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Pyridine Adducts of Iron(II)–Schiff Base Complexes

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Five-coordinate iron(II) complexes prepared from Schiff base ligands and pyridine have been synthesized. The Schiff base ligands were formed from salicylaldehyde or 5-bromosalicylaldehyde and ethylenediamine or *o*-phenylenediamine. Three of the four complexes react with oxygen in the solid state to produce five-coordinate μ-oxo compounds. The formation of a μ-oxo complex in the solid state is compared with the reaction of dioxygen and hemerythrin to form methemerythrin. For both systems a dioxygen complex intermediate is proposed which is stabilized in the case of hemerythrin. The relevance of the Schiff base complexes as model compounds is discussed.

Introduction

The importance of iron complexes in natural systems needs no elaboration. In order to better understand these systems, various model compounds have been studied.[1] Results of these investigations have been extrapolated more or less successfully to the naturally occurring compound. There are several reasons for studying model systems. The natural compounds may be difficult to obtain, therefore limiting the type and number of experiments which can be performed. The active site (the iron center and immediate donor groups) may be obscured by the surrounding matrix such as large proteins. A model compound may serve simply as a comparison, perhaps providing a better behaved system.

A good example of a model compound is the "picket fence" iron(II) porphyrin.[1] This complex has been used as a model for the bonding of dioxygen to hemoglobin. It is the only well-defined dioxygen complex of iron. By its reversible behavior, it has provided substantial insight into the reactivity and bonding associated with a naturally occurring compound. No doubt continued studies will provide even greater understanding of the active site in complex molecules such as hemoglobin.

Another natural iron protein, hemerythrin, has also received considerable attention in recent years.[2] This compound, although quite different from hemoglobin, also binds oxygen reversibly. Even though much information has been gathered, the mechanism of oxygen binding and the structure of the active site are still only speculative. A recent investigation by X-ray analysis was unable to determine exactly the number and type of ligands attached to the iron atoms.[3] So far, a good model for hemerythrin has not been found. The present report deals with a group of five-coordinate iron(II) compounds which react with oxygen in the solid state. Although the reaction is irreversible, the nature of the solid reaction suggests a mechanism involving an intermediate which may be responsible for the reversibility observed in hemerythrin.

Experimental Section

Materials. Ferrous sulfate ($Fe(SO_4)\cdot 7H_2O$) was obtained from Fischer Scientific Co. Salicylaldehyde (SAL), ethylenediamine (EN), and *o*-phenylenediamine (*o*-PhEN) were purchased from Aldrich Chemical Co. Salicylaldehyde was distilled and *o*-phenylenediamine was recrystallized prior to use. 5-Bromosalicylaldehyde was prepared from the reaction between bromine and salicylaldehyde in acetic acid. The compound was then recrystallized from 2-propanol. All other compounds and solvents were reagent grade or better, and all gases were used without further purification.

Preparation of the Complexes. In a typical reaction, a 250-mL round-bottom flask was fitted with a nitrogen intake and stirring bar. The Schiff base ligand was made in situ prior to the addition of the metal. Ethylenediamine or *o*-phenylenediamine (0.010 mol) in 25 mL of 1-propanol was added to 0.020 mol of salicylaldehyde or 5-bromosalicylaldehyde in 50 mL of pyridine. The mixture was refluxed under nitrogen for 30 min after which a pressure-equalizing dropping funnel with a coarse frit was connected to the flask. Solid ferrous sulfate (0.010 mol) was added through the top of the funnel and was dissolved by adding 25 mL of deoxygenated water. The solution was added dropwise to the Schiff base. A dark crystalline precipitate formed about halfway through the addition. In some cases, the reaction mixture was again heated to reflux and a better product formed upon cooling. The contents of the flask were filtered under nitrogen, and the precipitate was washed with a deoxygenated propanol–water mixture. The complex was dried by vacuum overnight. Analytical data for the compounds are presented in Table I. With the exception of Fe(5-BrSAL-*o*-PhEN)py, exposure to atmospheric oxygen produced a color change from purple to orange accompanied by loss of pyridine. These compounds are μ-oxo complexes and their analytical data are presented in Table I.

Physical Measurements. Carbon, hydrogen, and nitrogen analyses were performed by the Center for Trace Characterization, Texas A&M University. Infrared spectra were measured as Nujol mulls between KBr plates on a Perkin-Elmer Model 237B grating spectrophotometer which was calibrated with polystyrene. Near-infrared and visible spectra were measured on a Cary 14 spectrophotometer. Magnetic susceptibility data were obtained by the Gouy method using $HgCo(CNS)_4$ as a standard.

Results and Discussion

Characterization of the Complexes. The reaction of dioxygen with ferrous compounds is well-known. In most cases the reactions lead to irreversibly oxidized ferric compounds.[4,5] The complex 1,2-disalicylideniminatoethaneiron(II) or Fe(SALEN) reacts with oxygen in solution to produce a well-characterized μ-oxo product.[6,7] In the solid state, reaction with oxygen is believed to produce the same μ-oxo compound,[8] although a well-defined μ-oxo complex has not been prepared by this method.

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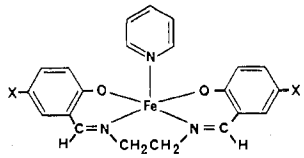
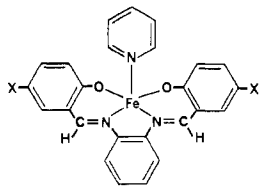
Table I. Analytical and Magnetic Susceptibility Data for the Complexes

iron complex	%C		%H		%N		μ_{eff},[a] μ_B
	calcd	found	calcd	found	calcd	found	
Fe(SALEN)py	62.86	63.08	4.77	4.80	10.47	10.45	4.95
Fe(5-BrSALEN)py	45.08	45.29	3.04	3.01	7.51	7.38	4.99
Fe(SAL-*o*-PhEN)py	66.82	67.05	4.23	4.32	9.35	9.55	4.87
Fe(5-BrSAL-*o*-PhEN)py	49.42	49.06	2.80	2.91	6.92	6.73	5.01
$[Fe(SALEN)]_2O$·py	60.43	60.50	4.55	4.61	10.06	9.74	1.91
$[Fe(5\text{-}BrSALEN)]_2O$	40.51	40.85	2.53	2.55	5.90	5.93	1.92
$[Fe(SAL\text{-}o\text{-}PhEN)]_2O$·py	64.67	64.12	3.95	3.98	8.38	8.24	1.89

[a] Solid state, room temperature.



(A)



(B)

Figure 1. Iron(II)–Schiff base complexes: (A) Fe(SALEN)py, X = H; Fe(5-BrSALEN)py, X = Br; (B) Fe(SAL-*o*-PhEN)py, X = H; Fe(5-BrSAL-*o*-PhEN)py, X = Br.

In 1969, Calderazzo et al. reported the preparation of a pyridine adduct of Fe(SALEN) which they stated was unreactive toward oxygen in the solid state.[7] With a somewhat different procedure, a compound with the same composition as that of the previously reported adduct has been prepared. This compound, however, does react with atmospheric oxygen at room temperature even after drying. Elemental analysis of the oxygenated material provided the empirical formula $[Fe(SALEN)]_2O$·py. The reaction with oxygen was accompanied by a color change from purple to orange. The characteristic odor of pyridine was also detected. The orange color of the oxidized material was identical with that of $[Fe(SALEN)]_2O$ obtained from solution reactions. Since the pyridine adduct prepared in this investigation and the one previously reported were prepared by different methods, the compounds may not be the same structurally. This could account for their differences in reactivity. However, considering that the magnetic moments of the two compounds are identical, a more logical explanation may be that, depending upon the method of preparation, there are different crystalline forms of the compound, not all of which bind oxygen.

In order to determine the exact nature of these compounds, other derivatives were prepared. These included Fe(5-BrSALEN)py, Fe(SAL-*o*-PhEN)py, and Fe(5-BrSAL-*o*-PhEN)py (see Figure 1). All were obtained as crystalline solids and thoroughly dried. Although Fe(5-BrSAL-*o*-PhEN)py was unaffected by oxygen; the other two compounds reacted with oxygen under normal conditions retaining their crystalline appearance. In both cases color changes and loss of pyridine were observed. For Fe(5-BrSALEN)py, all the pyridine was lost as a result of oxygenation. Fe(SALEN)py and Fe(SAL-*o*-PhEN)py lost only half the original amount of pyridine, although it was later found that the residual pyridine could be removed under vacuum. The presence of pyridine was determined by both elemental analysis and infrared spectroscopy. Fe(5-BrSAL-*o*-PhEN)py retains its pyridine (and color) even when heated to 100 °C in the presence of oxygen.

Table II. Major Peaks in the Electronic Spectra of the Complexes[a]

compd	band maxima, Å
Fe(SALEN)py	24 000, 14 550, 4750, <4000
Fe(5-BrSALEN)py	>25 000, 14 450, 5250, 4000
Fe(SAL-*o*-PhEN)py	>25 000, 14 400, 7000, 5750, 4500
Fe(5-BrSAL-*o*-PhEN)py	25 000, 14 600, 7500, 5750, 4250
$[Fe(SALEN)]_2O$·py	4000
$[Fe(5\text{-}BrSALEN)]_2O$	4500
$[Fe(SAL\text{-}o\text{-}PhEN)]_2O$·py	4250

[a] Solid state, Nujol mull.

All the compounds that react with oxygen form well-defined μ-oxo complexes. The room-temperature magnetic moments ($\sim$1.9 μ_B) are essentially the same as those of other μ-oxo complexes[9] and quite different from the high-spin Fe(II) values observed for the precursors (see Table I). The electronic spectra of the oxidized compounds show a broad band centered about 4000 Å whereas the ferrous complexes exhibit a much more complicated spectrum (see Table II). Furthermore an Fe–O–Fe asymmetric stretching frequency observed in the infrared spectra was not present in the precursor. For $[Fe(SALEN)]_2O$·py it occurs at 805 cm^{-1}, while for the spectrum of $[Fe(SALEN)]_2O$ obtained from solution reactions[7] this peak was found at 825 cm^{-1}. Since removal of residual pyridine in the former compound does not affect the position of this peak, the difference must be due to the way in which the compounds were prepared. The solid-state reaction probably produces certain steric constraints on the bonding of oxygen since the iron centers are restricted in their movement. Therefore a shift in frequency from that observed in the compound formed in solution is not unexpected. For $[Fe(5\text{-}BrSALEN)]_2O$ and $[Fe(SAL\text{-}o\text{-}PhEN)]_2O$·py, the Fe–O–Fe peaks occur at 830 and 820 cm^{-1}, respectively.

The reactivities of the complexes that form μ-oxo adducts also varied. The reaction with Fe(SAL-*o*-PhEN)py was quite vigorous. During the reaction, pyridine actually condensed on the sides of a tube containing the compound. The reaction with Fe(5-BrSALEN)py was very slow and in the presence of atmospheric oxygen took several days to complete. If pure oxygen was used, the reaction proceeded much faster and was complete within a day or two. The time varied somewhat depending upon the amount of compound used and the amount of stirring during the reaction.

The differences in reactivity raised a question as to the nature of the pyridine binding in the precursor. Whether or not the pyridine was coordinated and to what extent could explain the difference in the reactivities. However, the electronic spectra of the ferrous complexes are very similar. Table II lists the band maxima of these compounds. An additional peak in the spectra of the *o*-phenylenediamine derivatives can be attributed to an additional charge-transfer band. These spectra are quite different from those of

square-planar or octahedral iron(II) species[10] but closely resemble five-coordinate ferrous complexes. For example, the electronic spectrum of Fe(SALDPT), bis(salicylideniminato-3-propyl)amineiron(II), exhibits d–d transitions at about 24 000 and 15 000 Å. Charge-transfer bands at 5000 Å and lower are also observed.[11]

Attempts to remove the pyridine by heating the ferrous compounds under vacuum at 100 °C were unsuccessful. The pyridine was retained, as evidenced by the infrared spectra. The electronic spectra also remained unchanged. This suggests that pyridine is tightly bound to the iron(II) center or the crystal packing is such that the pyridine cannot diffuse out. This latter explanation seems unlikely since upon reaction with oxygen, the pyridine can be removed readily. The similarity in the electronic spectra of the μ-oxo complexes with and without pyridine suggests that the residual pyridine is simply trapped in the crystal lattice after reaction with oxygen. Since $[Fe(5\text{-}BrSALEN)]_2O$ contains no pyridine, it would seem that the bromines are taking up the space in which a residual pyridine might remain. This is only speculative but may account for the lower reactivity of this compound since diffusion of oxygen into the crystal and/or diffusion of pyridine out of the crystal may be difficult. By the same reasoning, the inability of Fe(5-BrSAL-*o*-PhEN)py to react with oxygen may also be attributed to the above considerations. At least there is no evidence to suggest that structurally the compound is any different from other derivatives. Weak dibridging between the phenolic oxygens and the iron centers[12] seems unlikely from a steric point of view because of the bulkiness of the attached bromines. However, differences in reactivity might be attributed to other effects created by the bromines.

If the iron(II) complexes are five-coordinate (square pyramidal), one may wonder why reaction with oxygen does not lead to an octahedral μ-oxo complex as in some other systems. However, it is well established that Fe(SALEN) reacts with dioxygen in coordinating solvents (including pyridine) to give μ-oxo complexes in which the solvent is not coordinated.[6,7] This is in contrast to Co(SALEN) which reacts with dioxygen in coordinating solvents to form μ-peroxo complexes with solvent coordinated in the axial position.[13] But five-coordinate μ-oxo complexes are not uncommon in other iron systems. Iron porphyrins also react with oxygen in pyridine to form μ-oxo complexes in which the pyridine is not coordinated.[14] This may in fact be a general characteristic of ferrous complexes with strong square-planar bonding.

The apparently strong bond between iron(II) and pyridine in the high-spin Schiff base complexes could be attributed to strong π bonding between the nitrogen pπ and iron dπ orbitals. This may explain why no aliphatic nitrogen adducts of Fe(SALEN) could be isolated. The stabilities of complexes such as Fe(SALEN)pip (pip = piperidine) are apparently less since π bonding is not possible in these compounds. With the pyridine adducts, reaction with oxygen produces an iron(III) complex. In this compound, π bonding is now associated with the μ-oxo oxygen as evidenced by a strong exchange interaction[9] and short metal–oxygen bond distances.[6] In the μ-oxo complex, the interaction between pyridine and iron probably becomes very weak and stability is not gained by coordination of a sixth donor.

Relevance to Methemerythrin. There have been many comparisons of μ-oxo complexes with oxy- and methemerythrin.[2] The reason is that in these compounds there is also a strong exchange interaction between the two iron centers. Mössbauer experiments have shown that $[Fe(SALEN)]_2O$ and oxyhemerythrin exhibit the same isomer shift.[15] One of the earliest theories concerning the bonding in oxyhemerythrin was suggested by Garbett et al. to involve a μ-oxo bridge.[16] Obviously this must be of an unusual type since normally μ-oxo complexes lead to irreversibly oxidized ferric complexes. However, the reversibility of oxyhemerythrin is limited since "aging" slowly results in the formation of irreversible methemerythrin.[15]

The difficulty in obtaining a model compound for hemoglobin is the prevention of μ-oxo formation.[17] Only when a ligand was prepared which prevented dimerization was a reversible dioxygen complex realized.[1,18] Various mechanisms were proposed to account for μ-oxo compounds. It is now well established that the first step is the formation of a 1:1 dioxygen complex.[1] The second step would then be the reaction of this compound with another molecule of unoxygenated complex to produce a μ-peroxo compound. Although no μ-peroxo iron complex has been isolated, it seems reasonable from studies with cobalt that an unstable μ-peroxo complex would be formed.[13] To account for the ultimate μ-oxo compound, it has been suggested[14] that the reaction proceeds as follows:

$$FeO_2Fe \rightarrow 2FeO$$

$$FeO + Fe \rightarrow FeOFe$$

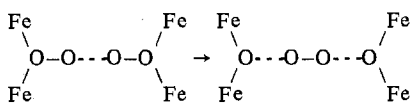
This mechanism assumes there is enough electron transfer into the antibonding orbitals of dioxygen to break the oxygen–oxygen bond. So far there has been no substantial evidence to support this. An alternate pathway involves a similar scheme:

$$FeO_2Fe + Fe \rightarrow FeOFe + FeO$$

$$FeO + Fe \rightarrow FeOFe$$

Here the breaking of the dioxygen bond is facilitated by the presence of a third metal ion. However, for large ligands such as SALEN, this pathway is sterically impossible.

Neither of these mechanisms are applicable in the case of solid-state reactions. This is the result of the fact that the metal ions are in fixed positions within the crystal lattice. This is also true of hemerythrin where the iron centers are positioned within the large surrounding protein and are essentially immobile.[19] Thus the similarity between hemerythrin and iron complexes that form μ-oxo adducts in the solid state has to do with the mechanism of this reaction. If the iron(II) centers are considered independent as they are in hemerythrin, then they must be far enough apart so that interaction cannot occur. However, since dimerization is ultimately necessary, the metal ions must be within a critical distance that will allow oxo bridging (Figure 2A). The first step is probably the formation of a μ-peroxo complex (Figure 2B). This may go through a superoxo intermediate or may be a concerted reaction. In order to form the μ-oxo bridge, it is necessary to break the O–O bond. This probably occurs by a rearrangement resulting in an unsymmetrically bound peroxide ion (Figure 2C). By interaction with a neighboring molecule, two peroxo complexes could disproportionate into μ-oxo compounds (Figure 2D) and an oxygen molecule:



This mechanism could possibly be tested by oxygen-labeling experiments.

Going from a peroxo bridge to an oxo bridge, of course, requires some movement of the iron centers. Although there could be some movement of the complex within the crystal lattice, it probably would not be enough to account for the differences in relative distances. Another method of iron movement that is possible is displacement out of the plane of the equatorial ligand(s). This type of movement seems to be common as evidenced by X-ray structure determinations of μ-oxo complexes such as $[Fe(TPP)]_2O$ (TPP = tetra-

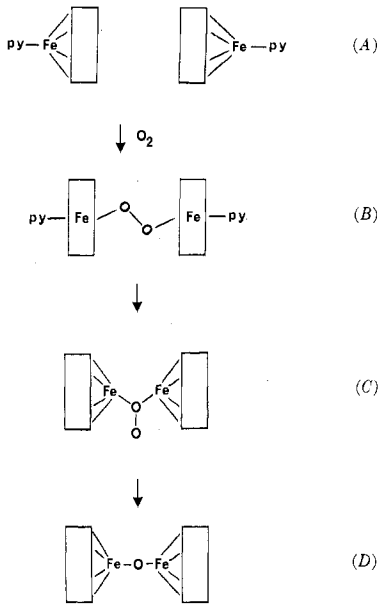


Figure 2. Schematic representation of the mechanism leading to the μ-oxo complex in the solid-state reaction.

phenylporphine[20]) and $[Fe(SALEN)]_2O$.[6] Initially, the iron(II) in the deoxygenated complex may also be displaced to the opposite side of the plane as in the case of hemoglobin.[1] This mechanism not only allows for the needed movement of the iron centers, but it also maximizes the distance between them in the deoxygenated complex and suggests another reason why the axial ligands are lost during oxo bridge formation.

Comparing this to methemerythrin, there are several things which should be taken into consideration.[15]

1. The O:Fe ratio in oxyhemerythrin is 2:2 and 1:2 in methemerythrin.
2. The oxygenation reaction is reversible, but methemerythrin will form irreversibly upon standing.
3. There is considerable interaction between the iron centers in oxyhemerythrin and methemerythrin, but there is no interaction in hemerythrin.
4. The iron centers are equivalent in hemerythrin and methemerythrin but nonequivalent in oxyhemerythrin.

The O:Fe ratio in oxyhemerythrin is that of a peroxo-type compound. However, a μ-peroxo bridge would not produce the exchange interaction that has been observed. On the other hand, the unsymmetrical peroxo bridge (Figure 2C) would allow interaction, and it is this type of compound that has been proposed herein as an intermediate leading to μ-oxo complexes in solid-state reactions. It is possible that in hemerythrin, this intermediate is stabilized in some manner such as hydrogen bonding to the neighboring protein. The compound is still somewhat unstable and this contributes to the reversibility of the reaction with dioxygen. Its instability is also manifested in its facile formation of the irreversible μ-oxo complex, methemerythrin.

This type of unsymmetrical bonding is the same as that proposed by McLendon et al.[21] as being the most likely to occur in hemerythrin as based on all available experimental evidence as well as precise steric arguments. The inequivalence of the iron atoms in oxyhemerythrin has been attributed to the hydrogen bonding of the dioxygen moiety.[16] While this could account for some nonequivalence, the overall effect would seem to be very small, especially if the dioxygen ligand has considerable μ-oxo character. From the studies just presented, it might be possible to account for another influence. Consider that the intermediate μ-peroxo complex of hemerythrin probably has ligands attached trans to the dioxygen ligand as in the case of peroxo cobalt complexes. Following the mechanism proposed for the solid-state reaction, as the μ-oxo compound is formed, the trans ligands are detached. Thus, in the case of oxyhemerythrin, which can be considered as intermediate between peroxo and oxo, these trans ligands may be nonequivalent in their bonding, therefore producing a nonequivalence in the two iron atoms. After the oxo complex is definitely formed in methemerythrin, the two iron centers are equal as they would be if both trans donors were completely lost.

The five-coordinate iron complexes reported herein seem to be good models for methemerythrin. The uniqueness of compounds which react in the solid state makes it possible to better understand the reaction of hemerythrin. However, in order to obtain a model compound for oxyhemerythrin, a means of stabilizing the intermediate dioxygen complex must be found. Perhaps the attachment of groups to which the dioxygen ligand can hydrogen bond may produce a reversible compound.[22] Such derivatives of the Schiff base ligand are certainly worthy of further investigation.

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Registry No. Fe(SALEN)py, 24323-09-9; Fe(5-BrSALEN)py, 66842-50-0; Fe(SAL-*o*-PhEN)py, 66842-49-7; Fe(5-BrSAL-*o*-PhEN)py, 66842-48-6; $[Fe(SALEN)]_2O$, 18601-34-8; $[Fe(5\text{-}BrSALEN)]_2O$, 18601-72-4; $[Fe(SAL\text{-}o\text{-}PhEN)]_2O$, 18601-73-5.

References and Notes

(1) J. P. Collman, R. P. Gagne, C. A. Reed, T. R. Halbert, G. Lang, and W. T. Robinson, *J. Am. Chem. Soc.*, **97**, 1427 (1975).
(2) E. Bayer, P. Krauss, A. Roder, and D. Schretzmann, "Oxidases and Related Redox Systems", Vol. I, T. E. Kine, H. S. Mason, and M. Morrison, Ed., University Park Press, Baltimore, Md., 1973, Chapter II.
(3) K. B. Ward, W. A. Hendrickson, and G. L. Klippenstein, *Nature (London)*, **257**, 818 (1975).
(4) S. J. Lippard, H. Schugar, and C. Walling, *Inorg. Chem.*, **6**, 1825 (1967).
(5) E. B. Fleischer, *Acc. Chem. Res.*, **3**, 105 (1970).
(6) M. Gerloch, E. D. McKenzie, and A. Towl, *Nature (London)*, **220**, 906 (1968).
(7) F. Calderazzo, C. Floriani, R. Henzi, and F. L'Eplattenier, *J. Chem. Soc. A*, 1378 (1969).
(8) A. Earnshaw, E. A. King, and L. F. Larkworthy, *J. Chem. Soc. A*, 1048 (1968).
(9) J. Lewis, F. E. Mabbs, and A. Richards, *J. Chem. Soc. A*, 1014 (1967).
(10) H. Kobayashi and Y. Yanagawa, *Bull. Chem. Soc. Jpn.*, **45**, 450 (1972).
(11) R. H. Niswander and A. E. Martell, *Inorg. Chem.*, **17**, 1511 (1978).
(12) R. DeIasi, S. L. Holt, and B. Post, *Inorg. Chem.*, **10**, 1498 (1971).
(13) C. Floriani and F. Calderazzo, *J. Chem. Soc. A*, 946 (1969).
(14) O. H. W. Kao and J. H. Wang, *Biochemistry*, **4**, 342 (1965).
(15) N. Y. Okamura and I. M. Klotz, "Inorganic Biochemistry", Vol. I, G. L. Eichhorn, Ed., Elsevier, New York, N.Y., 1973, Chapter II.
(16) K. Garbett, D. W. Darnall, I. M. Klotz, and R. J. P. Williams, *Arch. Biochem. Biophys.*, **103**, 419 (1969).
(17) A. R. Amundsen and L. Vaska *Inorg. Chim. Acta*, **14**, L49 (1975).
(18) J. E. Baldwin and J. Huff, *J. Am. Chem. Soc.*, **95**, 5757 (1973).
(19) K. B. Ward, W. A. Hendrickson, and G. L. Klippenstein, *Nature (London)*, **257**, 818 (1975).
(20) E. B. Fleischer and T. S. Srivastava, *J. Am. Chem. Soc.*, **91**, 2403 (1969).
(21) G. McLendon, W. Harris, and A. E. Martell, *Bioinorg. Chem.*, **7**, 117 (1977).
(22) A. Avdeff and W. P. Schaefer, *J. Am. Chem. Soc.*, **98**, 5153 (1976).