Electronic and Solvent Effects in the Reaction of Zinc Porphyrins with a Metal Imidazolate Complex or 1-Methylimidazole

JOHN B. COOPER, CYNTHIA T. BREWER and GREG BREWER
Department of Chemistry, The Citadel, Charleston, S.C. 29409, U.S.A.

(Received September 22, 1986)

Abstract

The reactions of Zn(p-XTPP) derivatives (X = CF_3, Cl, F, H, CH_3, OCH_3, $N(Et)_2$) with a copper imidazolate complex to yield imidazolate bridged binuclear axial adducts of the porphyrin were followed in the visible region between 700–450 nm. The α and β bands of the porphyrin shift to lower energy and the $\epsilon_\beta/\epsilon_\alpha$ ratio decreases upon adduct formation. Equilibrium constants for the reaction were measured in toluene at 25.3 °C using the β band maximum of the parent zinc porphyrin. A plot of $\log K_{eq}$ with the Hammett constant is linear with a slope of 0.208, which indicates that the formation of the binuclear adducts is aided by electron withdrawing substituents on the porphyrin. Replacement of the copper atom in the imidazolate complex with nickel significantly reduces the value of K_{eq} for the reaction with Zn(TPP) while the free ligand fails to react at all. The reduced reactivity with the nickel imidazolate complex is attributed to entropy effects and that of the non-reacting metal free complex to conformational effects. Equilibrium constants for the reaction of N-CH_3Im with Zn(TPP) conducted in dichloromethane, toluene, dimethoxyethane, and dimethylsulfoxide reveal a linear dependence of $\log K_{eq}$ on the position of the α or β band in a given solvent. The relative ordering of K_{eq} in various solvents is given by the position of the α or β band maximum of the parent zinc porphyrin. The lower the energy of the bands the smaller the value of K_{eq}.

Introduction

The binding of imidazole and its derivatives to metalloporphyrins has long been a subject for investigation because of its relevance to biological systems. One such system is the enzyme cytochrome *c* oxidase, which contains Fe(III) ($S = 5/2$) in a porphyrin environment and Cu(II) ($S = 1/2$) in a non-porphyrin environment antiferromagnetically ($-J > 200$ cm^{-1}) coupled by a bridging group to give a $S = 2$ system [1]. Although the identity of the bridging group is structurally undetermined, both imidazolate [1] and thiolate [2] have been postulated. We have recently begun investigations of the imidazolate bridged model by examining the binding of metal imidazolate complexes to metalloporphyrins to give imidazolate bridged bi- or trinuclear metalloporphyrin complexes. Systems investigated to date include the trinuclear adduct from the reaction of Fe(TPP)Cl (TPP is the dianion of tetraphenylporphyrin) with a metal imidazolate complex, M[CBP-PHEN-4-CHO-Im] (MIm, M = Cu or Ni, Y = Cl, see Fig. 1) [3], and binuclear adducts formed in the reaction of Co(TPP) [4] or Zn(TPP) [5] with MIm. In these adducts, binding to the central metal atom of the porphyrin occurs through the imidazolate nitrogen such that the metal centers are bridged by an imidazolate.

Preliminary investigation [5] of the imidazolate bridged model was conducted with Zn(TPP) due to the simplicity imposed by its d^{10} electron configuration. Reactions of the CuIm or NiIm complexes with Zn(TPP) were compared to the analogous reaction with N-methylimidazole, N-CH_3Im, to determine what effect the presence of the metal would have on the ability of the imidazole portion of the complex to bind. Striking spectral and thermodynamic similarities were found between N-CH_3Im and its MIm analogues in spite of obvious structural differences and the fact that the MIm complexes contain a formal imidazolate.

Axial ligation of metalloporphyrins with simple nitrogenous donors has been shown to be sensitive to substituents on the periphery of the porphyrin and to solvent effects. In reactions with axial bases, Co(II) [6], V(IV) [7], Ni(II) [7], Zn(II) [8], and Fe(p-XTPP)Cl [9] (p-XTPP is the dianion of the symmetrically *para* X substituted tetraphenylporphyrin) exhibit a dependence of K_{eq} on substituents of the phenyl rings. These reactions have been shown to follow the linear free energy relationship

$$\log K_X = \log K_H + 4\sigma\rho$$

where σ is the Hammett constant for the substituents, ρ is the sensitivity of the reaction to electronic effects, and K_H and K_X are the equilibrium constants for the reaction of an axial base with M(TPP) or M(p-XTPP), respectively. The magnitude and sign

0020-1693/87/$3.50

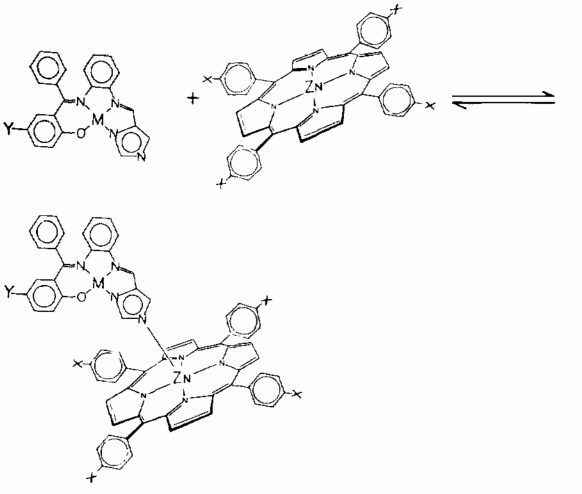

Fig. 1. Reaction of Zn(p-XTPP) with MIm complexes. X = CF_3, Cl, F, H, CH_3, OCH_3 or $N(Et)_2$. M = Cu, Ni or 2H. Y = F, Cl or Br.

of this dependence varies with the metal ion, charge of the ion, and the stoichiometry of the adduct. Solvent effects are also important in determining the value of K_{eq}. The formation constant for the reaction of Fe(TPP)Cl with an axial base [9] shows a complicated dependence on solvent polarity which may arise from a combination of bulk effects and specific molecular interactions. Electronic and solvent effects on the reaction of Zn(TPP) with CuIm or N-CH_3Im are the subjects of this investigation.

Three aspects of the electronic dependence of K_{eq} for the reaction of Zn(p-XTPP) with a metal imidazolate complex (see Fig. 1) were examined as part of this study – the variation of K_{eq} with the para substituent, X, the dependence of K_{eq} upon the metal in the metal imidazolate complex, and the effect of substituent variations on the base while keeping the metal constant. The results for the reaction of Zn(p-XTPP) with CuIm has revealed a linear dependence of log K_{eq} on the Hammett constant similar to the systems discussed above. Solvent effects for the reaction of N-CH_3Im and Zn(TPP) reveal a linear dependence of log K_{eq} on the visible band positions of the porphyrin.

The information obtained from these studies is being used to optimize conditions for the formation of imidazolate bridged adducts between pairs of paramagnetic metals. These adducts will allow an investigation of the ability of imidazolate to mediate magnetic exchange in Cu(II)–Im–Fe(III) and Cu(II)–Im–Co(II) complexes for comparison with the known magnetic properties of cytochrome c oxidase.

Experimental

Reagents

N-Methyl imidazole (N-CH_3Im) was obtained from Aldrich, vacuum distilled, and stored over molecular sieves prior to use. Toluene and dimethoxyethane (DME) were distilled from sodium ribbon and stored over molecular sieves. Dimethylsulfoxide (DMSO, spectrophotometric grade Aldrich) was stored over sieves prior to use.

Cu[YBP-PHEN-4-CHO-Im] (Y = F, Cl, Br) and Ni[CBP-PHEN-4-CHO-Im]

The metal imidazolate complexes, MIm, were prepared by the literature procedure [10] and recrystallized from ethanol before use.

H_2[CBP-PHEN-4-CHO-Im]

The free ligand was prepared by the reaction of imidazole-4-carboxaldehyde [11] (0.030 g, 0.311 mm) and the Schiff base condensate of 5-chloro-2-hydroxybenzophenone and 1,2-diaminobenzene (0.1 g, 0.311 mm). The reaction was conducted in refluxing absolute ethanol (80 ml) for one hour. The yellow product separates on cooling and is collected by filtration (yield 56%).

H_2(p-XTPP)

The *para* substituted tetraphenylporphyrins were prepared by the method of Adler [12] by the reaction of the appropriately substituted benzaldehyde (Aldrich) with pyrolle in propionic acid. The H_2(p-CF_3-TPP) and H_2(p-$N(Et)_2$-TPP) porphyrins obtained in this manner were impure and were chromatographed on dry alumina with chloroform prior to metal insertion.

Zn(p-XTPP)

Zinc was inserted into the porphyrin by the method of Adler [13] and the complexes were chromatographed before use in subdued light on dry alumina with chloroform as the eluting solvent [14]. The chloroform solution was evaporated to dryness and the Zn(p-XTPP) was dried in an oven at 120 °C for several hours and stored at 0 °C in the dark until needed.

Spectra

Visible spectra were obtained on a Perkin-Elmer lamda 3B spectrophotometer equipped with a model 3600 data station or model 124 spectrophotometer. A thermostatted cell compartment attached to a circulating thermostatted bath was used to maintain a constant temperature during measurements. Absorbance data were obtained as follows. A fixed aliquot of Zn(p-XTPP) and variable amounts of axial base were mixed and diluted to 2.5 ml giving a total metalloporphyrin concentration of ~4.0 X 10^{-5} M. The absorbance of the β band was followed as a function of concentration of the base.

Calculations

Equilibrium constants were determined by the method of Rose and Drago [15] and of Miller and Dorough [16] as described previously [5].

Results and Discussion

The reaction of Zn(*p*-XTPP) with CuIm in toluene is easily followed in the visible region. Scanning spectrophotometric titrations were conducted in the 700–450 nm region to determine the presence of isosbestic points and to insure that all the systems consisted of a single equilibrium between the parent porphyrin and its mono axial adduct. The spectral behavior of Zn(*p*-OCH_3-TPP) and CuIm is shown in Fig. 2 and is typical of the other systems. Table I summarizes the positions of the α and β bands and the $\epsilon_\beta/\epsilon_\alpha$ ratio for both the four and five coordinated Zn(*p*-XTPP) complexes. For the seven compounds investigated it is observed that the α and β bands move to lower energy and that $\epsilon_\beta/\epsilon_\alpha$ decreases upon adduct formation. These trends were also observed in the reaction of symmetrically and unsymmetrically substituted zinc porphyrins with 3-picoline [17]. There is also a general shift in the position of the α and β bands to lower energy as the electron donating nature of the substituents increases. Both effects can be explained in terms of Gouterman's theory [18]. The electronic transitions shift to lower energy as more electron density is added to the porphyrin ring either from substituents at the periphery of the molecule or by axial ligation.

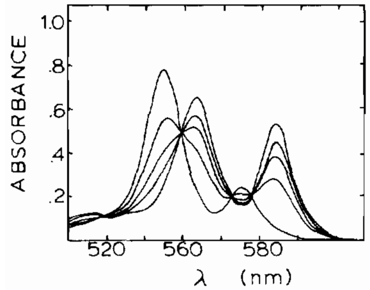

Fig. 2. Visible spectral changes observed upon addition of Cu[CBP-PHEN-4-CHO-Im] to Zn(*p*-OCH_3TPP) in toluene.

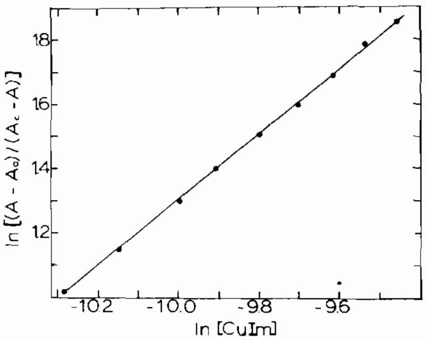

Fig. 3. Plot of $\ln[(A - A_0)/(A_c - A)]$ *vs.* $\ln(\mathrm{CuIm})_{eq}$ for the reaction of Zn(*p*-OCH_3TPP) and CuIm in toluene at 25 °C.

Equilibrium constants for the reaction of Zn(*p*-XTPP) and CuIm in toluene at 25.3 °C were calculated by the method of Drago [15] and of Miller and Dorough [16] as previously described from spectrophotometric data obtained at the β band maximum of the parent porphyrin. Good agreement between the two methods was obtained. In all cases the plots of $\ln[A - A_0)/(A_c - A)]$ *versus* $\ln[\mathrm{CuIm}]_{eq}$ (where A_0 is the absorbance of the Zn(*p*-XTPP) in the absence of base, A_c is the absorbance of the product, and A is the absorbance value of an intermediate solution) are linear with a slope of 1.00 indicating that the products of the reactions are the 1:1 imidazolate bridged binuclear complexes of copper and zinc. The plot for the reaction of Zn(*p*-OCH_3-TPP) and CuIm is shown in Fig. 3. Table II gives the formation constants with their standard deviations in parentheses and the Hammett [19] constants for the seven substituents investigated. The Hammett plot shown in Fig. 4 is linear with a slope of 0.208 indicating that the formation of the imidazolate bridged binuclear adducts of Zn(*p*-XTPP) is aided

TABLE I. Visible Peak Positions (cm^{-1}) and $\epsilon_\beta/\epsilon_\alpha$ ratio for Zn(*p*-XTPP) and the Adduct with CuIm

X	4σ	Zn(*p*-XTPP)			Zn(*p*-XTPP)–CuIm		
		$\bar{\nu}_\beta$	$\bar{\nu}_\alpha$	$\epsilon_\beta/\epsilon_\alpha$	$\bar{\nu}_\beta$	$\bar{\nu}_\alpha$	$\epsilon_\beta/\epsilon_\alpha$
CF_3	2.16	18250	17070	8.05	17700	16530	2.31
Cl	0.908	18240	17030	6.21	17690	16520	1.81
F	0.248	18260	17040	8.45	17720	16560	2.01
H	0.00	18250	17020	5.81	17670	16500	1.82
CH_3	−0.680	18220	17010	4.67	17680	16500	1.49
OCH_3	−1.072	18180	16950	3.17	17640	16420	1.23
$N(Et)_2$	−2.04	17890	16530	1.00	17460	16100	0.711

TABLE II. Equilibrium Constants and Hammett Values for the Reaction of Zn(*p*-XTPP) and CuIm at 25 °C

X	4σ	K_{eq} (M^{-1})
CF_3	2.16	421000(44700)
Cl	0.908	261000(9550)
F	0.248	172000(4660)
H	0.0	152000(3400)
CH_3	−0.680	113000(1710)
OCH_3	−1.072	81900(985)
$N(Et)_2$	−2.04	61500(1710)

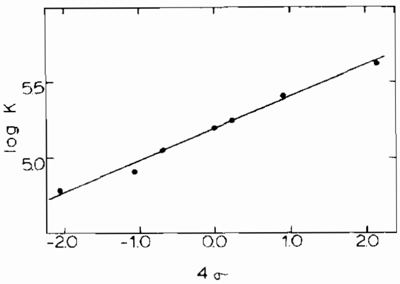

Fig. 4. Plot of log K_{eq} *vs.* 4σ for the reaction of Zn(*p*-XTPP) and CuIm in toluene at 25 °C.

by the presence of electron withdrawing substituents which enhance the Lewis acidity of the Zn(*p*-XTPP).

It was found that the electronic dependence of the reaction of Zn(*p*-XTPP) with pyridine in benzene is 0.188 [20] and that of symmetrically and unsymmetrically substituted Zn(TPP)s with 3-picoline in toluene is 0.180 [17]. The present value of 0.208 is only slightly greater although the reaction differs in two significant aspects. First, the nitrogen donor is an imidazole, formally an imidazolate, rather than a pyridine. Secondly, the axial base is covalently attached to a larger molecule and bound to a transition metal ion. This indicates that the electronic effect in the reaction of Zn(*p*-XTPP) with axial bases is only slightly dependent on the nature of the axial base, even for as unusual a base as in the present study, at least among nitrogen donors. The electronic dependence of the reaction of Co(II) and VO(*p*-XTPP) complexes with axial bases to give monoadducts have been reported as 0.145 and 0.113. The greater sensitivity of the zinc porphyrins has been attributed to the ability of the d^{10} electron configuration to interact with the porphyrin pi system in a metal to ligand backbonding manner [20]. The reactions of Ni(*p*-XTPP) and piperidine in toluene [7] and of Fe(*p*-XTPP)Cl and N-CH_3Im in chloroform [9], which give bis adducts, yield ρ values of 0.331 and −0.39, respectively. The sign for the latter system reflects the +3 charge on the metal and the fact that the product is an ion pair. However, both the sign and magnitude are highly solvent dependent for this system as the same reaction conducted in DMSO yields a ρ of 0.113 [21].

The dependence of the formation constant for the reaction of Zn(TPP) with MIm was also investigated as a function of the metal (M = Cu, Ni, or 2H). It was previously reported that the difference in formation constants of CuIm (152 000) and NiIm (110 000) with Zn(TPP) is attributed, not to differences in basicities between the two, but to a more favorable entropy term for CuIm. As part of this study it was found that the free ligand (M = 2H) does not bind to Zn(TPP), as determined by lack of spectral changes, even at a ligand to zinc ratio of 643:1. Two changes occur on the formation of NiIm or CuIm from the free ligand. The imidazole loses a proton to become a formal imidazolate, and the metal holds the ligand in a square planar geometry positioning the imidazolate for subsequent binding to the metalloporphyrin. The latter of these two effects is probably the more important in comparing the reactivities of the free ligand and its metal complexes. The $\epsilon_\beta/\epsilon_\alpha$ ratio and the position of the α band for the adduct of NiIm or CuIm with Zn(TPP) (1.82 and 16 500 cm^{-1}) is similar to those for the adduct of *N*-CH_3Im (1.72 and 16 470 cm^{-1}) as opposed to those of the imidazolate adduct [22] (1.34 and 16 210 cm^{-1}), which suggests that the MIm complexes are closer in electron donating properties to imidazole than to imidazolate. Without the metal present, the free ligand is not conformationally constrained. Although it could bind through its imidazole ring, it is apparently not oriented properly in solution to do so. The formation constant of the adduct of Zn(TPP) with imidazole-4-carboxaldehyde, which is electronically similar to the imidazole portion of the free ligand but sterically less hindered, is 2030 ± 120 M^{-1}, which is significantly smaller than that observed for the adduct of Zn(TPP) with CuIm (152 000). This suggests that the presence of the metal enhances adduct formation in some manner in addition to controlling the geometry of the complex.

The effect on K_{eq} of varying the halogen which is *para* to the phenolic oxygen of the CuIm was also investigated. The equilibrium constants for the reaction of Zn(TPP) with CuYIm (Y = F, Cl, or Br) in toluene at 31.5 °C are 104 000, 111 000 and 101 000 M^{-1}, respectively. The similarities among these bases are not surprising as they are all imidazole donors, and the atom being varied is remote from the imidazole ring with its effects being transmitted through the copper ion.

It has been observed that the visible band positions of Zn(TPP) are solvent dependent with large red shifts (measured from their positions in cyclohexane) occurring in strongly interacting solvents. The reaction of Zn(TPP) with *N*-CH_3Im in DMSO, DME, toluene, and dichloromethane [23] was chosen to

TABLE III. Position of Visible Peaks of Zn(TPP)[a] (cm^{-1}) and Formation Constants of the Adduct with N-CH_3Im at 25 °C

Solvent	$\bar{\nu}_\alpha$	$\bar{\nu}_\beta$	K_{eq} (M^{-1})
Dichloromethane	17080	18260	240000[b]
Toluene	16980	18200	54100
Dimethoxyethane	16880	18070	1680
Dimethylsulfoxide	16660	17830	13.0

[a]Taken from ref. 22. [b]Taken from ref. 23.

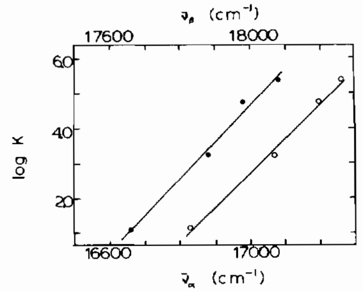

Fig. 5. Plot of log K_{eq} for the reaction of Zn(TPP) and N-CH_3Im in various solvents *vs.* the positions of the parent α band (closed circles) and β band (open circles) in the same solvent.

investigate the effect of solvent on K_{eq} for axial ligation. An interesting correlation is observed between log K_{eq} in a given solvent and the positions of the α and β bands in that solvent. Results are given in Table III and a plot of log K_{eq} *versus* the α and β band positions is shown in Fig. 5. It is clear from the data that strongly interacting solvents, such as DMSO, substantially lower the value of K_{eq} for an axial ligation reaction. For the case of a coordinating solvent, an explanation is readily available in terms of a competition between the base and solvent for the vacant coordination site of Zn(TPP). This is probably the case with solvents such as DMSO, DMF, and, to a lesser extent, DME. This is in agreement with the results of Nappa and Valentine, who suggested that ligation is responsible for the large red shifts (measured from their positions in cyclohexane) observed in coordinating solvents [22]. For non-coordinating solvents the interaction is less obvious, perhaps a loose attraction to the metal or a pi–pi interaction with the porphyrin ring. Nappa and Valentine correlated the position of the α band with a solvent parameter, $(n^2 - 1)/(2n^2 + 1)$ (n is the refractive index of the neat solvent) [22]. The solvents investigated fell into one of two distinct categories, coordinating and non-coordinating, as judged by the fit. For non-coordinating solvents, the solvent parameter varied linearly with the α band position. Coordinating solvents fell off the line as the α band energies in these solvents were substantially less than predicted by the function. They concluded that the observed band shifts (*versus* the α band position in cyclohexane) arise from a combination of two separate effects – solvation and ligation. This work fails to make that distinction since α and β band positions for both coordinating and non-coordinating solvents vary linearly with log K_{eq} for the reaction of Zn(TPP) and N-CH_3Im in these solvents.

This study has shown that the formation of imidazolate bridged binuclear adducts in the reaction of Zn(p-XTPP) with CuIm is aided by the presence of electron withdrawing groups and that log K_{eq} follows the Hammett equation with a slope of 0.208 which is slightly greater than that exhibited in the analogous reaction with pyridine donors. The competition between an axial base and solvent has been demonstrated by the correlation of log K_{eq} and the positions of the α and β bands of the parent porphyrin in the solvent in the reaction of N-CH_3Im and Zn(TPP). The value of the equilibrium constant for an axial ligation reaction can be maximized by appropriate choice of porphyrin and solvent. These results are being applied to the reactions of CuIm with Co(II) and Fe(III)(p-XTPP)Cl since solution magnetic susceptibility experiments using the above systems to measure the extent of magnetic exchange fostered by the imidazolate bridge will require conditions of high K_{eq} to insure that the adduct is the prominent species in solution. These results may shed some light on the plausibility of such a bridge in cytochrome c oxidase.

Acknowledgement

Funds for the computer interfaced spectrophotometer used in this work were provided by The Citadel Development Foundation. This and other CDF support is gratefully acknowledged.

References

1 M. F. Tweedle, L. J. Wilson, L. Garcia-Iniguez, G. T. Babcock and G. Palmer, *J. Biol. Chem., 253*, 8065 (1978).
2 L. Powers, B. Chance, Y. Ching and P. Angiolillo, *Biophys. J., 34*, 465 (1981).
3 C. Brewer and G. Brewer, *Inorg. Chem.*, (1986) submitted for publication.
4 C. Brewer and G. Brewer, *Inorg. Chim. Acta, 111*, L5 (1986).
5 C. Brewer and G. Brewer, *Inorg. Biochem., 26*, 247 (1986).
6 F. A. Walker, D. Beroiz and K. M. Kadish, *J. Am. Chem. Soc., 98*, 348 (1976).
7 F. A. Walker, E. Hui and J. M. Walker, *J. Am. Chem. Soc., 97*, 2390 (1975).
8 F. A. Walker, V. L. Balke and G. A. McDermott, *Inorg. Chem., 21*, 3342 (1982).

9 (a) F. A. Walker, M. W. Lo and M. T. Ree, *J. Am. Chem. Soc., 98*, 5552 (1976); (b) K. M. Kadish and L. A. Bottomley, *J. Am. Chem. Soc., 99*, 2381 (1977); (c) V. L. Balke, F. A. Walker and J. T. West, *J. Am. Chem. Soc., 107*, 1226 (1985).

10 R. Atkins, G. Brewer, E. Kokot, G. M. Mockler and E. Sinn, *Inorg. Chem. 24*, 127 (1985).

11 E. P. Papadopoulos, A. Jarrar and C. H. Issidorides, *J. Org. Chem., 31*, 615 (1966).

12 A. D. Adler, F. R. Longo, J. D. Finarelli, J. Goldmacher, J. Assour and L. Korsakoff, *J. Org. Chem., 32*, 476 (1967).

13 A. D. Adler, F. R. Longo, F. Kampas and J. Kim, *J. Inorg. Nucl. Chem., 32*, 2443 (1970).

14 G. C. Vogel and L. A. Searby, *Inorg. Chem., 12*, 936 (1973).

15 N. J. Rose and R. S. Drago, *J. Am. Chem. Soc., 81*, 6138 (1959).

16 J. R. Miller and G. D. Dorough, *J. Am. Chem. Soc., 74*, 3977 (1952).

17 G. A. McDermott and F. A. Walker, *Inorg. Chim. Acta, 91*, 95 (1984).

18 M. Gouterman, *J. Chem. Phys., 30*, 1139 (1959).

19 (a) L. P. Hammett, 'Physical Organic Chemistry', McGraw Hill, New York, 1970, p. 356; (b) J. M. Harris and C. C. Wamser, 'Fundamentals of Organic Reaction Mechanisms', Wiley, New York, 1976, p. 115; (c) E. Pelizzetti and C. Verdi, *J. Chem. Soc., Perkin Trans. 2*, 808 (1973).

20 G. C. Vogel and B. A. Beckmann, *Inorg. Chem., 15*, 483 (1976).

21 C. Brewer and G. Brewer, *191st National ACS Meeting*, New York, N.Y., 1986.

22 M. Nappa and J. S. Valentine, *J. Am. Chem. Soc., 100*, 5075 (1978).

23 K. M. Kadish, L. R. Shiue, R. K. Rhodes and L. A. Bottomley, *Inorg. Chem., 20*, 1274 (1981).