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Electron Paramagnetic Resonance Study of the Interaction of Nitrosyl(protoporphyrin IX dimethyl ester)iron(II) with Sulfur- and Oxygen-donor Ligands

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The interaction of nitrosyl(protoporphyrin IX dimethyl ester)iron(II) with various sulfur (S)- and oxygen (O)-donor ligands has been studied by electron paramagnetic resonance (EPR) measurements. It was found that some of these ligands coordinate to the iron in the position trans *to the nitrosyl group at low temperature, while at room temperature such an axial coordination is impossible, or very weak. It was also shown that the axial coordination of the S-donor ligand is stronger than that of the O-donor one and that the bonding ability of the thioether sulfur is somewhat more pronounced than that of the thiol one. The structure of the Fe–N–O unit in the complex formed at low temperature is compared with the case of the nitrogen (N)-donor ligands.*

Introduction

The investigations for the EPR spectra of nitrosylporphyrinatoiron(II) complexes with the axial ligand *trans* to a nitrosyl group have been extensively undertaken to characterize the axial ligand, which has been limited to nitrogenous bases in relation to a histidine ligand to heme iron in the majority of hemoproteins (hemoglobin, myoglobin, cytochromes, *etc.*) [1]. The imidazole nitrogen, thioether sulfur (cytochromes c) [2], and, probably, thiolate sulfur (cytochrome P-450) [3], have all been known as axial ligands to heme iron in hemoproteins. The O-donor group has been possibly considered as the axial ligand in abnormal hemoglobins [4]. Thus, we have been interested in the interaction of nitrosyl(protoporphyrin IX dimethyl ester)iron(II) (or nitrosylprotoheme dimethyl ester, Fe(PPDME)(NO)) with S- and O-donor ligand.

In preceeding papers [1c, d], it was reported that the pyridine and the imidazole derivatives differ in exchange rate between the five- and six-coordinate species in reaction with the Fe(PPDME)(NO) and that two molecular species can exist in the Fe(PPDME)(NO) complex with the nitrogenous bases.

The present paper presents EPR evidence for the coordination of various S-(thioethers and thiols) and O-donor ligand (ethers, alcohols, *etc.*) to the iron in the position *trans* to the nitrosyl group of Fe(PPDME)(NO) at low temperature. The structure of Fe–N–O unit in the complex formed is discussed on the basis of the EPR parameters and is compared with that in the complex with N-donor ligands.

Experimental

Nitrosyl(protoporphyrin IX dimethyl ester)iron(II) was prepared as described previously [5]. The thioethers, thiols and ethers were obtained as the best available grade and were used without further purification. All other chemicals including tetrahydrothiophen, tetrahydrofuran, and furan were purified and dried by the usual method [6]. The solvents and the liquid ligands were deoxidized by bubbling pure N_2 prior to use. N-Acetylmethionine methyl ester was prepared by the esterification of methionine with methanol-HCl on an ice bath and then the acetylation with acetic anhydride.

EPR measurements were carried out as described previously [1d]. EPR samples, in which the concentration of Fe(PPDME)(NO) was 5 *mM* unless otherwise stated, were prepared under N_2.

Results

At room temperature, Fe(PPDME)(NO) systems with S- and O-donor ligand exhibited the EPR spectra with an isotropic triplet structure, similar to that of the systems without a *trans* axial ligand [5]. This was the case both in neat ligands and in organic solvents such as toluene, chloroform, dichloromethane, and acetone. The isotropic g values at the center of the triplet and coupling constants (A values) of these systems were only slightly smaller than those of the systems without a *trans* axial ligand (Table I). This is

TABLE I. EPR Parameters[a] in Various Solvents at Room Temperature.

Ligand[b]	neat	toluene $E_T{}^c = 33.9$	$CHCl_3$ 39.1	CH_2Cl_2 41.1	acetone 42.2
None		2.052_3 (16.2)	2.052_1 (16.0)	2.051_9 (16.1)	2.050_9 (16.1)
Me_2S^d	2.049_5 (15.8)	2.051_7 (16.0)	2.051_9 (16.0)	2.050_0 (15.6)	2.050_6 (15.7)
$EtMeS^d$	2.051_0 (15.9)	2.051_6 (16.1)	2.052_4 (16.0)	2.051_6 (16.1)	2.051_4 (16.1)
THT^d	2.049_7 (16.1)	2.051_9 (16.0)	2.051_9 (16.1)	2.051_2 (15.9)	2.050_8 (15.8)
$NAcMetME^e$					2.051_7 (16.0)
THF^f	2.050_8 (16.0)	2.052_5 (16.2)	2.052_1 (16.0)	2.050_7 (15.9)	2.051_1 (15.7)

[a] Isotropic g value and isotropic coupling constant (in parentheses) in gauss. [b] Abbreviations: Me_2S, dimethyl sulfide; EtMes, ethyl methyl sulfide; THT, tetrahydrothiophene; NAcMetME, N-acetylmethionine methyl ester; THF, tetrahydrofuran. [c] Taken from ref. 7. [d] [Ligand]/[Fe(PPDME)(NO)] (m.r.) ≈ 400. [e] m.r. ≈ 800. [f] m.r. ≈ 600.

very different from the systems with imidazoles and pyridines, in which the g and A values distinctly decrease with an increase in ligand concentration [1c, d]. As shown in Table I, both g and A values slightly decrease with an increase in E_T value [7] (the polarity of the solvents), which is similar to the results obtained with the systems without a *trans* axial ligand [8].

At 77 K, the systems with S- and O-donor ligand (Fig. 1b, c) exhibited clearly distinguishable spectra from those of the system without a *trans* axial ligand (Fig. 1d).

The temperature dependence of the spectra of the system with tetrahydrothiophen in acetone from room temperature to 77 K was illustrated in Fig. 2. On lowering the temperature from 293 K, the triplet signal was sharpened and then broadened and the triplet structure disappeared around the freezing point of the solution (melting points of acetone and tetrahydrothiophene: 178 and 177 K, respectively). The spectra at 153 K appeared to exhibit overlapping of Fig. 1d- and 1c-type spectra, and at lower temperature varied to spectra identical to Fig. 1c.

Accordingly, the interaction of S- and O-donor ligands with iron seems to be intensified with an decrease in temperature.

Figure 3 shows the spectra (first- and second-derivative display) of the systems with dimethyl sulfide and N,N-dimethyl formamide in frozen acetone glass at 77 K. The line shape of the spectra appparently resembles that of the system with N-donor ligand (Fig. 1a). As shown in Fig. 3, the g_2- and g_3 absorptions split into a triplet, which can be originated from the hyperfine interaction of the

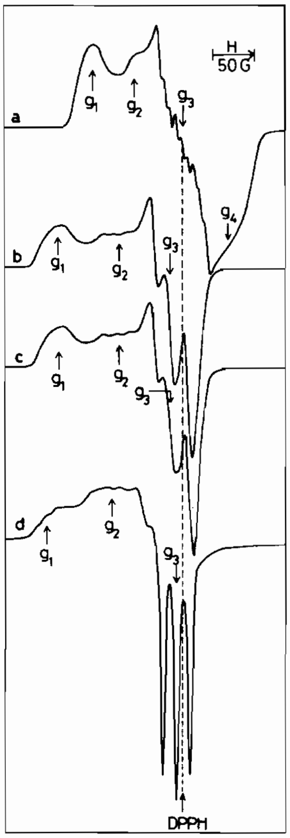

Fig. 1. The EPR spectra in frozen acetone glass at 77 K: Fe(PPDME)(NO) systems (a) with 4-aminopyridine, (b) with tetrahydrothiophen, (c) with tetrahydrofuran, and (d) without a *trans* axial ligand.

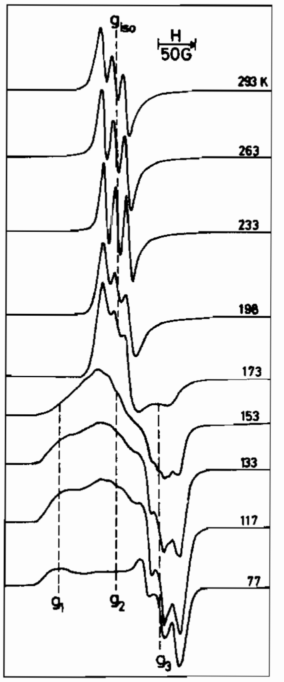

Fig. 2. Temperature dependence of EPR spectra for the Fe(PPDME)(NO)-tetrahydrothiophen system in acetone.

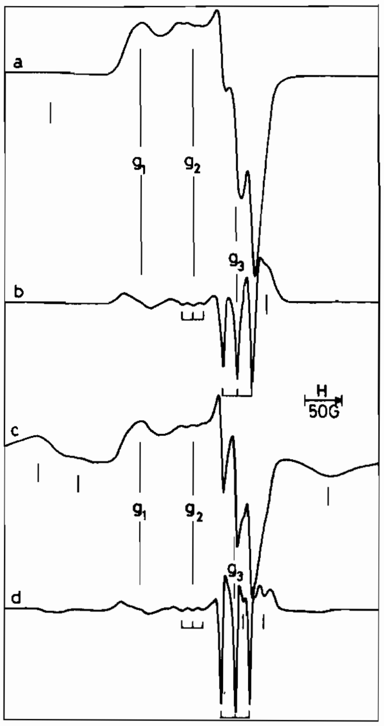

Fig. 3. The EPR spectra in frozen acetone glass at 77 K: (a) first- and (b) second-derivative displays of Fe(PPDME)(NO)-dimethyl sulfide system; (c) first- and (d) second-derivative displays of Fe(PPDME)(NO)-dimethyl formamide system.

unpaired electron with the ^{14}N nucleus of the NO group. The second-derivative display exhibited the existence of additional absorptions at the lower and higher magnetic field sides of the third line in the g_3 absorption. The measurement of EPR spectra at Q-band frequency, in which this additional absorptions would be resolved, is in progress.

The EPR parameters of the system with S- and O-donor ligand at 77 K are shown in Tables II and III respectively. When the spectral line shape and the A_3

TABLE 11. EPR Parameters of Fe(PPDME)(NO) System with S-donor Ligand in Acetone at 77 K.

Ligand[a]	m.r.[b]	g_1	g_2	g_3	Coupling Const. (G)		
					A_1	A_2	A_3
None		2.109	2.059	2.009_5	13	16	16.5
EtSH	400	2.096	2.05	2.011			18.2
nPrSH	800	2.11	2.06	2.009_8			16.6
PhSH	800	2.10	2.06	2.009_9			16.5
Me_2S	400	2.092	2.047	2.009_3		14	19.7
Et_2S	400	2.095	2.049	2.010_9			18
Ph_2S	800	2.10	2.059	2.009_5		15	16.1
EtMeS	400	2.093	2.048	2.009_6		14	20.2
MePhS	400	2.095	2.05	2.009_1			17.5
Me_2S_2	800	2.10	2.06	2.009			16.3
Thiop	400	2.103	2.058	2.009_8	14	14	16.2
THT	400	2.094	2.049	2.010_0		15	19.6
NAcMet	sat.[c]	2.10	2.049	2.010_8		17	18.4
NAcMetME	800	2.094	2.05	2.010_3		16	19.4

[a] Abbreviations except for those in the footnote b of Table 1: EtSH, ethanethiol; nPrSH, n-propanethiol; PhSH, benzenethiol; Et_2S, diethyl sulfide; Ph_2S, diphenyl sulfide; MePhS, methyl phenyl sulfide; Me_2S_2, dimethyl disulfide; Thiop, thiophene; NAcMet, N-acetylmethionine. [b] m.r. = [Ligand]/[Fe(PPDME)(NO)]. [c] sat., saturated.

TABLE III. EPR Parameters of Fe(PPDME)(NO) System with O-donor Ligand in Acetone at 77 K.

Ligand[a]	m.r.[b]	g_1	g_2	g_3	Coupling Const. (G)		
					A_1	A_2	A_3
None		2.109	2.059	2.009_5	13	16	16.5
MeOH	800	2.09	2.047	2.010_8			21
EtOH	800	2.11	2.059	2.009_8		15	16.4
PhOH	800	2.10	2.060	2.009_5		15	16.6
Et_2O	800	2.10	2.06	2.009_7		14	16.6
MenPrO	(neat)	2.10	2.05	2.010_9			20
MePhO	800	2.10	2.06	2.009_9		15	16.7
Furan	800	n.r.[c]	n.r.[c]	2.009_8			16.6
THF	400	2.096	2.050	2.011_4		14	20.6
Me_2SO	600	2.10	2.05	2.010_4			20
nBu_2SO	600	2.093	2.046	2.009		15	20.1
Ph_2SO	600	2.099	2.050	2.011		15	19.0
DMF	400	2.091	2.046	2.009_8		15	19.9
DMAc	600	2.10	2.06	2.009_8			16.5
$MeNO_2$	800	n.r.[c]	n.r.[c]	2.009_7			16.3
$(MeO)_3PO$	800	n.r.[c]	n.r.[c]	2.010			16.5
NAcGlyEE	400	2.10	2.06	2.009_9			16.6

[a] Abbreviations: MeOH, methanol; EtOH, ethanol; PhOH, phenol; Et_2O, diethyl ether; MenPrO, methyl n-propyl ether; MePhO, methyl phenyl ether; THF, tetrahydrofuran; Me_2SO, dimethyl sulfoxide; nBu_2SO, di-n-butyl sulfoxide; Ph_2SO, diphenyl sulfoxide; DMF, dimethyl formamide; DMAc, dimethyl acetamide; $MeNO_2$, nitromethane; $(MeO)_3PO$, trimethyl phosphate; NAcGlyEE, N-acetylglycine ethyl ester. [b] See footnote b of Table II. [c] n.r. = not resolved.

value are Fig. 1d type and around 16.5 G (corresponding to those of the system without a *trans* axial ligand), the interaction of ligand with iron seems to be very weak. In these systems, the g_1, g_2, and g_3 values may be assigned to g_x, g_y, and g_z ones, respectively, on the basis of the assignments for the system without a *trans* axial ligand [5]. On the contrary, when the spectral line shape and the A_3 value are Fig. 1b (or c) type and more than 18 G, then the interaction seems to be pronounced. When the assignment of g values follows that for the system with the N-donor ligand [1c, d], g_1- and g_3 absorptions are to be assigned to g_x- and g_z ones respectively, and g_2 absorption may be assigned to $g_\perp$ of second species [1c]. In the systems with thiols, thioethers, alcohols and ethers, the interaction is complicated by the effect of the carbon numbers of alkyl groups and the symmetry of ligand molecules, as described later. Dimethyl disulfide is unlikely to interact with iron, due to the participation of the lone-pair electron of sulfur in double bond formation in a disulfide [9]. In the systems with tetrahydrothiophen and tetrahydrofuran, the interaction is however possible, although impossible in those with thiophen and furan because the lone-pair electron of donor atom is utilized in the conjugation with hetero-aromatic ring. The carbonyl oxygen in N,N-dimethyl-, N-methyl-, and formamide can coordinate to iron, while that in N,N-dimethyl acetamide, which is interposed by neighbouring two methyl groups, cannot. Sulfoxides clearly exhibited such interaction.

Although N-acetylmethionine methyl ester has sulfur and oxygen as possible donor atoms, in this case sulfur appeared to coordinate to iron because interactions can not be observed in the system with N-acetylglycine ethyl ester with oxygen donor. From the dependence of EPR spectra on the concentration of ligand, N-acetylmethionine methyl ester seems to be of the same order in bonding ability as n-butyl methyl sulfide, which has a structure similar to methionine among simple thioethers.

The spectra were measured in various solvents and the parameters of representative system at 77 K are shown in Table IV. The g_3 value increases slightly with polarity of the solvents. The A_3 value of the system with asymmetric thioether is more than 18 G, both in neat ligand and in solvents, while that of the system with asymmetric ether is only in neat ligand and that of the system with the other ligand is only in solvents. Thus the spectra of these systems are sensitive to solvents. Taking into account the possibility that the spectra of Fig. 1b or c type result from the interaction with the solvents, the spectra of Fe(PPDME)(NO) were measured in toluene, chloroform and acetone, and these mixed solvents in various ratios. All the spectra thus obtained were of Fig. 1d type with A_3 value of about 16.5 G.

As is partly seen in the low and high field side of Fig. 3b, in the systems with S- and O-donor ligand a group of four satellite absorptions at g = 2.28, 2.19, 1.93 and 1.83, and another weaker satellite absorption were sometimes observed. These absorptions

TABLE IV. EPR Parameters in Various Solvents at 77 K.

Ligand[a]	Solvent	g_1	g_2	g_3	A_3(G)
Me_2S[b]	neat	2.10	2.058	2.009_3	16.5
	toluene	2.090	2.046	2.007_9	20.5
	$CHCl_3$	2.092	2.046	2.009_0	19.0
	CH_2Cl_2	2.091	2.046	2.009_3	19.0
	acetone	2.092	2.047	2.009_3	19.7
EtMeS[b]	neat	2.09	2.05	2.011_1	19.2
	toluene	2.092	2.046	2.007_0	19.8
	$CHCl_3$	2.092	2.045	2.008_5	19.0
	CH_2Cl_2	2.094	2.046	2.008_9	19.2
	acetone	2.093	2.048	2.009_6	20.2
THT[b]	neat	2.10	2.059	2.009_6	16.8
	toluene	2.094	2.050	2.008_6	20
	$CHCl_3$	2.092	2.047	2.009_3	19.3
	CH_2Cl_2	2.094	2.049	2.009_7	19.0
	acetone	2.094	2.049	2.010_0	19.6
THF[c]	neat	2.104	2.061	2.009_0	17.1
	toluene	2.096	2.051	2.008_9	21
	$CHCl_3$	2.096	2.05	2.011	18
	CH_2Cl_2	2.097	2.052	2.010_9	19.7
	acetone	2.096	2.050	2.011_4	20.6

[a] Abbreviations, see footnote b of Table I. [b] [Ligand]/[Fe(PPDME)(NO)] (m.r.) ≈ 400. [c] m.r. ≈ 600.

were markedly intense in the system with very weak ligand or without a *trans* axial ligand in nonpolar solvent, *e.g.*, in the system with thiols or alcohols in toluene. The former group of absorptions was first observed in nitrosylhemoglobin-salicylate system [10] and recently assigned to absorptions resulting from the dimer formation of nitrosylporphyrinatoiron(II) by Kon *et al.* [1, 29].

Discussion

EPR spectra of Fe(PPDME)(NO) and Its Complexes with Various Axial Ligands

The N-donor ligands have been known to coordinate to iron in Fe(PPDME)(NO) at room temperature and the complex formation constants have been evaluated by the dependence of EPR spectra on the concentration of the ligand [1d]. On the contrary, the interaction of the S- and O-donor ligand with Fe(PPDME)(NO) can not be found in the EPR measurements at room temperature, but only at lower temperature as shown in Fig. 2. Thus, the bonding ability of the S- and O-donor ligands can be much less than that of the N-donors. This seems to arise mainly from markedly low basicity (or σ-bonding ability) of the former [12] compared with the latter [13]. Furthermore, the system with the S- and O-donor ligand is more sensitive to solvents than that with N-ligand [1d], both at room temperature (Table I) and at 77 K (Table IV). We consider therefore, that the former is susceptible to influence from the medium since the interaction with iron is smaller, while the latter (relatively) is not.

The deviation of g_z value from the free electron value (2.0023), which is a measure of the interaction with iron [14], decreases almost linearly for donor atom: free ligand (g_z = 2.010) [5], S- and O-coordination (g_z = 2.007-2.011), and N-coordination (g_z = 2.004-2.007) [1c, d]. The axial coupling constant (A_z value) increases in the same order for donor atom: free ligand (16.5–16.7 G) [5], S- and O-coordination (18–21 G), and N-coordination (20.5–21.9 G) [1c, d], which indicates that the unpaired electron density at the nitrogen nucleus of the NO group increases in that order. Accordingly, iron to NO bond strength can decrease in the following order for donor atom: free ligand, S- and O-coordination, and N-coordination. Consequently, it seems likely that iron to NO bond (Fe–N(NO)) distance or the displacement of the iron atom from the heme plane toward NO group (Fe---Ct distance) increases or decreases in the same order, respectively. These speculations are supported by the structural data of Fe(TPP)(NO) (Fe–N(NO) = 1.717 Å, Fe---Ct = 0.21 Å) [15] and Fe(TPP)(NO)(NMeIm) (Fe–N(NO) = 1.743 Å, Fe---Ct = 0.07 Å) [16], though these structural analyses were undertaken at room temperature (TPP, α, β, γ, δ-tetraphenylporphyrinatio dianion; NMeIm, 1-methylimidazole). The fact that a triplet structure in g_x- and g_y absorption was found in the system without a *trans* axial ligand, instead of that with a ligand (Ref. 1c, d, Table II, and III) suggests that d_π(Fe)–p_π(NO) interaction increases with a decrease in Fe–N(NO) distance and an increase in Fe---Ct one.

It was reported [1c] that two molecular species which differ in structure of Fe–N–O unit are observed in the EPR spectra of the system with N-donor ligand, and the second species (species II) show the $g_\perp$ value ranging from 2.03 to 2.04. In the system with S- and O-donor ligand the $g_\perp$ value was around 2.05 and a triplet structure was observed in $g_\perp$ absorption (Fig. 3 and Tables II, III). Since it was pointed out [1d] that the $g_\perp$ value in the system with N-donor ligand increases with decreasing strength of iron to the ligand bond, the $g_\perp$ value in the system with S- and O-donor ligand seems to reflect the weaker bond of iron to the ligand. The triplet structure in $g_\perp$ absorption in the system with S- and O-donor ligand probably arises from the structural changes of Fe–N–O unit similar to that in species I described above.

Comparison between Sulfur- and Oxygen-donor Ligand

A_z values of the system with thiols and alcohols, thioethers and ethers at 77 K are summarized in

TABLE V. Comparison between Thiols and Alcohols in Acetone at 77 K.

Ligand[a]	m.r.[b]	A_z (G)	±[c]
thiols			
EtSH	(neat)	19.1	+
	400	18.2	+
	800	18.7	+
nPrSH	(neat)	16.3	–
	800	16.6	–
alcohols			
MeOH	600	16.5	–
	700	20.3	+
EtOH	800	16.4	–
nPrOH	800	16.5	–

[a,b] See footnote a of both Table II and III and b of Table II, respectively. [c] See text.

TABLE VI. A_z Values of Fe(PPDME)(NO) System with Thioether (R•S•R′) at 77 K.

R	R′	in neat		in $CHCl_3$[a]	
		A_z (G)	±[b]	A_z (G)	±[b]
sym. thioethers					
Me	Me	16.5	–	19.0	+
Et	Et	17.4	–	19.1	+
nPr	nPr	17.0	–	19.2	+
iPr	iPr	16.8	–	16.6	–
nBu	nBu	17.0	–	16.8	–
nPe	nPe	16.7	–	16.9	–
Ph	Ph	16.3	–	16.3	–
asym. thioethers					
Et	Me	19.2	+	19.0	+
Et	nPr	19.3	+	19.2	+
Et	iPr	16.7	–	18	+
Et	nBu	18.4	+	18.9	+
Me	Ph	16	–	18	+

[a] [Ligand]/[Fe(PPDME)(NO)] ≈ 400. [b] See text.

TABLE VII. A_z Values of Fe(PPDME)(NO) System with Ether (R•O•R′) at 77 K.

R	R′	in neat		in acetone[a]	
		A_z (G)	±[b]	A_z (G)	±[b]
sym. ethers					
Et	Et	16.6	–	16.6	–
nPr	nPr	16.9	–	16.6	–
asym. ethers					
Me	nPr	20	+	16.8	–
Me	nBu	16.9	–	16.5	–
Et	nPr	21	+	16.8	–
Me	Ph	n.r.[c]		16.7	–

[a] [Ligand]/[Fe(PPDME)(NO)] ≈ 800. [b] See text. [c] n.r. = not resolved.

Tables V–VII. The plus or the minus sign in Tables V–VII refers respectively to pronounced ($A_z \geq 18$) or very weak ($A_z < 18$) interaction of the ligand with iron.

The interaction of thiols with iron is apparently greater than that of alcohols with the same alkyl group (Table V), though it should be noted that alcohols have greater ability for hydrogen bonding than do thiols [17]. The interaction of both thiols and alcohols decreases with the carbon numbers of the alkyl group. Although the basicity of thiols increases slightly with the carbon numbers of the alkyl group [18], the structural stability to maintain the iron to ligand bond probably decreases with the alkyl chain length because both thiols and alcohols are a unidentate ligand: in this case, the decrease in structural stability seems to surpass the increase in basicity.

It is evident from Tables VI and VII that the interaction of thioethers with iron is greater than that of ethers with the same substituents. The decrease in interaction with the carbon numbers of the substituents is observed in the system with symmetric thioethers, but not apparently in that with asymmetric ones (Table VI). The symmetric thioethers require solvents to interact with iron, while the asymmetric thioethers can interact with iron even in neat ligand (except for those with bulky groups such as isopropyl- and phenyl group). Asymmetric ethers also have greater ability for the interaction with iron. This difference in bonding ability between the symmetric- and the asymmetric ligands seems to result from a difference in magnitude of the steric interaction of the substituents with porphyrin core, rather than that in electronic property of the donor atom; the detail remains to be clarified.

For the ligand concentration required for showing pronounced interaction, observed by EPR spectra at 77 K, thiols are much higher than thioethers.

The S- and O-donor ligands are, respectively, classified into soft- and hard ligands on the basis of the properties of a donor atom, such as electronegativities, polarizabilities, and atomic radii [19, 20]. It has been inferred [20–22] that the S-donor ligands have greater ability for the coordination to iron(II) with low-spin $3d^6$ configuration than do the O-donor ligands, owing to the participation of d_π–d_π interaction to utilize the 3d vacant orbital of sulfur.

Although in the nitrosylprotoheme complexes the unpaired electron of NO group is delocalized to iron d_{z^2} orbital [1a] and thus the electronic configuration should be represented by $\{FeNO\}^7$ [23], the facts described above indicate that also in the interaction with Fe(PPDME)(NO), the S-donor ligands have somewhat greater ability than the O-donor ligands.

Relation of Model Systems with Nitrosylhemoproteins

Cytochromes c [2], cytochrome P-450 [3], and possibly chloroperoxidase [24] are all hemoproteins in which the sulfur atom axially coordinates to heme iron. The thioether sulfur of the methionine in cytochromes c [2] and the thiolate sulfur of the cysteine in cytochrome P-450 [3] have been reported to be the donor atom.

It has been demonstrated in the EPR study of their nitrosyl derivatives that in cytochrome c [25], the ligand *trans* to a nitrosyl group can be the imidazole nitrogen of the histidine and the nitrosyl group can replace the methionine, and that in cytochrome P-450 [26], the observation of the triplet structure in the g_z absorption can be consistent with the proposal of the thiolate sulfur as the ligand *trans* to the nitrosyl group.

The axial ligand groups of heme in Fe(PPDME)(NO) system with thioether correspond to those in nitrosylcytochrome c in which the axial histidine is replaced by a nitrosyl group. Since, as mentioned above, the bonding ability of N-acetylmethionine and its methyl ester was comparable to that of simple thioether, the amino nitrogen and the carbonyl group in these methionine derivatives seem to be ineffective in enhancement of the bonding ability of the sulfur donor. It was recently reported in the study of the model compound for cytochrome c [27] and cytochrome P-450 [28] that the thioether sulfur coordinates relatively strongly to heme iron. Accordingly, the weak bonding of iron to sulfur in the Fe(PPDME)(NO) system with thioether is attributable to the *trans* effect of the nitrosyl group.

The fact that the EPR parameters of nitrosylcytochrome P-450 (g_x = 2.068, g_y = 1.978, g_z = 2.008, and A_z = 20 G) [26] are similar to those of the Fe(PPDME)(NO) system with unhindered N-donor ligand (for imidazole; g_x = 2.072, g_y = 1.971, g_z = 2.004, and A_z = 21.7 G) [1c], suggests that the bonding ability of thiolate-sulfur ligand is comparable to that of unhindered N-donor ligand. Consequently, the thiolate-sulfur ligand can be much greater for the bonding ability to iron in position *trans* to a nitrosyl group than the thiol- and thioether-sulfur ligands.

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