)$_2$, 99685-51-5; Ni(4,6-Bn-D-Glc-β-ala)$_2$, 99656-39-0; Ni(β-ala)$(H_2O)$(3-Me-D-Glc-β-ala), 99656-40-3; Ni(β-ala)$_2(H_2O)_2$, 22585-11-1; D-Glc, 50-99-7; D-Gal, 59-23-4; D-Xyl, 58-86-6; D-Rib, 50-69-1; 4,6-Bn-D-Glc, 30688-66-5; 3-Me-D-Glc, 146-72-5; 2-De-D-Glc, 154-17-6.

(15) Maillard, L. C. *C. R. Hebd. Seances Acad. Sci.* **1912**, *154*, 66-68.

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## Crystal and Molecular Structure of Bis[*N*-[2-(4-imidazolyl)ethyl]salicylaldiminato]iron(III) Hexafluorophosphate Ethanol Solvate: A Model for Iron(III) Sites with Tyrosine and Histidine Ligands in Proteins

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Iron-tyrosinate proteins[5] are a diverse group, including transferrin,[6] the catechol dioxygenases,[7] and the purple acid phosphatases.[8] The presence of tyrosine phenolate ligands to iron(III) is indicated by intense low-energy ligand to metal charge-transfer transitions; irradiation into this band gives rise to a set of resonance-enhanced Raman modes that are characteristic of coordinated phenolates. The identity of other ligands to iron is, however, more difficult to ascertain. Proton NMR studies of the purple acid phosphatases[9] have confirmed the presence of tyrosyl ligands to iron and have implicated histidine imidazoles as well. These conclusions have been reinforced by EXAFS studies.[10] A major problem in analyzing the EXAFS data of the proteins, especially the purple acid phosphatases,[10c] is the existence of several sets of nearest neighbors at relatively similar distances in the first shell. A lack of structurally characterized iron(III) complexes containing phenolate and imidazole ligands has made it difficult to distinguish between tyrosinate oxygens at relatively short distances and bridging oxo groups.[10c] Although to date no synthetic complex containing imidazole, phenolate, and bridging oxo groups has been prepared, Que et al.[7a] have briefly reported the preparation and resonance Raman spectrum of a mononuclear complex containing both phenolate and imidazole ligands, $[Fe(salhis)_2]ClO_4 \cdot H_2O$.[11] This complex provides a convenient model for mononuclear Fe(III) sites and for comparison to bridged binuclear sites. We have now obtained crystals of the $PF_6^-$ salt of $[Fe(salhis)_2]^+$, and we describe herein

**Table I.** Summary of Crystal Data and X-ray Data Collection and Reduction for $[Fe(salhis)_2]PF_6 \cdot EtOH$

| | |
|---|---|
| **Crystal Parameters** | |
| cryst syst | orthorhombic |
| space group | *Pbca* |
| cryst habit | rectangular needle elongated along *c* |
| cryst dimens, mm$^3$ | 0.83 × 0.09 × 0.13 |
| *a*, Å | 16.43 (1) |
| *b*, Å | 18.21 (1) |
| *c*, Å | 19.85 (1) |
| *V*, Å$^3$ | 5940.6 (2) |
| *Z* | 8 |
| *d*(calcd), g cm$^{-3}$ | 1.510 |
| abs coeff, cm$^{-1}$ | 5.814 |
| formula | $C_{26}H_{30}F_6FeN_6O_3P$ |
| fw | 675.38 |
| **Data Collection and Reduction[13a]** | |
| diffractometer | Picker FACS-I VDODS[13b] |
| radiation | Mo $K\alpha_1$ (λ = 0.709 26 Å), graphite monochromated |
| temp, °C | 20 |
| scan technique | $\theta$-$2\theta$ |
| scan rate, deg/min | 2 |
| scan range ($2\theta$), deg | 1.5-50 |
| octant collcd | $+h,+k,+l$ |
| transmissn factor | 0.976-0.962 |
| no. of total reflcns | 5822 |
| no. of unique data with $I > 2\sigma(I)$ | 2160 |

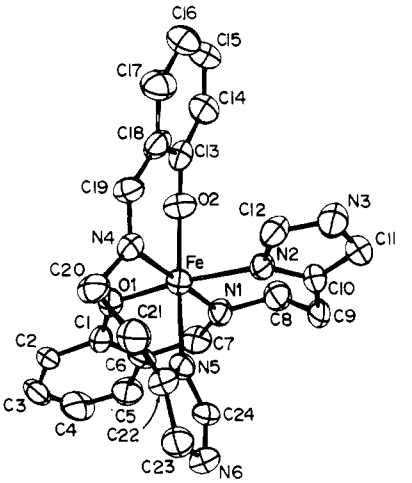


**Figure 1.** ORTEP diagram of the $[Fe(salhis)_2]^+$ cation (50% probability ellipsoids), showing the atomic numbering scheme. Hydrogen atoms have been omitted for clarity.

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(5) (a) Que, L., Jr. *Coord. Chem. Rev.* **1983**, *50*, 73-108. (b) Keyes, W. E.; Loehr, T. M.; Taylor, M. L. *Biochim. Biophys. Res. Commun.* **1978**, *83*, 941-945.
(6) (a) Ainscough, E. W.; Brodie, A. M.; Plowman, J. E.; Bloor, S. J.; Loehr, J. S.; Loehr, T. M. *Biochemistry* **1980**, *19*, 4072-4079. (b) Aisen, P.; Listowsky, I. *Annu. Rev. Biochem.* **1980**, *49*, 357-393.
(7) (a) Que, L., Jr.; Heistand, R. H., II; Mayer, R.; Roe, A. L. *Biochemistry* **1980**, *19*, 2588-2593. (b) Que, L., Jr.; Epstein, R. M. *Biochemistry* **1981**, *20*, 2545-2549. (c) Que, L., Jr. *Struct. Bonding (Berlin)* **1980**, *40*, 39-72.
(8) (a) Antanaitis, B. C.; Aisen, P. In "Advances in Inorganic Biochemistry"; Thiel, E., Eichhorn, G., Marzilli, L., Eds.; Elsevier: Amsterdam, 1983; Vol. 5, pp 111-136. (b) Antanaitis, B. C.; Strekas, T.; Aisen, P. *J. Biol. Chem.* **1982**, *257*, 3766-3770. (c) Davis, J. C.; Averill, B. A. *Proc. Natl. Acad. Sci. U.S.A.* **1982**, *79*, 4623-4627.
(9) (a) Lauffer, R. B.; Antanaitis, B. C.; Aisen, P.; Que, L., Jr. *J. Biol. Chem.* **1983**, *258*, 14212-14218. (b) Que, L., Jr.; Averill, B. A., unpublished results.

 