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Approaches to Artificial Macromolecular Oxygen Carriers

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Approaches to Artificial Macromolecular Oxygen Carriers

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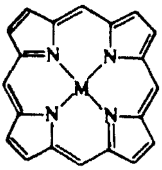
ABSTRACT

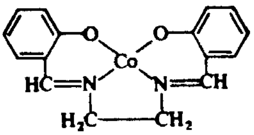
Construction of artificial oxygen carriers by use of iron or cobalt complexes bound to synthetic polymers was attempted. Radical copolymerization of porphyrin vinyl monomers with styrene gave the metalloporphyrins covalently bonded to a polymer chain at low concentration. For these metalloporphyrin polymers, irreversible oxidation via dimerization was prevented in aprotic solvents and reversible oxygenation was observed. The chemical environment around the oxygen-binding site was presumed to play an important role on the stability of oxygenated complex as in the case of the tetraamide groups on the porphyrin plane. When ethylenebis(salicylideniminato)cobalt chelate coordinated to a polymer-ligand, it formed a stable oxygenated complex at room temperature. Rotational motion of the chelate was decreased markedly by the polymer chain to enhance the coordinate bond between the metal ion and the bound oxygen molecule. Furthermore, the iron porphyrin with bulky substituents was oxygenated even in homogeneous aqueous solutions by combining it with the rigid, hydrophobic domain of a water-soluble block copolymer.

INTRODUCTION

Metal complexes of π-conjugated planar tetradentate ligands, such as metalloporphyrin (I) and Schiff-base cobalt chelates (II), have a tendency to form oxygenated complexes. But, for example, if a "naked" metalloporphyrin is mixed with a nitrogenous axial ligand in a solution at room temperature, the porphyrin complex is immediately oxidized upon exposure to air.



I



II

For the reversible desorption of molecular oxygen it is important to form a stable 1:1 metal-dioxygen complex, as shown in Eq. (1), where Fe denotes iron porphyrin and B represents axial base.

Reversible oxygenation:

$$B\overset{|}{\underset{|}{\mathrm{Fe}}}{}^{(II)} + O_2 \rightleftharpoons B\overset{|}{\underset{|}{\mathrm{Fe}}}O_2 \tag{1}$$

Irreversible oxidation via dimerization:

$$B\overset{|}{\underset{|}{\mathrm{Fe}}}O_2 + \overset{|}{\underset{|}{\mathrm{Fe}}}B \longrightarrow B\overset{|}{\underset{|}{\mathrm{Fe}}}{}^{(III)}{-}O_2{-}\overset{|}{\underset{|}{\mathrm{Fe}}}{}^{(III)}B \text{ or } 2\overset{|}{\underset{|}{\mathrm{Fe}}}{}^{(IV)} = 0$$

$$\xrightarrow{\overset{|}{\underset{|}{\mathrm{Fe}}}} \overset{|}{\underset{|}{\mathrm{Fe}}}{-}O{-}\overset{|}{\underset{|}{\mathrm{Fe}}} \tag{2}$$

Monomolecular oxidation:

$$B\overset{|}{\underset{|}{\mathrm{Fe}}}O_2 + \underset{(H_2O)}{H^+} \longrightarrow B\overset{|}{\underset{|}{\mathrm{Fe}}}{}^{(III)}X + HO_2^{\bullet} \tag{3}$$

$$B\overset{|}{\underset{|}{\mathrm{Fe}}}O_2 \longrightarrow B\overset{|}{\underset{|}{\mathrm{Fe}}}{}^{(III)}X + O_2^{\bullet -} \tag{4}$$

The following conditions are considered to be required for this reversible oxygenation [1-4]. An oxygenated complex reacts with another porphyrin complex, and this binuclear complex is irreversibly oxidized to μ-oxodimer [Eq. (2)]. Thus the first condition is that the porphyrin complex must be isolated and hence steric factors of the porphyrin complex are important for inhibiting the oxidation via dimerization. Another oxidation mechanism is a monomolecular process [Eq. (3)] facilitated by hydrogen ion. So the second condition is that the oxygenated complex must be surrounded by an aprotic environment in order to exclude protons or water molecules from the vicinity of the oxygenated complex. Certain simple monomolecular oxidations occur by an electron transfer from the Fe(II) ion to the bound oxygen molecule, as shown in Eq. (4). A chemical environment is sometimes presumed to be effective in suppressing charge separation and to restrict this oxidation process.

Much recent work has been aimed at overcoming these problems and has been partially successful in aprotic solvents. In aprotic solvents the monomolecular oxidation by proton is excluded, so that the first problem of reversible oxygenation is how to inhibit the dimerization [Eq. (2)]. The successful approach is an elegant steric modification of porphyrins: porphyrins have been substituted in a fashion that inhibits the irreversible oxidation via dimerization. Some interesting metalloporphyrins have been produced by clever synthetic techniques. Collman et al. [4-7] synthesized the iron complex of picket-fence porphyrin to favor the five coordinate structure and inhibit dimerization by steric bulkiness on one side of the porphyrin plane. Baldwin et al. synthesized capped porphyrin [8-10] and strapped porphyrin [11], and crowned porphyrin was synthesized by Chang et al. [12] from the same viewpoint of steric hindrance preventing dimeric oxidation. On the other hand, Traylor et al. [13-15] considered the effect of the proximal base and synthesized porphyrins to which a proximal base was covalently bonded. Collman et al. [16] recently reported the proximal based picket-fence porphyrin. These studies on the synthesis of oxygen carriers are of great significance because they have demonstrated both steric and environmental effects on reversible oxygenation.

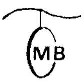
On the other hand, in hemoglobin and myoglobin, the globin protein protects the iron porphyrin complexes which are tucked separately into a hydrophobic domain of the protein. That is, the globin protein prevents the iron porphyrin complexes from dimerization by embedding them separately in the macromolecule, and the hydrophobic domain of the globular protein suppresses the monomolecular oxidation and excludes water molecules. A "synthetic" polymer might be expected to protect the oxygenated complex against autoxidation in much the same way as the globin protein does.

In a classic experiment Wang [3] reported the first synthetic oxygen carrier of iron porphyrin based on use of solid polymer. He embedded the diethyl ester of Fe(II) protoporphyrin IX in a hydrophobic matrix of polystyrene and 1-(2-phenylethyl)imidazole. The iron porphyrin embedded in the polystyrene film was indeed found to combine reversibly with molecular oxygen and remained stable for a few days without irreversible oxidation. Wang considered that the low dielectric constant of the hydrophobic polystyrene matrix excluded water molecules and suppressed charge separation in the oxygenated complex. Oxidation via dimerization was also thought to be prevented since the embedded hemes were isolated from each other by the matrix.

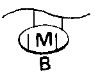
Other results reported concern the oxygen binding ability of iron-porphyrin attached to the surface of a solid. Basolo et al. [17] found the attachment of iron tetraphenylporphyrin to a rigid modified silica gel support which contained an imidazolyl group bonded to the surface atoms of silicon produced an efficient oxygen carrier. Collman et al. [18] prepared iron tetraphenylporphyrin coordinated to an imidazolyl group bonded to crosslinked polystyrene and immersed it in benzene. Treatment with oxygen caused oxidation and formed the μ-oxodimer. It was concluded that the crosslinked polystyrene ligand was not rigid enough in benzene to prevent dimerization upon treatment with oxygen. The authors [19] also studied the oxygenation of iron porphyrin bound to a polymer ligand in the solid state. The rate of oxygen uptake depended upon the surface condition or gas permeability of the polymer matrix in the case of solid-state oxygen binding.

As mentioned above, the dimerization of iron porphyrin was considerably inhibited by embedding the porphyrin complex in polymer matrices or by attaching the porphyrin complex to the surface of rigid polymers, and oxygen carriers composed of iron porphyrin were produced by using solid-state polymers. However, the rates of oxygenation and deoxygenation of these polymer-iron porphyrin complexes were much lower than those of complexes in homogeneous solutions, because ligand-exchange reactions of metal complexes in the solid state occur very slowly. Thus, the attempt should be made to synthesize a polymer-metalloporphyrin complex which will form a stable oxygenated complex even in a homogeneous solution.

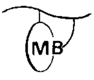
The authors have already studied the chemical properties of the synthetic polymer-metal complexes in homogeneous solutions and have found that the chemical reactivity of a metal complex is often affected by a polymer that exists outside the coordination sphere and surrounds the metal complex [20]. The effects of polymers have been already summarized under the following two terms [20]: (1) the steric effect, which is determined by the conformation and density of the polymer chain, and (2) the special environment constituted by a polymer chain. From this point of view, the authors are now attempting to construct artificial oxygen carriers in homogeneous solutions using the iron and cobalt complexes bound to soluble, synthetic polymers. In the present paper, various types of metalloporphyrin polymers III-VIII were reported. III-VI represent the metalloporphyrin covalently bonded to a polymer chain. In the types V and VI, an axial base ligand is also covalently bonded either to a polymer chain or to the porphyrin ring. Metalloporphyrins coordinate to polymer ligand in VII and VIII.



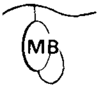
III



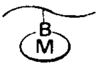
IV



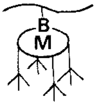
V



VI



VII



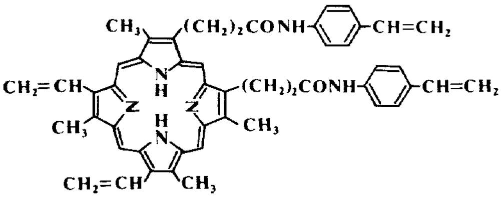
VIII

For example, when porphyrin complexes are bound to a polymer chain at low concentration so as to prevent two complexes from approaching each other, a reversible oxygen binding by the porphyrin complexes is expected to be achieved in aprotic solvents. Furthermore flexible motion and microenvironment of a polymer chain are also assumed to affect the stability of oxygenated complex. The latest result is also reported where reversible oxygenation is successful even in water by fixing iron porphyrin in the hydrophobic domain of water-soluble polymer.

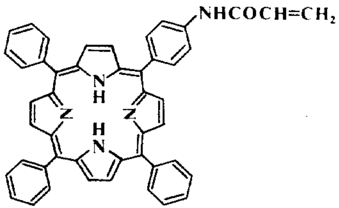
METALLOPORPHYRIN POLYMERS

Porphyrin vinyl monomers synthesized were: N,N'-bis(p-vinylphenyl)-7,12-divinyl-3,8,13,17-tetramethylporphyrin-2,18-dipropylamide (protoporphyrin IX styrylamide, PPSt) (IX), 5-mono(p-acrylamidophenyl)-10, 15,20-triphenylporphine (ATPP) (X); 5,10,15,20-tetra($\alpha,\alpha,\alpha,\alpha$-o-methacrylamidophenyl)porphine (TmPP) (XI), which corresponds to the vinyl monomer of Collman's picket-fence porphyrin, and N-(p-vinylbenzyl)-N'-(imidazolylpropyl)-7,12-divinyl-3,8,13,17-tetramethylporphyrin-2,18-dipropylamide (protoporphyrin IX styryl-imidazolylamide, BPPSt) (XII) which has both vinyl group and proximal base.

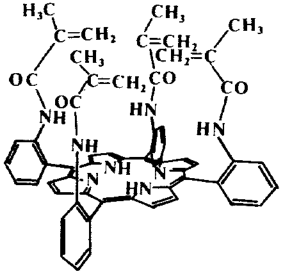
The vinyl monomers of tetraphenylporphyrin type were synthesized according to the schemes shown in Eqs. (1) and (2). Nitrophenylporphin rings were prepared by the reaction of pyrrole and


CH₃
(CH₂)₂CONH
CH=CH₂
CH₂=CH
(CH₂)₂CONH
CH=CH₂
CH₃
CH₃
CH₂=CH
CH₃
N
H
N
N
H
N

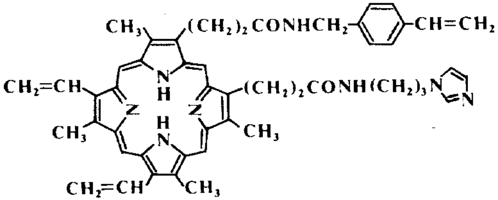
IX


NHCOCH=CH₂
N
H
N
N
H
N

X

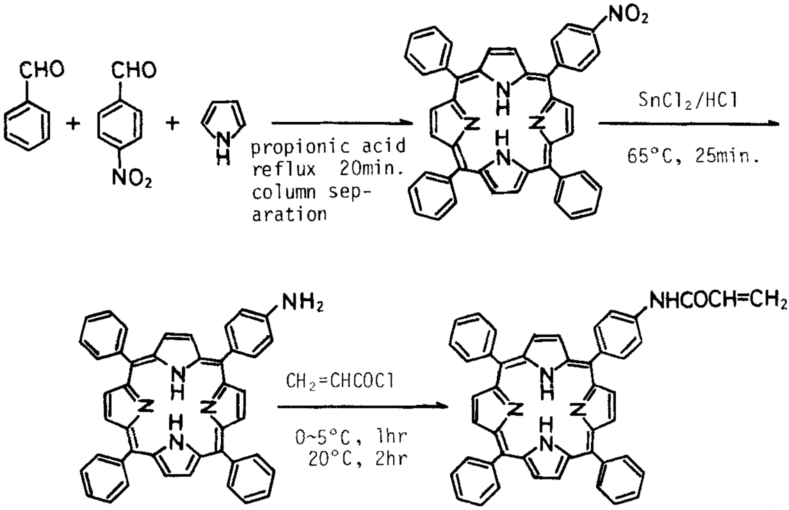

H₃C
C=CH₂
CH₃
C=CH₂
CH₃
CH₂=C
CH₃
C=CH₂
OC
OC
CO
CO
NH
NH
HN
HN
N
NH
N
HN

XI


CH₃
(CH₂)₂CONHCH₂
CH=CH₂
CH₂=CH
(CH₂)₂CONH(CH₂)₃N
N
CH₃
CH₃
CH₂=CH
CH₃
N
H
N
N
H
N

XII

nitrobenzaldehyde and reduced to the amino derivatives. Then, by reacting with acrylic or methacrylic chloride the vinyl derivatives were obtained. Each derivative was purified by column chromatography on silica gel. The structures of vinyl monomers were determined by elemental analyses, infrared, NMR, and mass spectra [21, 22].

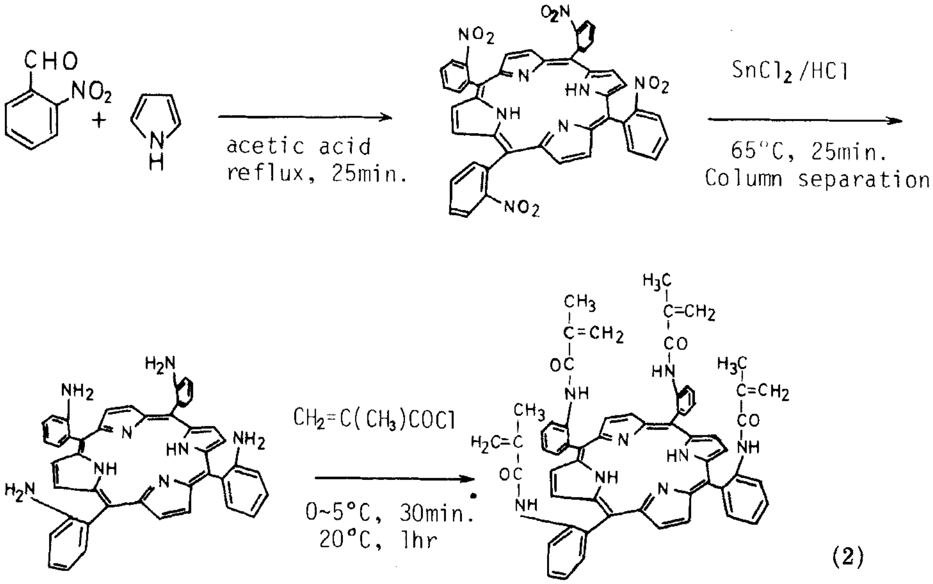


(1)

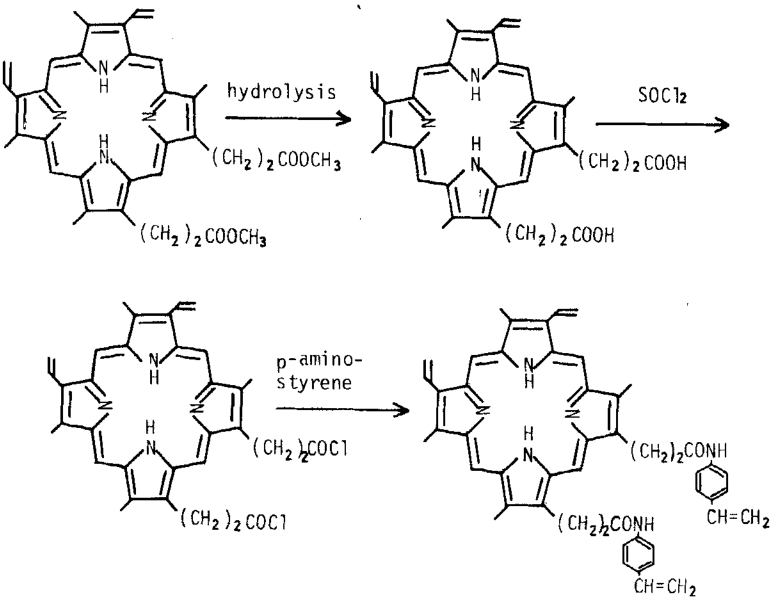
The vinyl derivatives of protoporphyrin IX were synthesized by the reaction of the acid chloride of protoporphyrin IX with p-aminostyrene [Eqs. (3) and (4)] [17, 18].

The process for synthesis of metalloporphyrin polymers is illustrated in Fig. 1. The method which includes the direct polymerization of metalloporphyrin was not used because a metal ion, like the Fe(III) ion of hemin, reacts with radicals to inhibit the radical polymerization. The metal-free porphyrin vinyl monomers IX-XII were radically copolymerized with styrene or with styrene and N-vinylimidazole by azobisisobutyronitrile as initiator. The copolymers were purified by gel permeation chromatography, and high molecular weight copolymers were obtained. The contents of porphyrin unit were determined spectroscopically under the assumption that the molar extinction coefficient of the porphyrin residue of the polymer is the same as that of the corresponding monomeric porphyrin. The contents were less than 1% for every copolymer (Table 1).

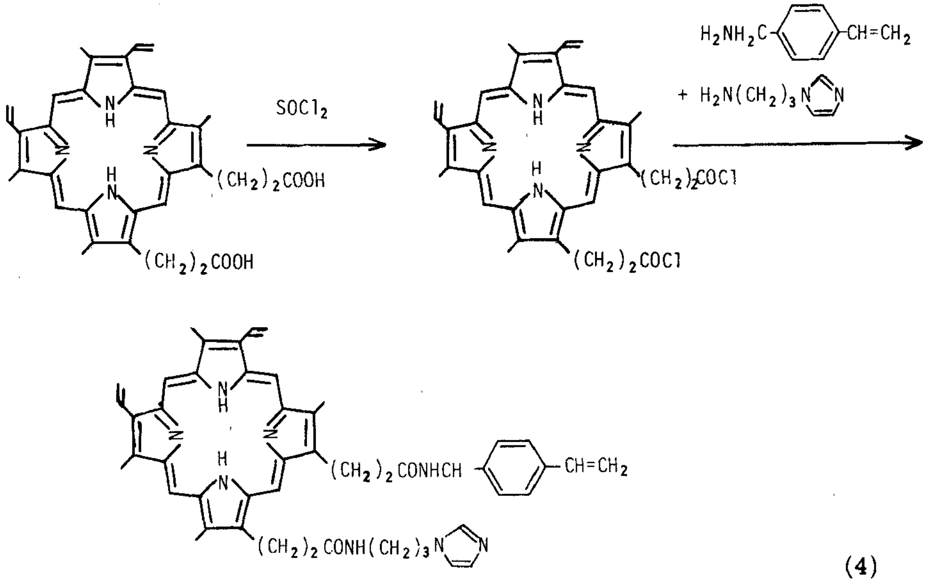
Then the central metal ion, Fe(III) ion or Co(II) ion, was incorporated and purified once more by chromatography. The incorporation of the metal ions into the porphyrin polymers was completed


CHO
NO_2
+
N
H
acetic acid
reflux, 25min.
NO_2
O_2N
N
HN
NO_2
NH
N
NO_2
$SnCl_2$/HCl
65°C, 25min.
Column separation
NH_2
H_2N
N
HN
NH_2
NH
N
H_2N
CH_2=C(CH_3)COCl
0~5°C, 30min.
20°C, 1hr
CH_3
C=CH_2
OC
NH
H_3C
C=CH_2
CO
HN
H_3C
C=CH_2
CO
NH
CH_3
H_2C=C
OC
NH
N
HN
NH
N

(2)


N
H
N
H
N
N
hydrolysis
$(CH_2)_2COOCH_3$
$(CH_2)_2COOCH_3$
$SOCl_2$
$(CH_2)_2COOH$
$(CH_2)_2COOH$
p-amino-
styrene
$(CH_2)_2COCl$
$(CH_2)_2COCl$
$(CH_2)_2CONH$
$(CH_2)_2CONH$
CH=CH_2
CH=CH_2

(3)



(4)

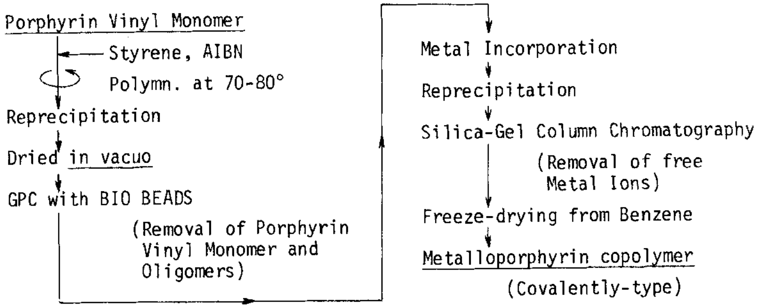


FIG. 1. Process for synthesis of polymeric covalently bonded metalloporphyrins.

within 15 min, except that it took about 2 hr for incorporation of Fe(III) ion into the TmPP polymer. The complete incorporation of metal ions was confirmed by the absence of spectral changes on HCl addition [23] and of emission bands due to metal-free porphyrins [24]. In types III and IV further addition of a low molecular weight axial ligand (B) was necessary to form the complexes. Before oxygenation the

TABLE 1. Copolymerization of the Porphyrin Vinyl Monomers[a]

Compound	Feed porphyrin content (mole %)	Solvent	Initiator (mole %)	Yield by GPC (wt %)	Porphyrin content (mole %)	$[\eta]^{30}$ (dl/g)
P(St-TmPP)	0.05	Bz	0.50	32.6	0.0156	
P(St-TmPP)	0.069	Bz	0.045	32.4	0.10	0.40(Bz)
P(St-ATPP)	0.033	DMF	0.385	21.8	0.0163	0.33 ($CHCl_3$)
P(St-PPSt)	0.030	DMF	0.20	33.8	0.0454	0.35 ($CHCl_3$)
P(St-BPSt)	0.33	-	0.664	22.0	0.416	

[a] Polymerization temperature, 80°C; time, 2-4 hr; initiator, azobisisobutyronitrile.

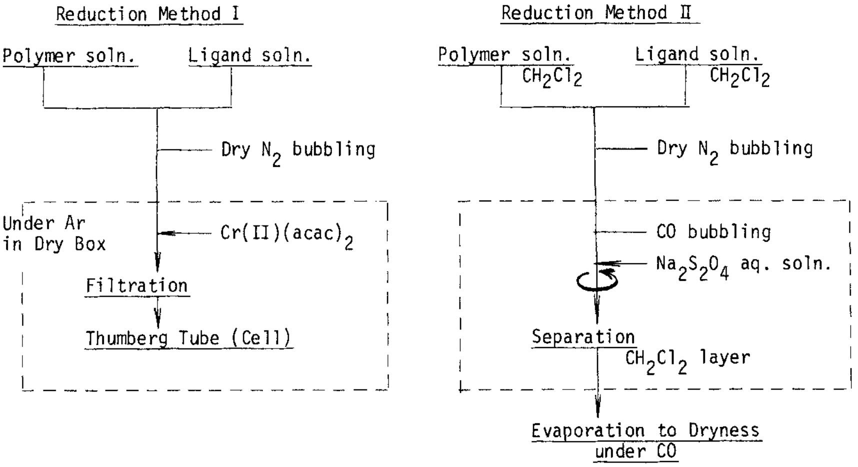


FIG. 2. Two reduction methods used for preparation of ferrous complexes.

central metal ion must be reduced from Fe(III) to Fe(II) ion. One must pay careful attention to this reduction procedure because the residues or fragments of the reducing agent often disturb the oxygenation reaction [25]. Two reduction methods were used (Fig. 2). One method (method I) is the heterogeneous reduction by solid bis (pentenedionato)chromium. Another method (II) also is shown. The methylene chloride solution of ironporphyrin was shaken with an aqueous solution of dithionite under a carbon monoxide atmosphere. The CO complex of Fe(II) porphyrin was isolated by evaporating the methylene chloride layer, and then the bound CO was eliminated from iron ion under high vacuum. The latter method is especially suitable for the coordinate type polymer complexes.

The absorption maxima of the Fe- and Co-porphyrin polymers at deoxy, oxygenated, and oxidized state are summarized in Table 2. Figure 3 is one example of reversible spectral changes of the iron porphyrin polymers. The visible spectrum of the copolymer of Fe(II)-TmPP with N-ethylimidazole changes reversibly at room temperature from 434, 537, and 608 nm in the deoxy state to 432, 540, and 628 nm in the oxy state in toluene. The half-life of the oxygenated complex was about 40 min under 760 Torr oxygen, as determined by measuring the time-decay curve of the absorbance at 432 nm at 20°C. The oxidation product, the absorption maxima of which were found at 428, 516, 606 (shoulder), and 660 nm (shoulder), was not the μ-oxodimer, but resembled the monomeric Fe(III) porphyrin. This indicated that a

TABLE 2. Visible Absorption Maxima of Various Porphyrin Complexes in Toluene

Complex[a]	Absorption maxima (nm)		
	Reduced	Oxygenated	Oxidized
P[St-TmPP Co(II)]-NEtIm	417, 529, 623	439, 550, 630	444, 555, 631
P[St-TmPP Fe(II)]-NEtIm	434, 537, 564, 608	432, 540, 628	428, 516, 606, 660
P[St-ATPP Fe(II)-NVIm]	430, 536, 570	428, 539	423, 510, 570, 601, 660
P[St-PPSt Co(II)]-NEtIm	402, 526, 556	422, 530, 560	-
P[St-BPPSt Fe(II)]	426, 562	-	419, 538

[a] NEtIm: N-ethylimidazole; NVIm: N-vinylimidazole.

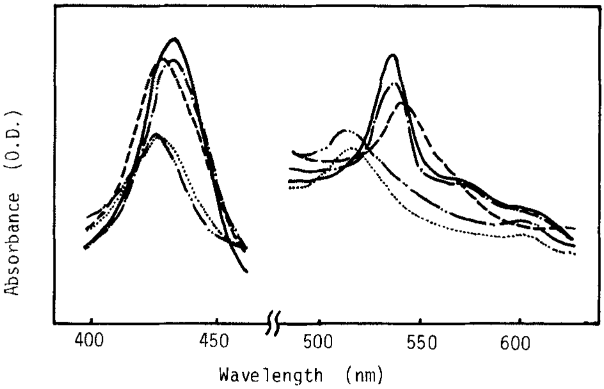


FIG. 3. Absorption spectra of P[St-TmPP Fe(II)] in toluene containing N-ethylimidazole as axial ligand: (– ·· –) before reduction, Fe(III); (—) reduced, Fe(II); (- -) immediately after contact with oxygen (760 Torr); (– · –) evacuated after contact with oxygen (760 Torr) for 15 min; (· · ·) oxidized. [Fe porphyrin] = 1.8 × 10^{-5} unit mole/liter; [N-ethylimidazole] = 1.29 × 10^{-3} mole/liter; 20°C.

dimeric oxidation was prohibited in this polymer-covalently bonded iron porphyrin complex. ESR spectra of the corresponding polymer of Co(II)-TmPP also indicated the formation of the dioxygen complex. While the ESR spectrum under nitrogen atmosphere was similar to that of the five-coordinate Co(II) porphyrin complex, a new signal with 8 shf lines developed in the vicinity of g = 2 when the solution was exposed to oxygen.

For the copolymer of Fe(II)ATPP with N-ethylimidazole, the absorption maximum due to the deoxy complex also changed rapidly upon contact with oxygen, resulting in a new band at 428 nm. After contact with oxygen for 5 min at 20°C, the bubbling of carbon monoxide gas changed the absorption maximum from 428 to 426 nm, which was attributed to the CO complex of Fe(II) ATPP. However, in this case, about 30-40% of the Fe(II) porphyrin residues had already been oxidized. But this half-life is much larger than that of the oxygenated complex of Fe(II)-tetraphenylporphyrin in toluene containing N-ethylimidazole, which is oxidized completely within 30 sec.

The stability of oxygenated complex or the half-life is shown by the data in Table 3. The values of the polymer systems are larger in comparison with those of the corresponding monomeric systems. Moreover, the oxidation products of metalloporphyrin polymers were not μ-oxodimers, as mentioned above. The degrees of incorporation

TABLE 3. Oxygenation Behavior and Stability of Oxygenated Complexes of Various Porphyrin Complexes in Homogeneous Solution

Metal ion	Porphyrin[a]	Oxygenation at 25°C[b]	Half-life	Oxidation product	Solvent
Co(II)	Tetraphenylporphin	No	-	μ-Dioxodimer	Toluene
	P(St-PPSt) (2200)[d]	"	-	No dimer	"
	P(St-TmPP) (1000)	Yes	1 day	"	"
Fe(II)	Tetraphenylporphin	Yes	30 sec	μ-Oxodimer	Toluene
	P(St-ATPP) (1700)	"	5-7 min	No dimer	"
	P(St-TmPP) (1000)	"	40	"	"
	P(St-ATPP-NVIm) (6040)	"	5-7	"	"
	"	"	15	"	DMF
	P(St-ATPP) (1700)	"	5-7	"	Cyclohexane

[a] St: styrene, NVIm: N-vinylimidazole.
[b] Under 760 Torr oxygen.
[c] Fe(II) TPP is completely oxidized to the μ-oxodimer within 30 sec in toluene.
[d] Numbers in parentheses indicate ratios of [St unit]/[porphyrin residue].

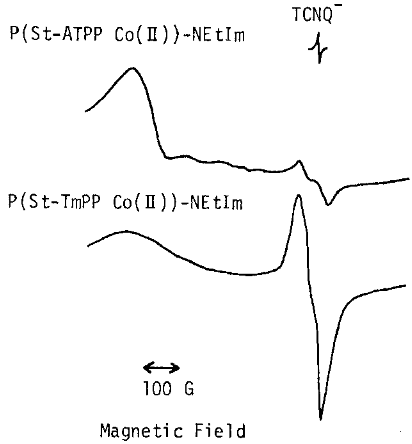


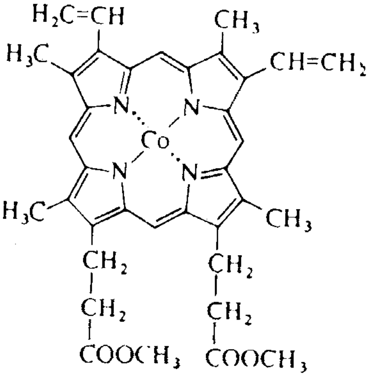
FIG. 4. ESR spectra of polymer-Co(II) complexes under oxygen in toluene containing N-ethylimidazole. [N-ethylimidazole] = 5%; 20°C. [Co(II) - porphyrin residue] = 1×10^{-4} unit mole/liter.

of metalloporphyrin unit are very small in these copolymers. Therefore it is quite difficult that the metalloporphyrin encounters each other to form a binuclear complex, and the irreversible oxidation via dimerization is inhibited.

From Table 3, one notices also the excellent stability of the oxygenated complex of the TmPP copolymer. Figure 4 shows the ESR spectra of oxygen adducts of the Co(II) complexes of TmPP copolymer and ATPP copolymer at room temperature. The absorption signal due to oxygenated complex at g = 2.0 is observed for the TmPP copolymer even at room temperature, with the small signal due to the deoxy penta-coordinated complex at g = 2.3. This result also supports that the tetraamide groups of TmPP form an extraordinarily stable oxygenated complex at room temperature. This effect of TmPP is explained by considering that the tetraamide groups of TmPP prevent the monomolecular oxidation by their chemical environment. One explanation is the holding of the bound oxygen molecule by the tetraamide groups on one side of the porphyrin plane. That is, the interaction between the amide groups and the bound oxygen molecule retards the monomolecular oxidation through charge separation to Fe(III) ion and dioxygen anion radical. This is somewhat similar to the solvent effect of dimethylformamide, which increases the oxygen-binding affinity of metalloporphyrin by solvating bound oxygen [26]. Another explanation of the effect of tetraamide groups is desolvation from the sixth-coordinate site of the porphyrin. The chemical environment around the oxygen-binding site is important to determine the stability of oxygenated complex.

COMPLEXES COORDINATED TO POLYMER LIGANDS

Meanwhile, oxygenation of cobalt porphyrin complexes takes place more easily than does that of iron porphyrin complexes when the solutions are cooled and exposed to air. Thus, the effects of polymer ligands on the oxygenation, i. e., the coordinate-type polymer complexes with Co(II) ion, are discussed next. The polymeric cobalt-porphyrin complexes were prepared from Co(II)-protoporphyrin IX dimethylester (PPME) (XIII) and copolymers of vinylpyridine and styrene (PSP) [27]. The PSP-Co(II)PPME complexes were oxygenated reversibly at low temperature, and the formation constant and thermodynamic data for reversible oxygen binding are summarized in Table 4. Greater oxygen affinity is found for the PSP complex having a large vinylpyridine content of the PSP-ligand is large. One notices that the polymer ligand makes a significantly favorable entropic contribution to oxygen binding [27].



XIII

A more obvious result was obtained for the polymeric cobalt Schiff-base chelates. Ethylenebis(salicylideniminato)cobalt(II) (salen) complex (II) of a nitrogenous ligand forms an oxygenated complex at 0°C but not at room temperature. The reaction at room temperature

TABLE 4. Thermodynamic Data for Reversible Oxygen Binding to the Polymeric Co(II) Complexes

Co(II) complex[a]	$K_{O_2} \times 10^3$ (Torr^{-1})	ΔH (kcal/mole)	ΔS (e. u.)
Py-Co PPME[b]	1.3	-8.4	-50
PSP -Co PPME[b]	0.91	-8.3	-50
PSP_{23}-Co PPME[b]	2.3	-7.6	-45
PSP_{42}-Co PPME[b]	7.6	-7.6	-43
Py-Co salen[c]	_[d]	–	–
PSP -Co salen[c]	0.40	-22	-65
PSP_{23}-Co salen[c]	8.4	-23	-61
PSP_{34}-Co salen[c]	19.1	-23	-59
Coboglobin[e]	50	-13.3	-53
Myoglobin[e]	2000	-18.1	-60

[a] PPME: protoporphyrin IX dimethyl ester, salen: ethylenebis-(salicylideniminato), PSP: copolymer of styrene and 4-vinylpyridine; suffix indicates the content of vinylpyridine-unit.

[b] -45°C, in toluene.

[c] 25°C, in toluene.

[d] The Py-Co(II) salen complex forms a μ-dioxodimer irreversibly.

[e] Sperm whale, 20°C, in water, pH 7.

was known to be the formation of binuclear μ-dioxo complex. However the authors found that the polymeric Co(II) salen complex of PSP (copolymer of vinylpyridine and styrene) was reversibly oxygenated even at room temperature. As can be seen in Fig. 5, reversible changes of the visible and ESR spectra are observed in toluene solution at room temperature on passage of a stream of oxygen or nitrogen gas. The uptake of molecular oxygen was measured by volumetry and was equimolar to cobalt ion. It was confirmed that the polymeric Co(II) salen complex forms 1:1 dioxygen-adduct without any trace of irreversible oxidation. The oxygenated complex remained stable for a few days without oxidation.

The immobilization of Co(II) salen onto the polymer ligand is considered to be one of the reasons for attainment of the oxygenated complex. The formation constant for the five-coordinate complex of PSP-Co(II) salen (K = 500 liter/mole) was much larger than that

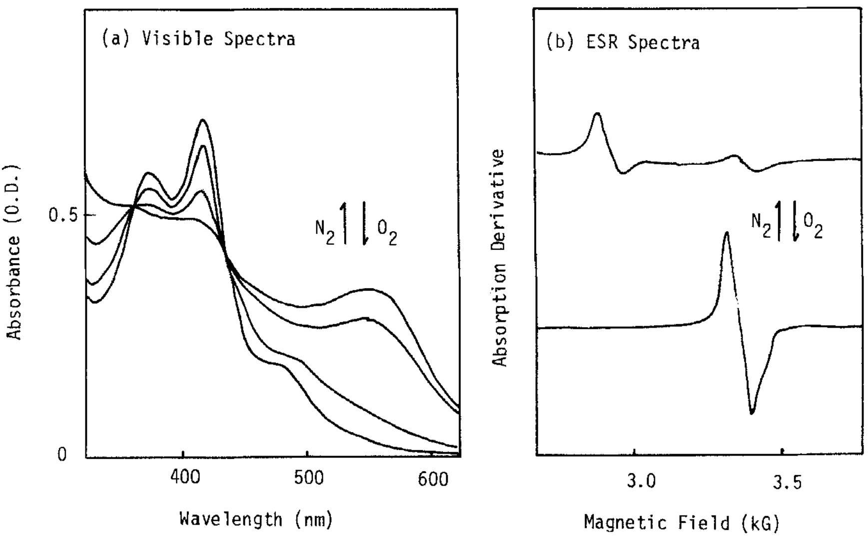
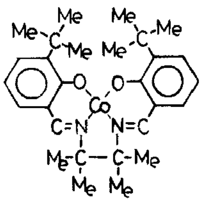


FIG. 5. Reversible changes of visible and ESR spectra of PSP$_{23}$-Co(II) salen in contact with oxygen; 23°C, toluene. [Co(II) salen] = 1×10^{-4} unit mole/liter; [pyridine unit of PSP] = 1×10^{-3} mole/liter.

for pyridine-Co(II) salen (K = 13 liter/mole) due to both favorable enthalpy and entropy changes. The detailed study on the ESR parameters of the complexes suggested also that the strong ligation of PSP to Co(II) salen increased the oxygen affinity of PSP-Co(II) salen and the complexes were separately distributed onto the polymer-ligand to prohibit the binuclear complex formation.

This effect of polymer ligand was studied clearly by using a



XIV

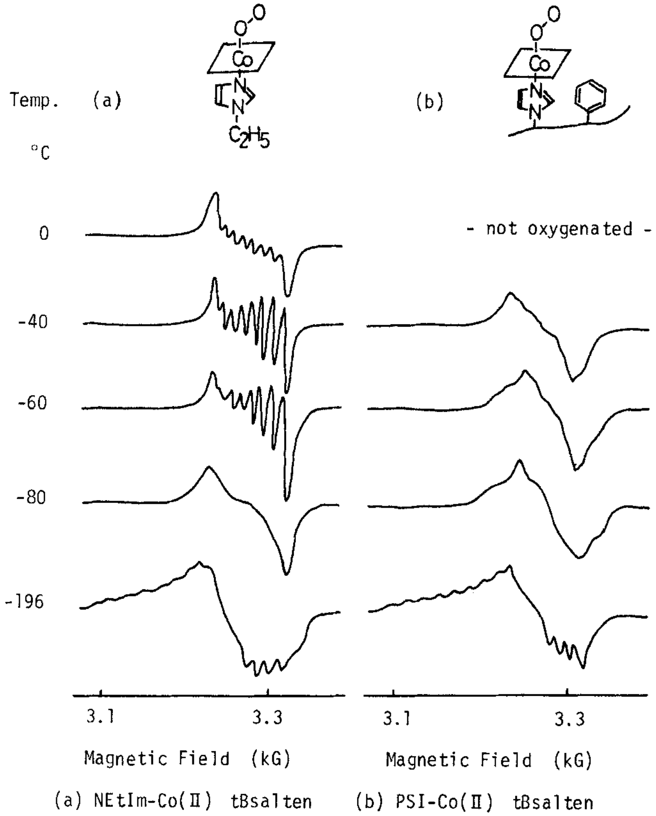


FIG. 6. Temperature dependence of ESR spectra of oxygenated Co(II)-complex under oxygen atmosphere in toluene. [Co(II) tBsalten] = 1×10^{-3} mole/liter; [imidazole unit] = 1×10^{-2} mole/liter.

sterically hindered cobalt Schiff-base compound: N,N'-[1,1,2,2-tetramethyl]ethylenebis(3-tert-butylsalicylideniminato) cobalt complex (XIV) here abbreviated as Co(II)tBsalten. The ESR spectra of oxygenated complexes are seen in Fig. 6. Down to freezing temperature, the ESR spectrum of oxygenated complex of the monomeric Co(II)-tBsalten, i. e., of the N-ethylimidazole complex remains isotropic. On the other hand, the polymer complex of tBsalten shows an anisotropic ESR spectrum even at near room temperature. This means that the rotational motion of the bound oxygen molecule is markedly restructed by the polymer ligand. This result is considered to indicate that the molecular movement of Co(II)tBsalten coordinately attached to the polymer ligand is strongly suppressed by the steric hindrance of the macromolecular chain. Therefore, the coordinate bond between Co ion and the axial base of the polymer ligand further enhances the oxygen affinity and decrease the rotational motion of coordinated oxygen molecule.

The formation constant and thermodynamic data for reversible oxygen binding to PSP-Co(II) salen are collected in Table 4. The entropy change is efficient also in this Co(II) salen system, as in the Co(II) PPME system. K_{O_2} and ΔS increase with the content of vinylpyridine units of the PSP ligand. Ibers et al. [28] studied previously the effects of nitrogenous base ligands in the trans position of the coordinate molecular oxygen. They reported that the larger the $pK_a(BH^+)$ of the base ligand, the smaller the ΔH value and the more stable the dioxygen complex formed. This result was considered to indicate that the electron donor property of the base ligand made the $Co-O_2$ bond stronger. On the contrary, the PSP-ligand produced an effect on the stability of the dioxygen complex through entropic contribution. This entropic contribution is presumed to relate to motional conditions of the bound oxygen molecule, as mentioned above.

POLYMER-IRON PORPHYRINS WITH HINDERING GROUPS

Collman et al. [4-7] succeeded in the reversible oxygenation in aprotic solvents by using their iron tetrapivalamidophenyl porphyrin so-called "picket fence" porphyrin. Their porphyrin derivative had steric bulkiness on the side of the porphyrin plane and yet left the other side unencumbered. They reasoned that the use of a suitable bulky axial base ligand such as N-alkylimidazole would allow coordination of the imidazole on the unhindered side of the porphyrin remaining as a pocket for binding molecular oxygen. Moreover, the hindrance would discourage the dimerization of the oxygenated complex. It was reported that the complex could bind molecular oxygen reversibly at room temperature when the picket-fence was constructed with the pivalamidophenyl group. Their result means that the steric bulkiness and the special environment around the oxygen binding site are important to form the reversible oxygen complex.

But their expectation mentioned above was not complete. For example, this complex often showed a characteristic visible absorption spectrum due to the six-coordinate structure. Therefore, the picket fence does not completely inhibit the dimerization, and the steric effect of the picket-fence configuration is not so important for oxygenation. As has been already mentioned about the TmPP com-

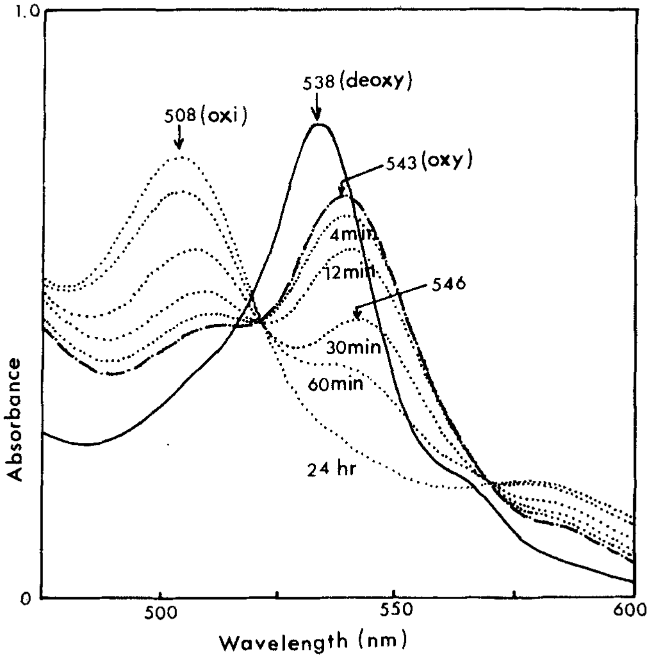


FIG. 7. Absorption spectra of PSI-Fe(II) prophyrin with hindrance groups (TpivPP) in toluene. [Fe porphyrin] = 3×10^{-5} mole/liter; [imidazole unit of PSI] = 3×10^{-4} mole/liter; 25°C.

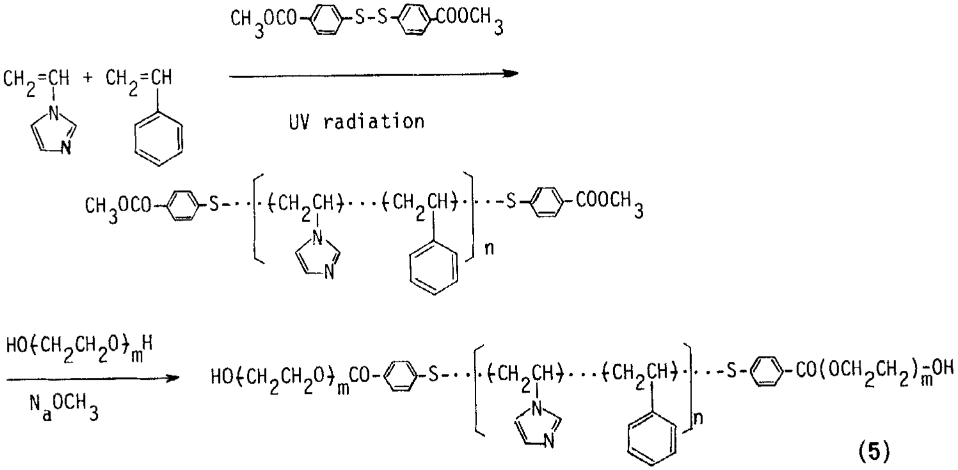
plex, the effect of the picket-fence configuration is possibly desolvation around sixth-coordinate site or a holding effect of dioxygen which prevents the monomolecular oxidation to Fe(III) ion and dioxygen anion radical.

We introduced the models similar to Collman's into a macromolecular chain through the coordinate bond. Firstly, that the steric hindrance between the bulky groups and macromolecular chain may increase the five-coordinate complex, for oxygen molecule just to coordinate to the sixth site. Secondly, the hydrophobicity of a polymer chain will prevent the attack of water molecule or proton to the oxygenated complex. Furthermore, the porphyrin can be dissolved in any solvent, especially in water, when it is bound to a polymer chain. Therefore, oxygenation can be studied even in water by utilizing water-soluble polymers. Under these expectations, the study was started from the toluene-soluble polymer system as shown in Fig. 7.

The complex between PSI (copolymer of styrene and N-vinylimidazole) and Fe(II)-porphyrin with hindrance groups showed a spectrum typical of those assigned to six-coordinate structure, probably because the steric hindrance of a polymer chain of such a flexible polymer is not satisfactory in order to obtain five-coordinate complex. The polymer complex can bind molecular oxygen, but the half-life of the oxygenated complex is several hours, which is shorter in comparison with Collman's result [5-7].

The reason for the smaller half-life is based on the method of reduction. Because the reduction of Fe(III) complex was carried out by the heterogeneous system of methylene chloride/aqueous dithionite solution, it was impossible to avoid contamination by water, which increases the monomolecular oxidation of oxygenated complex by the attack of water molecules. But it is important that the half-life of oxygenated complex is very long in the case of polymer complex (Table 5). Although the complex of N-ethylimidazole was rapidly oxidized in water-saturated toluene when it was exposed to oxygen, the complex of PSI had a half-life of 12 min under the same experimental conditions. The hydrophobic polymer chain composed of styrene residue is presumed to retard the monomolecular oxidation caused by water.

From this result the possibility of oxygenation in an aqueous medium by utilizing hydrophobic and water soluble polymers can be ensured. When the complex of a water-soluble random copolymer such as the copolymer of N-vinylimidazole and N-vinylpyrrolidone was used, no oxygenated complex was detected and the porphyrin complex was immediately oxidized. Thus, water-soluble hydrophobic triblock copolymer, as shown in Eq. (5), was next chosen. The central block is hydrophobic and composed of the copolymer of styrene and N-vinylimidazole (PSI), in which the iron porphyrin can



(5)

TABLE 5. Life-time of Oxygenated Complex of PSI-Iron Porphyrin with Hindrance Groups (TpivPP)[a]

Solvent	Ligand	[Im]/[Fe][b]	Visible absorption (nm)			Half-life
			Oxidized	Reduced	Oxygenated	
Toluene	EtIm	3	508	537	546	15 min
		10	508	536	544	15 min
	PSI	10	508	537	543	2-3 hr
		100	508	538	543	5-6 hr
H_2O-sat.	EtIm	10	508	537	(508)	0
Toluene	PSI	10	508	538	543	12 min

[a] TpivPP: meso-[tetra-$\alpha,\alpha,\alpha,\alpha$-(o-pivalamidophenyl)porphine].
[b] [Fe] = 0.01-0.02 mmole/liter.

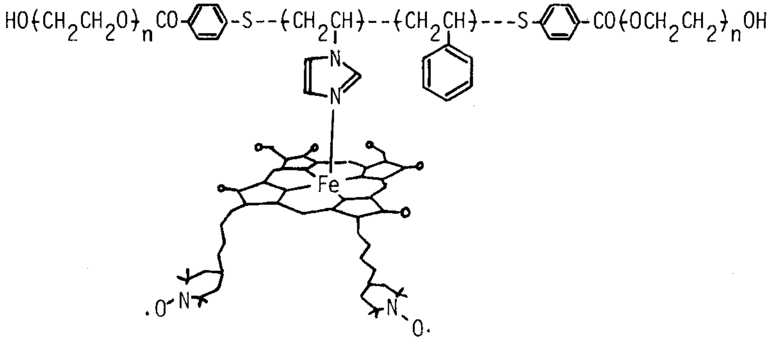
be bound through coordinate bond. This central block was synthesized by UV-radiation polymerization by telechelic initiator of bis(4-carbomethoxyphenyl) disulfide. The reaction of telechelic block with poly(ethylene oxide) gave the block copolymer. Triblock copolymer having a pure polystyrene chain (PSt) as hydrophobic block was also synthesized. PEO-PSI-PEO and PEO-PSt-PEO are used to denote the PSI block copolymer and the PSt block copolymer, respectively.

Equation (6) illustrates the method of preparation of Fe(II)-porphyrin bound to the block copolymers; P denotes porphyrin with hindering groups and NEtIm denotes N-ethylimidazole. The block copolymer and ferric complex were dissolved in methylene chloride, and the central metal ion was reduced by aqueous dithionite solution. The methylene chloride layer was separated and evaporated to dryness. Then, degassed dioxane was added to the polymer powder under an inert atmosphere. To this solution, water was slowly added. The content of dioxane was controlled to 3 vol %. In the case of PSt block copolymer, N-ethylimidazole was added as axial ligand.

$$
\begin{aligned}
&\text{Block copolymer} + (\text{NEtIm}) + \text{Fe(III)P/CH}_2\text{Cl}_2 \xrightarrow{\substack{\text{Heterogeneous reduction} \\ \text{by Na}_2\text{S}_2\text{O}_4/\text{H}_2\text{O}}} \\
&\text{Block copolymer-Fe(II)P-(NEtIm)/CH}_2\text{Cl}_2 \xrightarrow[\text{Addition of dioxane}]{\text{CH}_2\text{Cl}_2\text{ evaporated}} \\
&\text{Block copolymer-Fe(II)P-(NEtIm)/dioxane} \xrightarrow{\text{Slow addition of H}_2\text{O}} \\
&\text{Block copolymer-Fe(II)P-(NEtIm)/H}_2\text{O-3\% dioxane} \qquad (6)
\end{aligned}
$$

In order to ascertain the environment of the porphyrin or in order to establish whether the porphyrin is immobilized in the hydrophobic block of the copolymer, an ESR study was carried out by use of spin-labeled hemin XV.

A comparison of the relative relaxation time of rotational motion of spin-labeled hemin indicates that the axial ligation of PSI block copolymer decreased the relaxation time by a factor of one order compared with N-ethylimidazole system. This means that the porphyrin is attached to the hydrophobic domain of PSI block copolymer. Furthermore, for the porphyrin with bulky substituents, which is more hydrophobic than hemin due to the large organic group, the central metal ion cannot be reduced in water by sodium dithionite when the complex is bound to PSI block copolymer. This result supports the view that a picket-fence porphyrin is included in the center of a hydrophobic sphere of the copolymer, to which a large molecule such as dithionite ion cannot approach.



XV

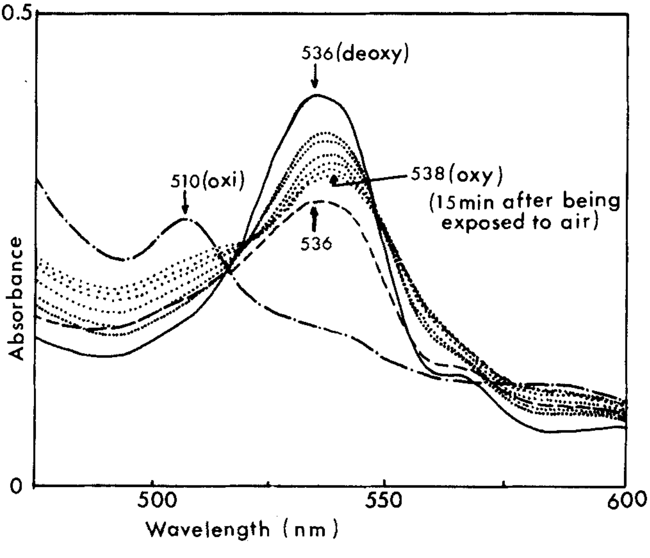


FIG. 8. Oxygenation of Fe(II) prophyrin with hindering groups (TpivPP) in aqueous solution: (—) in vacuo (deoxy); (· · ·) in air; (- -) in vacuo after 3 hr exposure to air; (– · –) oxidized. [Fe porphyrin] = 2 × 10^{-5} mole/liter; [imidazole unit of PSI block copolymer] = 4 × 10^{-4} mole/liter; 3% (v/v) dioxane-water; pH 7.0; 25°C.

Figure 8 shows the spectral change in the Fe(II) picket-fence porphyrin bound to the PSI block copolymer in water. The absorption maximum red-shifted slowly when the solution was exposed to air. After evacuation the maximum shifted back to 540 nm, although the absorbance decreased about half by partially irreversible oxidation. This is the first success in binding oxygen reversibly in homogeneous water solution. On the other hand, the PSt type block copolymer was not enough to protect the iron picket-fence porphyrin in water. In order to achieve oxygenation in water, it is considered that the iron porphyrin must be tightly coordinated to the hydrophobic microphase of a water-soluble block copolymer. This method was generally applicable to other prophyrins which have bulky tetraamido groups on the porphyrin plane such as XI and which are reversibly oxygenated in organic solution.

CONCLUSION

The roles of macromolecular chain in oxygenation of metal complexes are as follows. Firstly, metal complexes must be attached onto a polymer chain at low concentration in order to prevent dimeric oxidation. Secondly, the chemical environment around the sixth coordination site must be constructed in order to retard the monomolecular oxidation as in the case of the tetraamide groups on the porphyrin plane. Thirdly, when a metal complex coordinates to a polymer ligand, its rotational motion is decreased markedly to enhance the coordinate bond between the metal ion and the bound oxygen molecule. Finally, if the complex is fixed in a rigid, hydrophobic domain, it prevents the oxidation caused by water or proton attack. Oxygenation becomes possible even in water by utilizing a water-soluble, hydrophobic block copolymer.

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