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Oxygenation of Iron(II) Picket-Fence Porphyrin Bound to Amphiphilic Block Copolymer in Water

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ABSTRACT: Several *meso*-$\alpha,\alpha,\alpha,\alpha$-tetrakis[*o*-(alkylamido)phenyl]porphyrin–iron(II) complexes were prepared and their NEI (*N*-ethylimidazole) or PSI [styrene (84 mol %)–*N*-vinylimidazole (16 mol %) copolymer] complexes were observed with respect to the oxygenation reaction in dry toluene. In H_2O-saturated toluene, the Fe(II) picket-fence porphyrin (alkyl = tert-butyl)–PSI complex formed a more stable oxygen complex than the NEI complex did, probably due to the hydrophobicity of PSI. The Fe(II) picket-fence porphyrin coordinately bound to a water-soluble polymer ligand, such as *N*-vinyl-2-pyrrolidone (80 mol %)–*N*-vinylimidazole (20 mol %) copolymer, was rapidly oxidized upon exposure to oxygen gas, while amphiphilic ABA-type block copolymer ligands, such as PEO–PSI–PEO [PEO = poly(ethylene oxide)], gave oxygen complexes which were observed even at pH 7.0 in aqueous solution at room temperature. Further attempts to bind the complex units covalently to the hydrophobic B block of such ternary block copolymers also produced a stable oxygen complex in water at room temperature.

Introduction

A naked heme or related iron(II) complexes free from apoprotein are known to be rapidly oxidized in homogeneous solution at room temperature due to the oxidation side-reactions shown below:[1-4]

Oxygenation

$$\mathrm{B\text{–}Fe^{II}P + O_2 \rightleftarrows [B\text{–}Fe^{II}P\text{–}O_2 \leftrightarrow B\text{–}Fe^{III}P\text{–}O_2^{-}*]}$$
$$\mathrm{B\text{–}Fe^{II}P\text{–}B + O_2 \rightleftarrows [B\text{–}Fe^{II}P\text{–}O_2 \leftrightarrow B\text{–}Fe^{III}P\text{–}O_2^{-}*] + B} \quad (1)$$

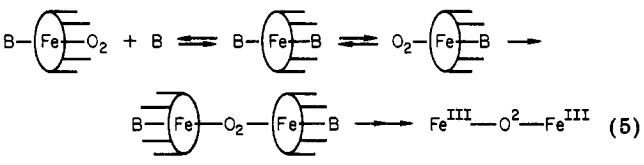
Oxidation

$$\mathrm{[B\text{–}Fe^{II}P\text{–}O_2 \leftrightarrow B\text{–}Fe^{III}P\text{–}O_2^{-}*] \rightarrow B\text{–}Fe^{III} + O_2^{-}*} \quad (2)$$
(monomeric aprotic)

$$\mathrm{[B\text{–}Fe^{II}P\text{–}O_2 \leftrightarrow B\text{–}Fe^{III}P\text{–}O_2^{-}*] + B\text{–}Fe^{II}P \rightarrow}$$
$$\mathrm{[B\text{–}Fe^{III}P\text{–}O_2^{2-}\text{–}Fe^{III}P\text{–}B] \xrightarrow[-2B]{} 2[Fe^{IV}{=}O] \xrightarrow[-2B]{2B\text{–}Fe^{II}P}}$$
$$\mathrm{2Fe^{III}P\text{–}O^{2-}\text{–}Fe^{III}P} \quad \text{(dimeric)} \quad (3)$$

$$\mathrm{[B\text{–}Fe^{II}P\text{–}O_2 \leftrightarrow B\text{–}Fe^{III}P\text{–}O_2^{-}*] \xrightarrow{H^+}}$$
$$\mathrm{B\text{–}Fe^{III}P + HO_2^{*}} \quad \text{(monomeric protic)} \quad (4)$$

Here $Fe^{II}P$ and $Fe^{III}P$ indicate iron(II)- and iron(III)–porphyrin complexes, respectively, and B represents a given axial base, such as an imidazole derivative. In an initial attempt to minimize oxidation process 3, Baldwin et al.[5,6] obtained an oxygen complex in aprotic organic solvents at room temperature. Collman et al. also succeeded in reversible oxygenation, using the Fe(II) picket-fence porphyrin *meso*-$\alpha,\alpha,\alpha,\alpha$-tetrakis[[*o*-(pivalamido)phenyl]porphyrinato]iron(II), or Fe^{II}TpivPP, in aprotic solvents at room temperature.[1,7-13] Its reversible oxygenation is attributed to the fact that the bulky *tert*-butyl groups attached to one side of the porphyrin plane prevent oxidation process 3 and that (4) is negligible in aprotic solvents. Collman et al. assumed an intramolecular solvation effect of the tetrapivalamide groups at the sixth coordination sphere,[1,10] to which an oxygen molecule was ligated, caused oxidation process 5 to be suppressed.



(5)

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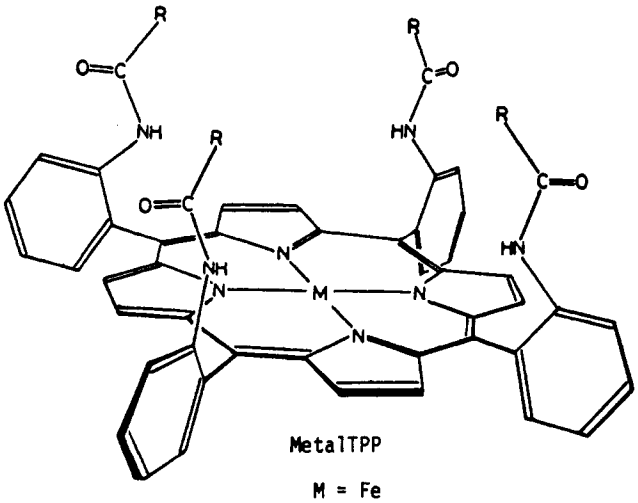
Chart I



MetalTPP

M = Fe

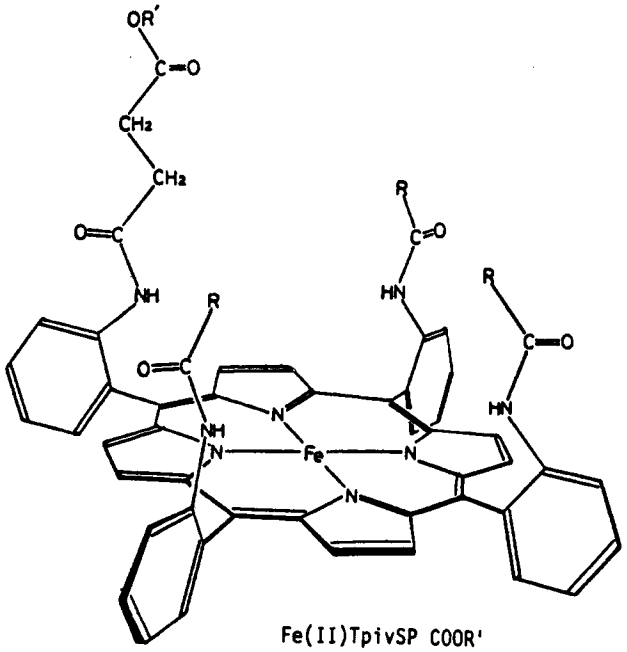
R = $-C_6H_5$ 1

$-CH_2C_6H_5$ 2

$-C(CH_3)_3$ 3

M = Co

R = $-C(CH_3)_3$ 4



Fe(II)TpivSP COOR'

R = $-C(CH_3)_3$

R' = $-CH_3$ 5

$-H$ 6

A similar attempt to prevent oxidation process 3 has been carried out by Chang,[14] who prepared a crowned deuteroporphyrin IX–iron(II) complex, with *N*-(triphenylmethyl)imidazole as the axial ligand. The imidazole ligand with the bulky substituent preferred to form a five-coordinate complex because it could only coordinate opposite to the crowned side. Therefore the selective ligation of oxygen at the axial position of the crowned side enabled reversible oxygenation.

As for aqueous media, a few attempts to achieve the oxygenation of iron(II)–porphyrin complexes have been reported. Bayer and Holtzbach demonstrated reversible oxygenation in water by using proximal- and distal-based (protoporphyrin IX)iron(II) covalently bound to endoglycinated poly(ethylene oxide) by an amide linkage.[15] Russian investigators have reported a proximal-based type iron(II)–protoporphyrin IX complex to be oxygenated in water when it was incorporated in a bilayer micelle of a phospholipid.[16] However, the details of their oxygenation phenomena are insufficient for further discussion.

One way to minimize process 4 is the inclusion of the Fe(II) complex into stiff hydrophobic substances solubilized in water. In the present paper, oxygenation reactions in water at room temperature are examined by using Fe^{II}TpivPP or a related complex and hydrophilic–hydrophobic–hydrophilic ABA-type block copolymers.

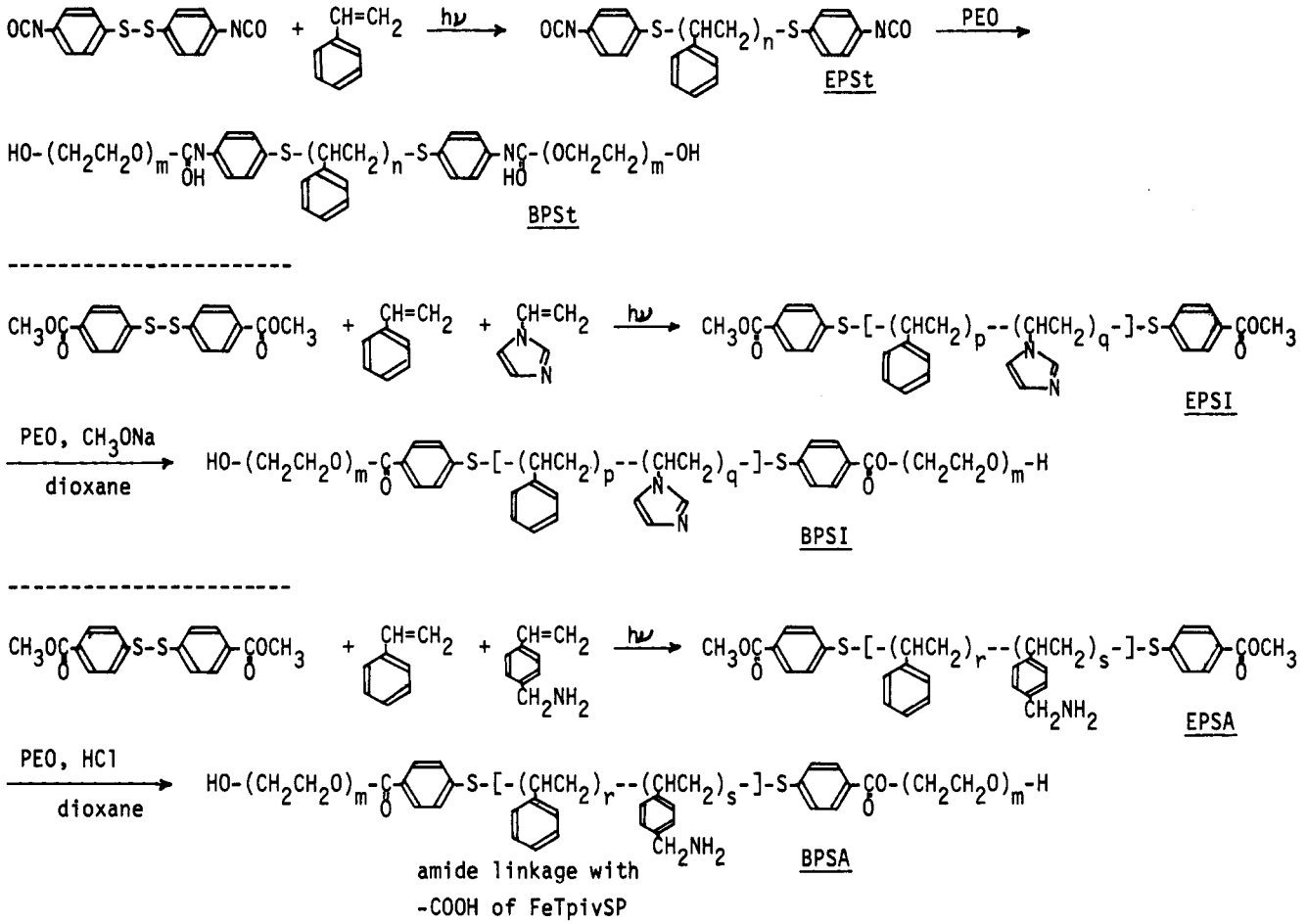
Experimental Section

Complexes. *meso*-$\alpha,\alpha,\alpha,\alpha$-Tetrakis(*o*-aminophenyl)porphyrin (H_2TamPP) was prepared according to Collman's report.[10] The corresponding (alkylamido)phenyl derivatives *meso*-$\alpha,\alpha,\alpha,\alpha$-tetrakis[*o*-(benzoylamido)phenyl]porphyrin (H_2TbzPP), *meso*-$\alpha,\alpha,\alpha,\alpha$-tetrakis[*o*-[(phenylacetyl)amido]phenyl]porphyrin (H_2TphPP), and *meso*-$\alpha,\alpha,\alpha,\alpha$-tetrakis[*o*-(pivalamido)phenyl]-porphyrin (H_2TpivPP) were stoichiometrically prepared by reaction of H_2TamPP with a slight excess of benzoyl chloride, phenylacetyl chloride, and pivaloyl chloride, respectively, in chloroform at 0–5 °C for 5 h. Each metal-free porphyrin derivative was reacted with a slight excess of $Fe^{II}Br_2{\cdot}2H_2O$ in THF containing pyridine as a HBr remover under unaerobic conditions according to Collman's method. After chromatography of the crude products on a basic alumina (grade I) column, they were recrystallized twice from the HBr-acidified $CHCl_3$–heptane–methanol solution, yielding about 70% for each Fe(III) complex, i.e., Fe^{III}TbzPP·Br (1), Fe^{III}TphPP·Br (2), and Fe^{III}TpivPP·Br (3), respectively.

meso-α-[*o*-[(Carboxysuccinyl)amido]phenyl]-tris-α,α,α-[*o*-(pivalamido)phenyl]porphyrin (H_2TpivSP) was prepared by reaction of H_2TamPP with a threefold excess of pivaloyl chloride (dropwise over 3 h) for 5 h, then with a large excess of succinyl chloride, and finally with a large excess of methanol for another 3 h, all at 0–5 °C. The crude product was chromatographed on a silica gel column (about 300 mesh, 3 × 30 cm for chromatography of 1.0 g of crude product). H_2TpivPP was first to elute with chloroform. After removal of the second band ($\alpha,\alpha,\alpha,\beta$ isomer of H_2TpivSP), the monomethyl ester of H_2TpivSP was obtained as the first eluent with 1:40 acetone–chloroform; yield about 40%. The corresponding Fe(III) complex, i.e., the methyl ester of Fe^{III}TpivSP·Br (5), was obtained as above; yield about 65%. Next, the resulting Fe(III) complex was dissolved in the minimum volume of DMF. An equal volume of 1 N KOH was added, and the solution was stirred for 2 h in order to hydrolyze the methyl ester group. The solution was acidified to pH 2 by adding aqueous HBr, and the resulting precipitate was collected and twice recrystallized from heptane–methanol to obtain the ester-hydrolyzed complex Fe^{III}TpivSP·Br (6); yield 85%. The structures and analyses of complexes are given below.

The Co(II) complex of H_2TpivPP, i.e., Co^{II}TpivPP (4), was obtained by reaction of H_2TpivPP with a slight excess of $Co(II)Cl_2{\cdot}6H_2O$ in THF for 10 h under reflux and unaerobic conditions. After chromatography on a basic alumina (grade I) column ($CHCl_3$), the eluted complex was recrystallized from

Scheme I
Syntheses of Ternary Block Copolymers



THF–heptane twice. Found (calcd.): C, 70.62 (70.64); H, 6.35 (6.32); N, 10.98 (10.98). After the complex was refluxed in methanol-d_4 for 1 week, the amide NH of Co^{II}TpivPP was replaced by ND, i.e., d-Co^{II}TpivPP. These Co(II) complexes were heated at 100 °C for 1 day in vacuo in order to deoxygenate them and then stored in vacuo.

Ligands. Reagent grade NEI (*N*-ethylimidazole) was dried over Na wire and distilled immediately before use. TMI [*N*-(triphenylmethyl)imidazole] was prepared by the conventional method.

Polymers and Block Copolymers. PSI (styrene$_{84}$–*N*-vinylimidazole$_{16}$ copolymer; subscripts indicate mol % content) was prepared by radical polymerization in 50 mL of toluene solution containing 6.3 g (60 mmol) of styrene (St), 1.14 g (12 mmol) of *N*-vinylimidazole (NVI), and 320 mg (2 mmol) of AIBN at 80 °C for 3 h, followed by precipitation from diethyl ether (Et_2O) twice; yield 2.3 g. The number-average molecular weight ($\bar{M}_n$) of PSI was determined to be 2.5×10^4 by vapor pressure osmometry (Hitachi Electric Co. Ltd., Model VPO-117) in benzene solution, using tristearin as reference. The contents of the St and NVI residues were as follows. Found (calcd. as St_{84}–NVI_{16} copolymer): C, 87.42 (87.47); H, 7.55 (7.50); N, 5.03 (5.03).

PPoI (*N*-vinyl-2-pyrrolidone$_{80}$–NVI_{20} copolymer) was also prepared by radical polymerization in 50 mL of toluene solution containing 5.56 g (50 mmol) of *N*-vinyl-2-pyrrolidone (NVPo), 1.41 g (15 mmol) of NVI, and 320 mg (2 mmol) of AIBN at 80 °C for 3.5 h. Two precipitations from Et_2O yielded 3.1 g. The $\bar{M}_n$ of PPoI was determined to be 2.3×10^4 by vapor pressure osmometry in methanol, using benzil as reference. Found (calcd. as $NVPo_{80}$–NVI_{20} copolymer): C, 64.60 (64.66); H, 7.91 (7.86); N, 15.60 (15.60).

A ternary block copolymer, abbreviated BPSt in Scheme I, was synthesized by coupling endo-telechelic polystyrene (EPSt) with poly(ethylene oxide) (PEO, $\bar{M}_n = 3.94 \times 10^4$).[17] EPSt was prepared by 15-h UV-irradiation polymerization at 30 °C (Toshiba Electric Co. Ltd. Model SHL-1000V high-pressure mercury lamp set 7.5 cm from the sample) of a solution containing 21 g (0.2 mol) of St and 3.00 g (10 mmol) of bis(*p*-isocyanatophenyl) disulfide as initiator in an evacuated 5 × 30 cm quartz tube. The yield was 3.8 g after two precipitations from petroleum ether. The $\bar{M}_n$ of the resulting EPSt was determined to be 5.4×10^3 by titration of the endo-NCO groups with *n*-butylamine, supposing both ends of EPSt to be attached to *p*-isocyanatophenyl sulfide groups. EPSt (1.0 g) (0.37 mmol of NCO) and PEO (17.4 g) (0.89 mmol of OH) were reacted in *o*-dichlorobenzene at 100 °C for 12 h. The resulting solution was concentrated and reprecipitated from Et_2O. The white powder obtained was chromatographed on a Sephadex LH-20 column (2.5 × 50 cm for chromatographing 0.5 g) eluted with methanol. The first eluate was collected, concentrated, and reprecipitated from Et_2O. Unreacted PEO was extracted with hot water. The electronic spectrum of the product in dioxane solution showed an absorption band at about 250 nm due to the St ring, indicating the existence of St units in the block copolymer. About 95% of the endo-isocyanate groups were determined to be reacted with PEO from the absorbance at 250 nm of the block copolymer referred to the absorbance of a dioxane solution of EPSt. The final product, BPSt, which contained a small amount of half-reacted EPSt (AB-type block copolymer), was used without further purification, as it was quite difficult to separate pure BPSt from the mixture.

A ternary block copolymer, abbreviated BPSI, containing NVI units in its center B block, was also synthesized by a similar coupling of endo-telechelic PSI (EPSI) with PEO. EPSI was prepared by UV-irradiation polymerization of St (3.75 g, 36 mmol), NVI (2.26 g, 24 mmol), and bis[*p*-(carbomethoxy)phenyl] disulfide (CPDS) (1.00 g, 3.0 mmol) under the above conditions for 15 h. A yield of 0.77 g was obtained after two precipitations from Et_2O. The $\bar{M}_n$ of the EPSI was determined to be about 3.7×10^3 by elemental analysis or by the NMR peak intensity ratio (total aromatic CH)/(methyl H), supposing both ends of EPSI to be

Table I
Analysis and Properties of Porphyrin Derivatives

porphyrin		anal. % C	% H	% N	NMR[b] δ	λ_{max},[c] nm Soret	Q band
H_2TbzPP	found	78.8	4.9	9.6	9.1 (8 H), 8.9 (4 H), 7.1, 8.0 (16 H), 6.3, 6.8 (20 H), −2.5 (2 H)	423	551, 596, 658
	calcd	78.8	4.6	10.2			
H_2TphPP	found	78.2	4.0	9.5	8.9 (8 H), 7.1, 8.0 (16 H), 8.8 (4 H), 6.1 (20 H), 2.8 (16 H), −2.5 (2 H)	425	518, 551, 596
	calcd	79.2	5.0	9.7			
H_2TpivPP	found	74.6	6.5	10.9	8.9 (8 H), 8.7 (4 H), 7.1, 8.1 (16 H), 0.05 (36 H), −2.6 (2 H)	418	515, 550, 592
	calcd	76.0	6.6	11.2			
H_2TpivSP[a]					8.9 (8 H), 8.8 (4 H), 7.3, 8.0 (16 H), 0.1, 0.5 (27 H), 2.6 (4 H), 3.8 (3 H), −2.5 (2 H)	423	519, 556, 594, 657
Fe^{III}TbzPP·Br	found	70.6	3.9	9.21		423	513, 591, 660
	calcd	70.6	4.0	9.15			
Fe^{III}TphPP·Br	found	71.3	4.4	8.81		421	512, 588, 656
	calcd	71.3	4.4	8.75			
Fe^{III}TpivPP·Br	found	65.5	5.3	9.36		421	510, 564, 650
	calcd	65.3	5.4	9.45			
Fe^{III}TpivSP·Br	found	64.4	5.3	9.81		421	509, 564, 650
	calcd	64.4	5.3	9.85			

[a] Monomethyl ester. [b] In $CDCl_3$. [c] In $CHCl_3$.

attached to *p*-(carbomethoxy) sulfide (CPS) groups. The content of NVI unit in EPSI was about 6 mol %, determined by elemental analysis. Found (calcd. as NVI = 6 mol %, $\bar{M}_n = 3.7 \times 10^3$): C, 63.4 (63.2); H, 7.16 (7.14); N, 1.34 (1.34). NMR (δ) in $CDCl_3$: CH_3, 3.8 (6 H), chain CH, 1.2–1.8 (ca. 106 H), aromatic CH, 6.4–6.9 (ca. 178 H). EPSI (0.74 g) (0.4 mmol of endo-methyl ester) and PEO (18.9 g) (0.96 mmol of OH group) were reacted in 100 mL of refluxed dry dioxane for 3 days with sodium methoxide (22 mg, 0.4 mmol) as catalyst. The resulting solution was concentrated and precipitated from Et_2O. The crude BPSI was purified in the manner described above; then after two reprecipitations from methanol–Et_2O, a yield of about 15 g was obtained. About 90% of the endo-methoxy groups were determined to be replaced by PEO from the absorbance at 250 nm of dioxane solution of block copolymer referred to that of EPSI.

A ternary block copolymer, abbreviated as BPSA, which contains amino groups in its center B block, was synthesized by coupling endo-telechelic copoly[styrene–*p*-(aminomethyl)styrene] (EPSA) with PEO in the same manner as described above for BPSI. EPSA was prepared by the UV-irradiation polymerization of St (13.5 g, 0.13 mol), *p*-(aminomethyl)styrene (AMS) (1.73 g, 13 mmol), and CPDS (1.73 g, 4.1 mmol) under the above-mentioned conditions for 16 h; yield 7.26 g. The $\bar{M}_n$ of EPSA was determined to be 4.2×10^3 by elemental analysis and NMR, supposing both ends of EPSA to be attached to CPDS. Found (calcd. as AMS = 12.5 mol %, $\bar{M}_n = 4.2 \times 10^3$): C, 88.04 (88.03); H, 7.53 (7.54); N, 1.51 (1.51). NMR (δ) in $CDCl_3$: CH_3, 3.83 (6 H), NH_2, 3.60 (ca. 6 H), chain CH, 1.80–1.18 (ca. 129 H), aromatic CH, 6.58–7.10 (ca. 212 H). EPSA (0.18 g) (0.04 mmol of the endo-methyl ester) and PEO (5.0 g) (0.13 mmol of OH group) were dissolved in 300 mL of dioxane containing 15 mL of concentrated HCl. With prolonged passage of HCl gas, the mixture was refluxed for 5 h and methanol and water were removed. The resulting solution was concentrated and reprecipitated from Et_2O. The crude BPSA thus obtained was purified in the manner described above for BPSI; yield 2.1 g. About 95% of the endo-methyl ester groups were determined to be replaced by PEO from the absorbance of dioxane solution of BPSA referred to that of EPSA.

BPSA–Fe^{III}TpivSP·Br. Fe^{III}TpivSP·Br (30 mg, 2.3×10^{-5} mol) was dissolved in 20 mL of dry dichloromethane. Triethylamine (4.7 mg) and ethyl chloroformate (5.06 mg) were added to this solution at 0 °C. The mixture was stirred at 0 °C for 1 h and 126 mg (NH_2 unit, 4.6×10^{-6} mol) of BPSA was added. The solution was stirred for another 2 h at 0 °C and then for a further 12 h at room temperature. The resulting solution was concentrated and precipitated from Et_2O. The brownish powder was dissolved in the minimum volume of dichloromethane and then reprecipitated from Et_2O twice; yield 70 mg. No unreacted Fe(III) complex was found by thin-layer chromatography (200-mesh silica gel, benzene eluent, polymer-bound complex $R_f = 0.0$, polymer-free complex $R_f = 0.2$). The degree of incorporation of complex unit into the amino groups was determined to be 22% from the absorbance of 419 nm of a dichloromethane solution of BPSA–Fe^{III}TpivSP(NEI)$_2$ referred to that of Fe^{III}TpivSP(NEI)$_2$.

Other Chemicals. Dichloromethane was distilled over calcium hydride immediately before use. Toluene was distilled over anhydrous calcium chloride and then redistilled over Na wire. Dioxane for spectroscopic measurements was treated with concentrated HCl, neutralized with KOH pellets, distilled, and then redistilled over Na wire. Reagent grade sodium dithionite was used as supplied.

Reagent grade hexadecakis(oxyethylene) dodecyl ether (HODE) was recrystallized from benzene solution twice. Sodium dodecyl sulfate (SDS) and octadecyltrimethylammonium bromide (OTA) of reagent grade were used without further purification.

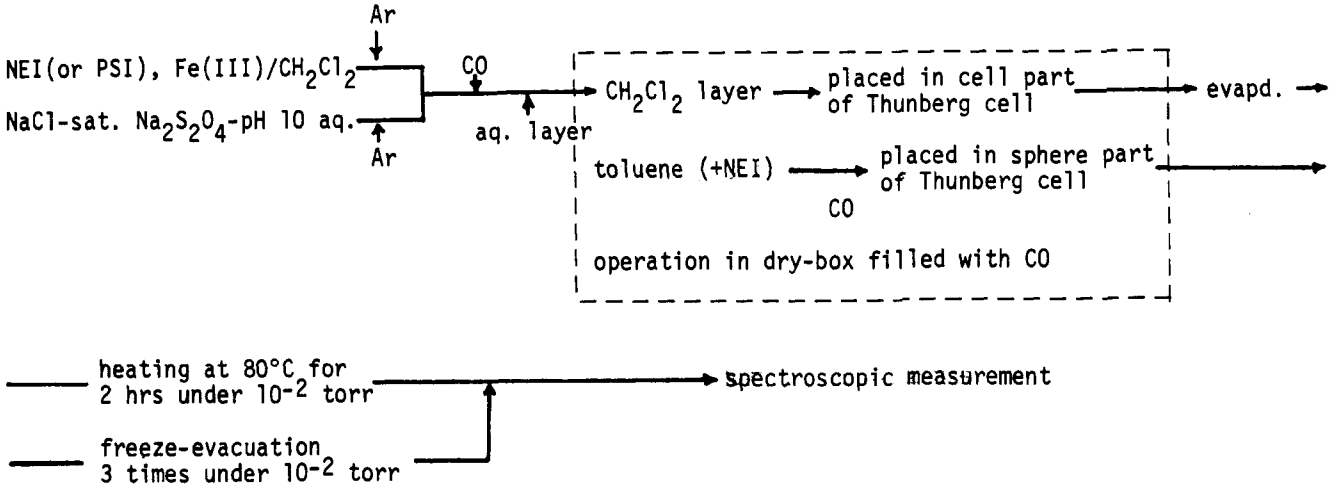
Measurements. Electronic absorption spectra were measured with a Union Giken SM-401 spectrophotometer. ESR spectra were measured with a JEOL JES-FE-3X ESR spectrometer.

Reduction of Fe(III) Complexes. A CO-saturated dichloromethane solution containing Fe(III) complex and NEI or PSI was vigorously stirred with an aqueous solution of sodium dithionite under a CO atmosphere. After separation of the dichloromethane layer under the CO atmosphere, the solution was placed in the cell part of a Thunberg-type cell and evaporated to dryness at 10^{-2} torr at 40 °C for 5 h. Under a pure CO atmosphere, dry CO-saturated toluene was placed in the sphere part of the Thunberg cell and was freeze-evacuated at 10^{-2} torr. Then the cell part was heated to about 80 °C at 10^{-2} torr in order to remove coordinating CO molecules from the complex; meanwhile the toluene solution in the sphere part was frozen by liquid N_2. After further freeze-evacuation, toluene was led into the cell part to obtain the corresponding Fe(II) complex solution free from CO coordination. When the axial ligand is NEI, some NEI must be in the toluene solution during the above-mentioned procedure. A flow chart is shown in Scheme II. Absence of contamination by sodium dithionite was confirmed by a lack of absorption at 330 nm. The preparations of pH 7.0 aqueous solutions of polymer micelle–Fe(II) complexes are illustrated in Schemes III–VI.

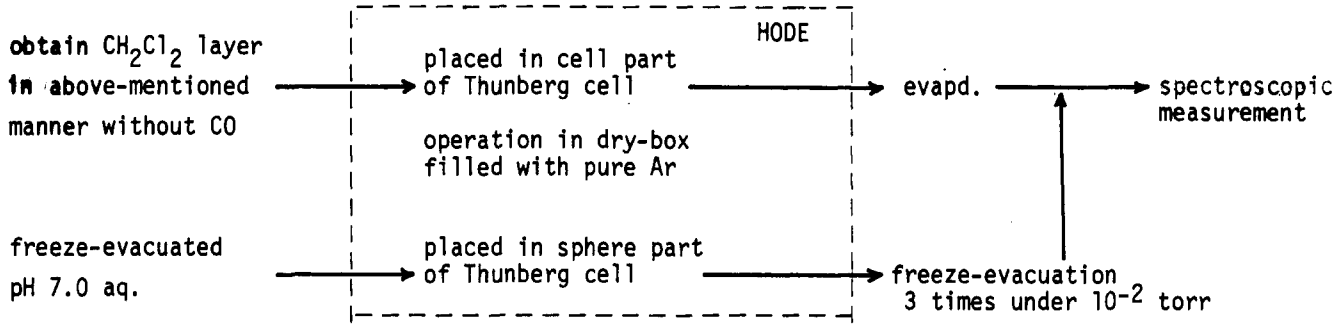
Results and Discussion

Effect of Steric Hindrance Group Attached to the Porphyrin Ring. Collman et al. examined the oxygenation of two iron(II)–tetraphenylporphyrin complexes with imidazole derivatives as axial ligands, namely, Fe^{II}TpivPP and [*meso*-*O*,*O*′:*O*″,*O*‴-diisophthalamidotetraphenylporphyrinato]iron(II) (Fe^{II}TphthPP), the latter of which was reported to be monomerically oxidized upon exposure to oxygen by proton donation from the acidic NH group of isophthalamide to the coordinated dioxygen (process 4).[10] Table II summarizes the results of oxygenation of $(NEI)_2Fe^{II}$ complexes, which indicate that $(NEI)_2Fe^{II}$TbzPP and $(NEI)_2Fe^{II}$TphPP are rapidly oxi-

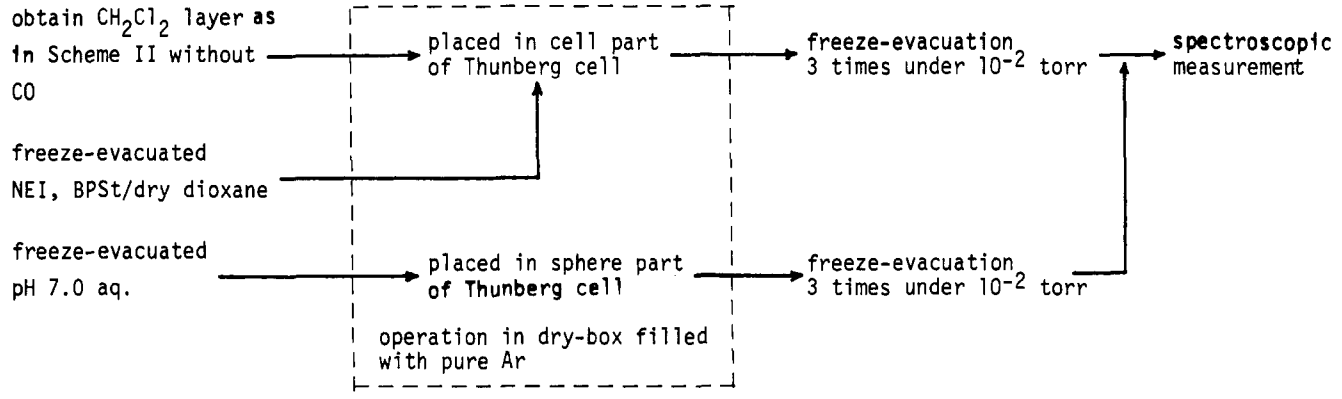
Scheme II
Fe(II) Complex/Toluene Solution



Scheme III
HODE-(NEI)$_2$Fe^{II}TpivPP/pH 7 (aq)



Scheme IV
BPSt-(NEI)$_2$Fe^{II}TpivPP/3 v/v % Dioxane, pH 7 (aq)



dized to μ-oxo dimers on exposure to oxygen, which suggests that oxygen ligates to the fifth coordination site and then the μ-oxo dimer is formed according to process 5. The reason that dissociation of the NEI-Fe^{II} bond scarcely occurs at the sixth coordination site may be attributed to the holding of the NEI molecule by the tetrakis(benzoylamide) or tetrakis[(phenylacetyl)amide] groups.

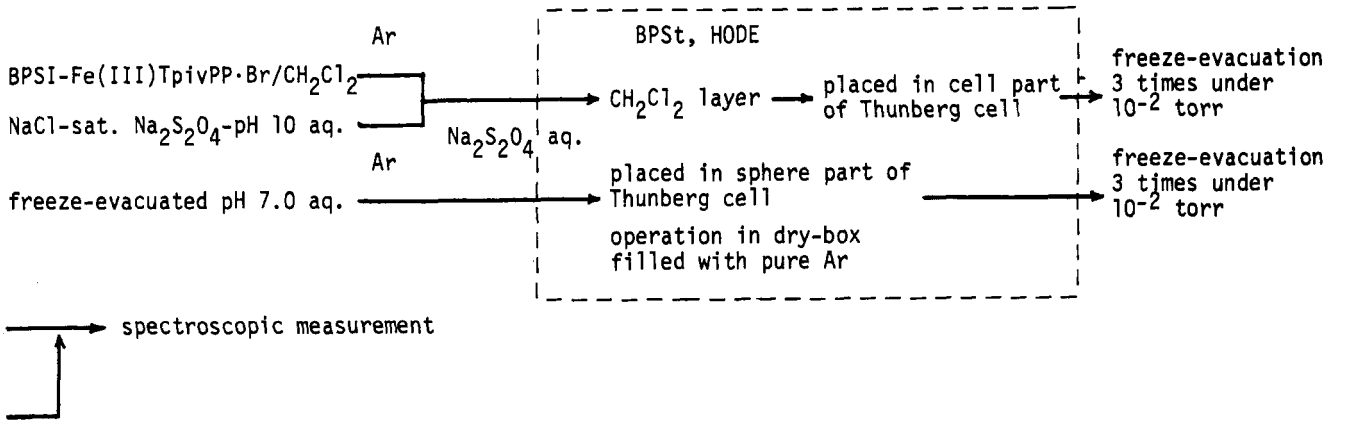
The (NEI)$_2$Fe^{II}TpivPP complex forms a stable oxygen complex in toluene at room temperature, as summarized in Table II and Figure 1a. Its lifetime ($t_{1/2}$) is more than 12 h when the solution is sufficiently dry. It is important that oxidation process 5 does not occur in the case of oxygenation of (NEI)$_2$Fe^{II}TpivPP. Collman et al. explained that the NH groups of the pivalamides interact with a coordinating oxygen molecule to stabilize the liga-

Table II
Effect of Steric Hindrance Groups on the Stability of Oxygenated (NEI)$_2$Fe^{II}TPP Complexes[a]

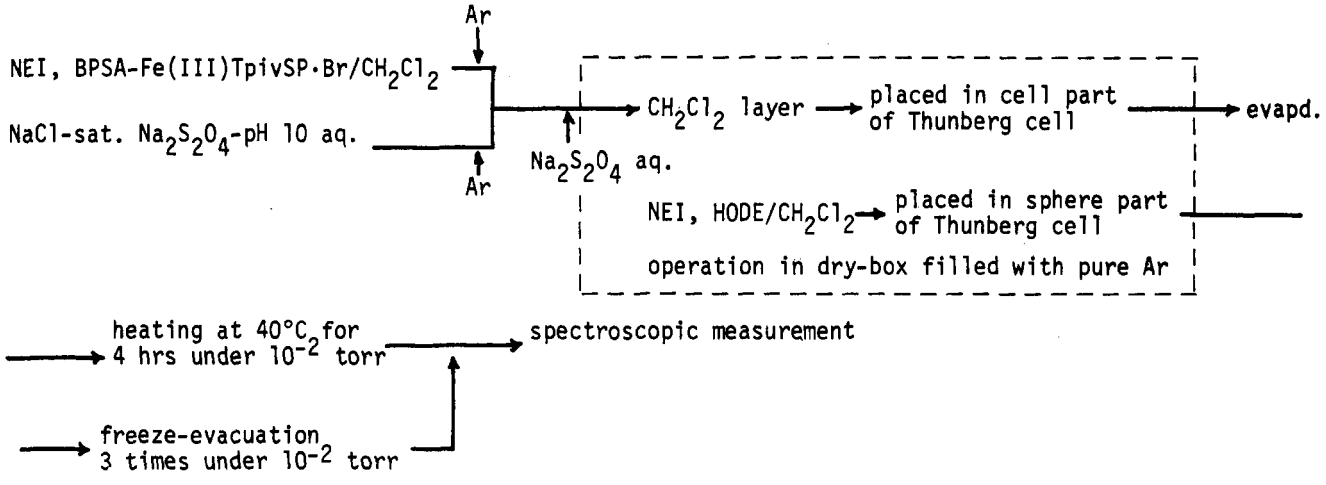
complex	λ, nm deoxy	λ, nm oxy	λ, nm oxid	$t_{1/2}$
Fe^{II}TbzPP	435, 537, 568	(426, 542)[b]	571 (μ-oxo)	<2 min
Fe^{II}TphPP	435, 538, 568	(426, 541)[b]	568 (μ-oxo)	~5 min
Fe^{II}TpivPP	433, 537, 568	425, 545		<12 h
Fe^{II}TpivSP	433, 537, 568	425, 544		<12 h

[a] TPP = tetraphenylporphine. [NEI]/[Fe] = 10, [Fe] = 2 × 10^{-5} mol/L, in toluene, at 25 °C. [b] Only short-lived. μ-oxo = oxidized to μ-oxo dimer.

Scheme V
HODE-BPSt-BPSI-Fe^{II}TpivPP/pH 7 (aq)



Scheme VI
HODE-BPSA-Fe^{II}TpivSP(NEI)$_2$/pH 7 (aq)



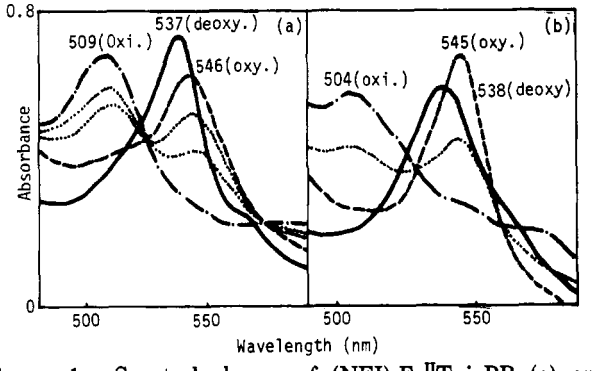


Figure 1. Spectral change of $(NEI)_2Fe^{II}$TpivPP (a) and (TMI)Fe^{II}TpivPP (b) on exposure to oxygen gas in toluene at 25 °C ([Fe] = 0.02 mM, [NEI] = 0.1 mM, [TMI] = 0.1 mM): (—) Fe^{II} (deoxy); (– –) Fe^{II}–O_2 (oxygenated); (···) intermediate states (changing from the oxygenated to the oxidized state); (–·–) Fe^{III} (oxidized).

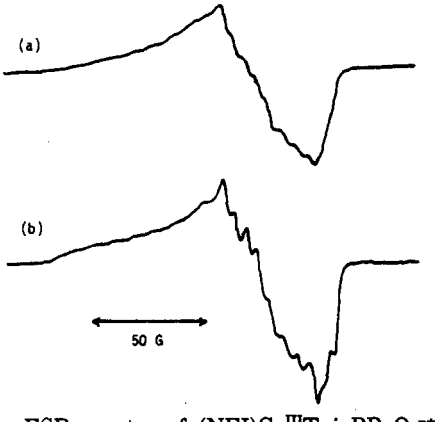


Figure 2. ESR spectra of (NEI)Co^{III}TpivPP–O_2^{-}* (a) and (NEI)*d*-Co^{III}TpivPP–O_2^{-}* (b) in toluene at 77 K ([Co] = 1 mM, [NEI] = 3 mM).

tion of dioxygen at the sixth coordination sphere but that the distance between the coordinated oxygen and the amide NH groups is 4.5–5 Å, too long for hydrogen bonding between them. The authors attempted to measure the interaction between the coordinating oxygen and the amide NH groups by using ESR spectroscopy. Figure 2 illustrates ESR spectra of (NEI)Co^{III}TpivPP–O_2^{-}* and (NEI)*d*-Co^{III}TpivPP–O_2^{-}*. When the amide NH groups are replaced by ND, the ESR spectrum due to O_2^{-}* is sharpened. This fact suggests that the coordinated oxygen actually interacts with the amide group.

The $(NEI)_2Fe^{II}$TpivSP complex also gave a stable oxygen complex. The $t_{1/2}$ value of its oxygenated complex is more than 12 h in dry toluene at room temperature, which is comparable to that of oxygenated (NEI)Fe^{II}TpivPP (Table II).

Effect of Substituents and Concentration of Ligand. Table III summarizes the effect of axial ligand or ligand concentration on the oxygenation in toluene. An example is illustrated in Figure 1b; deoxygenated Fe^{II}TpivPP formed a five-coordinate structure[18] when the axial ligand was TMI [(triphenylmethyl)imidazole] due to the strong steric hindrance between the bulky tetrapivalamide

Table III
Effect of Kind of Ligand and Ligand Concentration on the Oxygenation of Iron(II)-Tetraphenylporphine Complexes in Toluene at 25 °C

complex	ligand	[ligand]/[Fe]	λ, nm deoxy	λ, nm oxy	Soret shift, nm	Q-band shift, nm	DO,[a] %	$t_{1/2}$
Fe^{II}TbzPP	TMI	5.0	436, 538, 568	oxidized to μ-oxo dimer (574 nm)				
Fe^{II}TphPP	TMI	5.0	438, 536, 566	oxidized to μ-oxo dimer (570 nm)				
Fe^{II}TpivPP	TMI	5.0	433, 539	425, 546	8	7		<12 h
Fe^{II}TpivPP	NEI	3.0	436, 537, 566	429, 548	7	11	100	
		5.0	435, 536, 565	428, 547	7	11	100	~12 h
		7.0	435, 536, 565	429.5, 545	5.5	9	80	
		8.0	435, 536, 565	430, 544	5	8	70	
		10	435, 536, 565	432.5, 540	2.5	4	35	12 h
		100	436, 537, 566	—, 538		1	10	
Fe^{II}TpivPP	PSI	2.2	432.5, 540.0, 568	425.6, 546.0	6.9	6.0	100	<12 h
		4.0	433.0, 540.0, 569	426.3, 546.0	6.7	6.0	98	1 day
		6.0	433.0, 540.0, 569	426.5, 545.5	6.5	5.5	90	
		10	433.0, 540.0, 569	427.5, 545.0	5.5	5.0	80	
		100	433.0, 540.0, 569	427.5, 545.0	5.5	5.0	80	
		1000	433.0, 540.0, 569	—, 543.0		3.0	50	

[a] Calculated from (Q-band or Soret-band shift) × 100/(that of completely oxygenated state). Q-band shift and Soret band shift; see text. [Fe] = 2.0×10^{-5} mol/L.

group and the bulky substituent of imidazole. On the other hand, Fe^{II}TbzPP and Fe^{II}TphPP formed six-coordinate complexes with a threefold excess of TMI due to the weaker steric hindrance of porphyrin substituents, so these complexes were easily oxidized to μ-oxo dimer.

The oxygen affinity of Fe^{II}TpivPP is extremely sensitive to the [ligand]/[Fe] ratio when the axial ligand is NEI and when the deoxygenated Fe(II) complex takes the six-coordinate structure, as summarized in Table III. The Q-band shift ([λ (nm) of oxygenated Fe^{II}TpivPP] − [λ (nm) of deoxygenated Fe^{II}TpivPP]) was reported to be 11 nm when the axial ligand was *N*-methylimidazole and when the complex was completely oxygenated.[10] Therefore we estimated the degree of oxygenation by using the parameter DO, which is calculated by (Q-band shift) × 100/11 (%) as shown in Table III. By measuring the Soret band shift ([λ (nm) of deoxygenated Fe^{II}TpivPP] − [λ (nm) of oxygenated Fe^{II}TpivPP]), a similar result can be obtained.

The spectrum of the deoxygenated Fe(II) complex of the PSI–Fe^{II}TpivPP system showed the characteristic six-coordinate spectrum,[18] being very similar to that of $(NEI)_2Fe^{II}$TpivPP, though the λ_{max} of the Q-band shifted to longer wavelength (weak ligand field side). Furthermore, the Q-band shift was 6.0 nm even if [ligand]/[Fe] was lowered to 2.2, while the Soret band shift was 6.9 nm, being similar to that in the $(NEI)_2Fe^{II}$TpivPP system. These are probably caused by the steric hindrance between the tetrapivalamide groups and the polymer chain or St units of PSI; namely, the sixth coordination of imidazole unit of PSI is somewhat weakened. A Q-band shift of 3 nm accompanying oxygenation can be observed for [NVI unit of PSI]/[Fe] = 1000, although the ligand-exchange reaction at the sixth coordination sphere becomes difficult and oxygenation hardly occurs as [NEI]/[Fe] is increased to 100. Thus, the difference between the NEI and PSI systems is brought about by the distorted axial coordination of the NVI unit of PSI at the sixth coordination sphere. The DO values shown in Table III for the PSI systems are calculated by (Q-band shift) × 100/6.0 or (Soret band shift) × 100/6.9.

Table IV
Effect of Polymer Ligand on the Oxygenation of Fe^{II}TpivPP in H_2O-Saturated Toluene at 25 °C[a]

ligand	λ, nm deoxy	λ, nm oxy	λ, nm oxid	$t_{1/2}$, min
NEI	435, 536, 565	oxidized (mono)	419, 510	0
PSI	433, 540, 569	427.5, 545	419, 509	12
PPoI[b]	434, 538, 569	oxidized (mono)	419, 509	0

[a] [Fe] = 2.0×10^{-5} mol/L, [ligand]/[Fe] = 10.0. [b] In pH 7.0 aqueous solution (phosphate buffer, 0.05 mol/L); mono = monomerically oxidized to the initial Fe(III) state.

Effect of Polymer Ligand on the Oxygenation of Fe^{II}TpivPP in H_2O-Saturated Toluene. As summarized in Table IV $(NEI)_2Fe^{II}$TpivPP is rapidly oxidized in H_2O-saturated toluene at 25 °C through process 4 on exposure to oxygen, while PSI–Fe^{II}TpivPP formed the oxygenated complex under the same conditions with a short lifetime ($t_{1/2}$ value is about 12 min). This may be due to the hydrophobic effect of PSI, which acts to suppress the H_2O attack on the polymer-bound complex units. Fe^{II}TpivPP coordinately bound to a water-soluble copolymer ligand, PPoI, was rapidly oxidized monomerically on exposure to air. Therefore the strong hydrophobic field around the complex units seems to be preferable in order to achieve the oxygenation in water.

Oxygenation of $(NEI)_2Fe^{II}$TpivPP Incorporated into Micelle or Mixed Polymer Micelle by Hydrophobic Interaction. Figure 3a illustrates the spectral change of $(NEI)_2Fe^{II}$TpivPP incorporated into hexadecakis(oxyethylene) dodecyl ether micelle solubilized in an aqueous pH 7.0 solution on exposure to oxygen. As the aqueous solution was not completely transparent, the maximum absorption band at 538 nm was rather diffuse. Under oxygen, the maximum absorption band shifted immediately to 540 nm, showing the formation of an oxygen complex. However, the Q-band and Soret band shift or DO of the complex is not so large. The $t_{1/2}$ value of this

Table V
Oxygenation of Fe^{II}TpivPP in pH 7.0 Aqueous Solution at 25 °C[a]

no.	[HODE], g/L	[BPSt], g/L	[BPSI], g/L	[BPSA-Fe^{II}TpivSP], g/L	ligand	[ligand]/[Fe]	λ, nm deoxy	λ, nm oxy	$t_{1/2}$	DO, %
1	1.0	0	0		NEI	5.0	434, 538, 568	431, 540	2 min	20
2	2.0	0	0		NEI	5.0	434, 538, 567	431, 539	3 min	10
3	0	1.0	0		NEI	5.0	435, 537, 568	oxidized	0	0
4	0	4.0	0		NEI	5.0	435, 537, 568	(433, 539)[b]		0
5	1.0	1.0	0		NEI	5.0	435, 537, 568	(433, 539)[b]		0
6	1.0	4.0	0		NEI	5.0	435, 537, 568	432, 539	5 min	30
7	0	0	0		BPSI	5	434, 537, 568	431, 539	12 min	30
8	0	0	4.0		BPSI	20	433, 536, 568	429, 539	20 min	50
9	1.0	0	1.0		BPSI	5	434, 538, 568	431, 540	30 min	20
10	1.0	2.5	1.0		BPSI	5	434, 535, 568	431, 537	30 min	20
11	1.0	2.5	1.7		BPSI	5	434, 536, 568	430, 539	60 min	30
12	1.0	2.5	3.3		BPSI	10	435, 537, 568	430, 541	90 min	65
13	1.0 2.0[c]	1.0	1.7		BPSI	5	435, 539, 569	oxidized	0	0
14	2.0 1.0[c]	1.0	1.7		BPSI	5	435, 539, 569	oxidized	0	0
15	1.0			1.0	NEI	5	434, 535, 562	428, 540.5	10 h	85 (100)[d]
16	1.0			1.0	NEI	10	433, 537, 564	429, 540.5	12 h	60
17	1.0			1.0	NEI	20	431, 537, 564	429, 539.0	10 h	30

[a] No. 3, 4, 7, and 8 are in 3 v/v % dioxane/pH 7.0 (aq). [Fe] = (2–5) × 10^{-5} mol/L. [b] Very short-lived. [c] PEO. [d] After 5-min exposure to oxygen gas; other values are for after 1-min exposure.

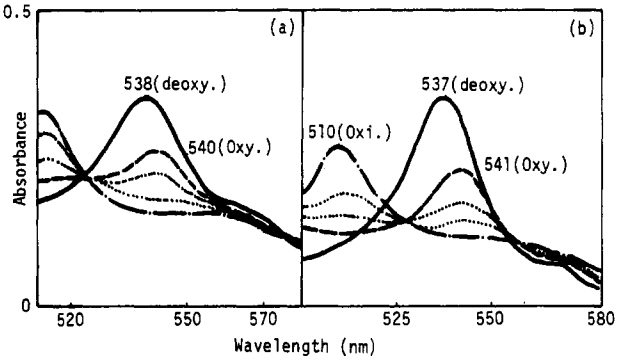


Figure 3. Spectral change of $(NEI)_2Fe^{II}$TpivPP incorporated into HODE micelle (a) and Fe^{II}TpivPP incorporated into HODE–BPSt–BPSI ternary mixed polymer micelle (b) on exposure to oxygen gas in pH 7.0–0.05 M phosphate buffer at 25 °C (a, [Fe] = 0.02 mM, [NEI] = 0.1 mM, [HODE] = 1.0 g/L; b, [Fe] = 0.02 mM, [BPSI] = 3.3 g/L, [ligand]/[Fe] = 10, [BPSt] = 2.5 g/L, [HODE] = 1.0 g/L): (—) Fe^{II} (deoxy); (– –) Fe^{II}–O_2 (oxygenated); (···) intermediate states (changing from the oxygenated to the oxidized state); (–·–) Fe^{III} (oxidized).

system was less than 2 min, and finally half the complex was monomerically oxidized according to proton attack and the other half was oxidized to give a μ-oxo dimer. The Fe(II) complex located in the hydrophobic core of the dodecyl chain forms a dioxygen complex, though the high local concentration of the complex in the micelle core makes more frequent the encounter of oxygen complex units with Fe(II) complex units to result in μ-oxo dimer formation. After several hours, the μ-oxo dimer was also degraded to the Fe(III) complex by water attack on the micelle core.

The detergents SDS (sodium dodecyl sulfate) and OTA (octadecyltrimethylammonium bromide) were not good for solubilizing the complex in water, and oxygen complexes were not observed in these systems.

Thus the hydrophobic field formed by the low molecular weight detergents is too weak for oxygenation in water. More hydrophobic substances, such as hydrophilic–hydrophobic–hydrophilic ABA-type ternary block copolymers, are needed. As the ternary block copolymer BPSt (see Experimental Section and Scheme I) is less soluble in water (>ca. 0.1 g/L), $(NEI)_2Fe^{II}$TpivPP is incorporated into the polymer micelle of BPSt solubilized in 3 v/v % dioxane/pH 7.0 (aq). The maximum absorption band of Fe(II) complex at about 537 nm gradually decreased on exposure to oxygen, while the absorption band at 509 nm identified with the Fe(III) complex increased.

BPSt was also solubilized in water by forming the mixed polymer micelle with HODE. $(NEI)_2Fe^{II}$TpivPP incorporated into the HODE–BPSt mixed polymer micelle formed the short-lived oxygen complex when the amount of added BPSt was sufficient to form a hydrophobic field. Therefore in order to immobilize the complex units into the core, the complex units should be attached to the hydrophobic B block of the ternary block copolymer by the coordinate or covalent bond.

Oxygenation Reaction of Fe^{II}TpivPP Immobilized in Mixed Polymer Micelle by Coordinate or Covalent Bond. The Fe^{II}TpivPP complex incorporated into BPSI (see Experimental Section) by the coordinate bond oxygenated in 3 v/v % dioxane/pH 7.0 (aq) at room temperature on exposure to oxygen is shown in Figure 4. The Fe(II) complex is located just around the hydrophobic B-block chain of BPSI due to both the coordinate bonding with NVI units of BPSI and the hydrophobic interaction. Water attack on the oxygen complex units is considered to be decreased compared with the HODE–BPSt–$(NEI)_2Fe^{II}$TpivPP system. The oxygen affinity of BPSI complex is apparently low, showing only 3 nm of Q-band shift. This may depend on the decrease in removability along the axis in the polymer micelle, resulting in the low oxygen affinity.

The oxygenated BPSI complex in 3 v/v % dioxane/pH 7.0 (aq) after exposure to oxygen for 20 min can be partially converted to the Fe(II) state by degassing the solution at 10^{-2} torr.

The Fe^{II}TpivPP complex incorporated into the mixed polymer micelle of HODE–BPSI forms a more stable oxygen complex, as summarized in Table V; however, the apparent oxygen affinity is still insufficient. Improved oxygen affinity can be achieved by adding BPSt to the HODE–BPSI–Fe^{II}TpivPP systems, as shown in Figure 3b and Table V (no. 12). The complex oxygenated at pH 7.0 (aq) at room temperature shows a $t_{1/2}$ of about 90 min and a Q-band shift of 4 nm. The addition of PEO, SDS, or

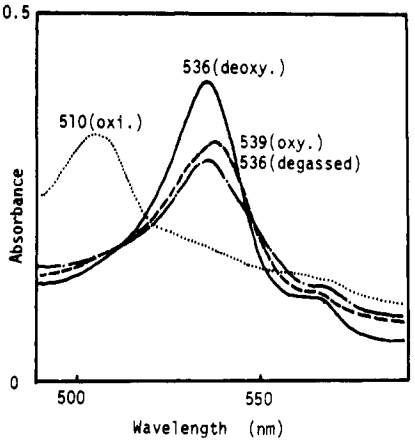


Figure 4. Spectral change of Fe^{II}TpivPP coordinately incorporated into BPSI on exposure to oxygen gas in 3 v/v % dioxane/pH 7.0 (aq) at 25 °C ([Fe] = 0.02 mM, [BPSI] = 4.0 g/L, [ligand]/[Fe] = 20): (—) Fe^{II} (deoxy); (--) Fe^{II}–O_2 (oxygenated); (-·-) degassed after 20-min exposure to oxygen gas; (···) Fe^{III} (oxidized).

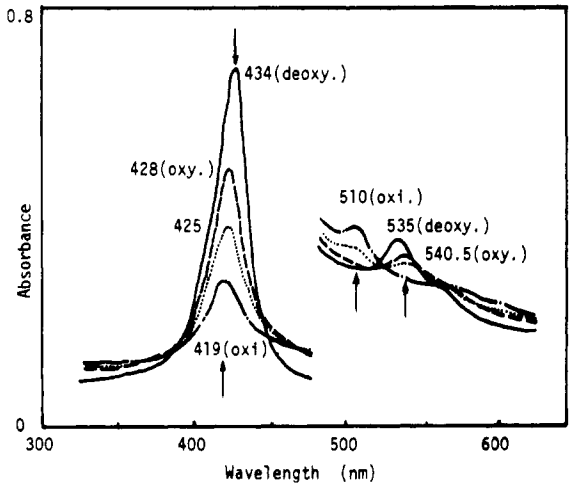


Figure 5. Spectral change of HODE–BPSA–Fe^{II}TpivSP$(NEI)_2$ on exposure to oxygen gas in pH 7.0 aqueous solution at 25 °C ([BPSA–Fe^{II}TpivSP] = 1.0 g/L, [ligand]/[Fe] = 5, [HODE] = 1.0 g/L): (—) Fe^{II} (deoxy); (--) Fe^{II}–O_2 (after 1-min exposure to oxygen gas); (···) intermediate state after 12-h exposure to oxygen gas; (-·-) Fe^{III} (oxidized).

OTA sharply decreases $t_{1/2}$ and the Q-band shift.

When the complex units are combined with a hydrophobic B block of such a ternary block copolymer by a covalent bond, the complex units can be expected to be completely immobilized into the micelle core. As summarized and illustrated in Table V and Figure 5, the HODE–BPSA–Fe^{II}TpivSP system formed a very stable oxygen complex even in pH 7.0 aqueous solution at room temperature. When the concentration of axial ligand NEI was low enough (5 equiv), this model showed a $t_{1/2}$ value of 12 h and a high oxygen affinity according to the Q-band and Soret band shifts.

Conclusion

In aqueous media, it is important that the proton-driven monomeric oxidation not occur for reversible oxygenation of iron(II)–porphyrin complexes. By combining the Fe(II) picket fence porphyrin into micelle-forming block copolymers coordinately or covalently, reversible oxygen complexes can be obtained in water at room temperature due to the hydrophobic field around the oxygen complexes.

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