

Inhibitory Effect of 2,6-Di-*tert*-butylphenol Groups in Iron and Manganese Porphyrins on the Catalytic Activity in the Oxidation of Hydrocarbons by Hydrogen Peroxide

O. A. Gerasimova, D. B. Shpakovskii, E. R. Milaeva, M. Louloudi*, and N. Hadjiliadis*

Organic Chemistry Department
e-mail: olgagerasimova@inbox.ru

Received April 9, 2007

Abstract—Iron and manganese porphyrins containing 2,6-di-*tert*-butylphenyl groups (R_4PFeCl and R_4PMnCl) have been synthesized to be further immobilized on silica gels via various spacers. The activity of these porphyrins in the oxidation of alkanes and alkenes by hydrogen peroxide has been studied. 2,6-Di-*tert*-butylphenol groups decrease the catalytic activity of porphyrins in oxidation processes.

DOI: 10.3103/S0027131407050100

The pharmacological and medical utility of porphyrins and their complexes with metals is due to their lipophilicity, which enables their accumulation in the lipid bilayer of cell membranes and transport to cells of living organisms [1]. However, the structural and functional affinity of synthetic metal porphyrins to the reactive sites of oxidoreductases makes them catalytically active in the oxidation of biosubstrates. As a result of these side processes, the use of porphyrins, e.g., in diagnostics, is complicated by the undesired oxidative destruction of biosubstrates. In this case, it is proposed to simultaneously use antioxidants. We demonstrated earlier that the introduction of 2,6-dialkylphenols into porphyrins or phthalocyanines generates polyfunctional systems. Such compounds express catalytic or antioxidant properties depending on the metal and the process parameters [2].

This work concerns the preparation of iron and manganese porphyrins with 2,6-di-*tert*-butylphenol moieties in their macrocycle and the study of their catalytic activity in oxidation processes. For modeling the oxygenase activity, silica-gel-immobilized metal porphyrins were prepared and studied. In choosing spacers with imidazole coordinating groups, we were guided by modeling of natural heme systems in which the iron metal is bound to the nitrogen atom of the imidazole ring of histidine.

PREPARATION OF PORPHYRINS IMMOBILIZED ON SILICA GELS

To determine the role of antioxidant groups in the catalytic activity of porphyrins, in this work we used compounds bearing 3,5-di-*tert*-butyl-4-hydroxyphenyl

substituents in *meso* positions. Free base 5,10,15,20-tetrakis(3,5-di-*tert*-butyl-4-hydroxyphenyl)-21H,23H-porphyrin (compound **1**) was synthesized by the Rothmund condensation of aldehyde with pyrrole in propionic acid, and its complexes with iron (compound **2**) or manganese (compounds **3**) were prepared (Fig. 1) [3–5] in 70–80% yields. These complexes were characterized by electronic absorption spectroscopy [4, 9].

To immobilize porphyrins on silica gel, we synthesized metalloporphyrins modified by various binding groups of silica gel (Scheme 1), by analogy with previously described methods [6, 7]. First, we prepared

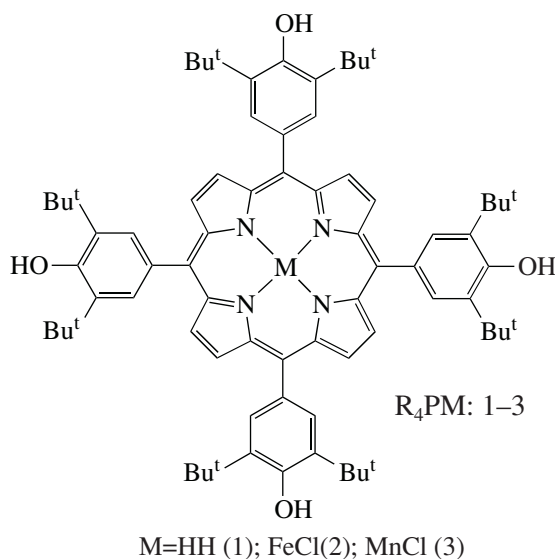
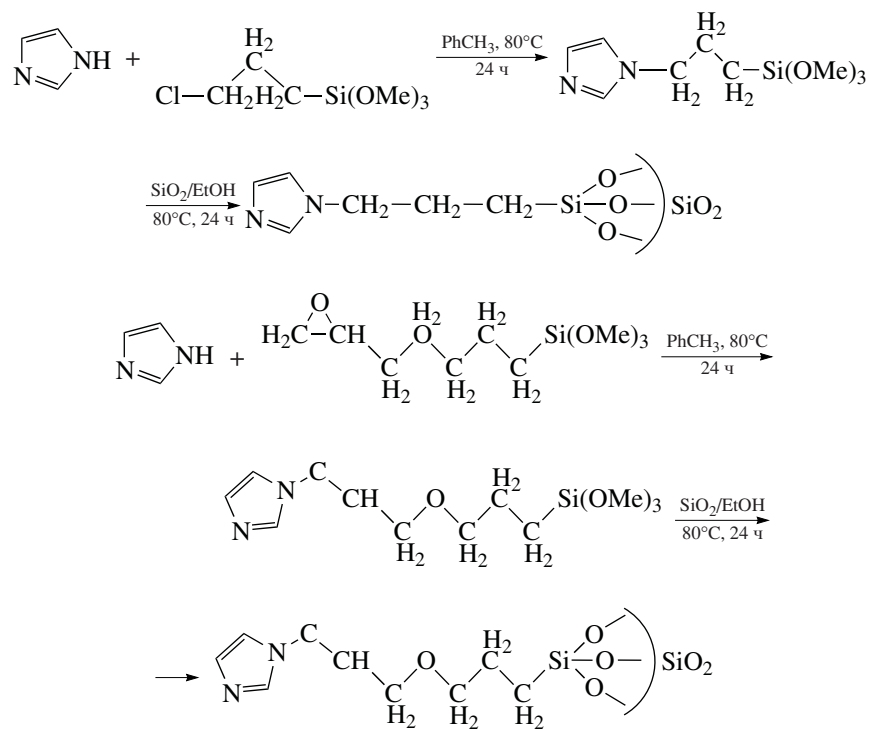


Fig. 1. Complexes of 5,10,15,20-tetrakis(3,5-di-*tert*-butyl-4-hydroxyphenyl)-21H,23H-porphyrin (compound **1**) with iron (compound **2**) and manganese (compound **3**).

* University of Ioannina, Greece.



Scheme 1.

modified silica gels bearing imidazole as the coordinating group (Fig. 2). The silica gel matrix was modified by porphyrins via a coordination link between the imidazole nitrogen atoms and the metal atoms of the macrocycle. With respect to metalloporphyrin, the imidazole groups are the axial ligands of spacers L_1 and L_2 .

The modified silica gels prepared in this work were identified by their IR spectra, electronic absorption spectra, and thermogravimetric analysis. All compounds bearing moiety L_1 display bands due to the C–O stretching vibrations at 1510–1520 cm^{-1} and the C=N vibrations in uncoordinated imidazole at

1675 cm^{-1} . For the complexes of L_1 with porphyrins, the C=N band shifts toward longer wavelengths (1655–1630 cm^{-1}), signifying the coordination of the metal ion and the nitrogen atom. For the O–H group, a broad band of the stretching vibrations is observed at 3300–3500 cm^{-1} for L_1 and immobilized porphyrins **4** and **6** and a narrow band, associated with the O–H stretching vibrations and characteristic of 2,6-di-*tert*-butylphenol groups, is observed at 3600 cm^{-1} . For the compounds bearing moiety L_2 , the C=N stretching vibrations in uncoordinated imidazole characteristically appear at 1671 cm^{-1} ; for complexes of L_2 with metalloporphy-

$R_4\text{PFeClL}_1$ (**4**), $R_4\text{PFeClL}_2$ (**5**), $R_4\text{PMnClL}_1$ (**6**), $R_4\text{PMnClL}_2$ (**7**)

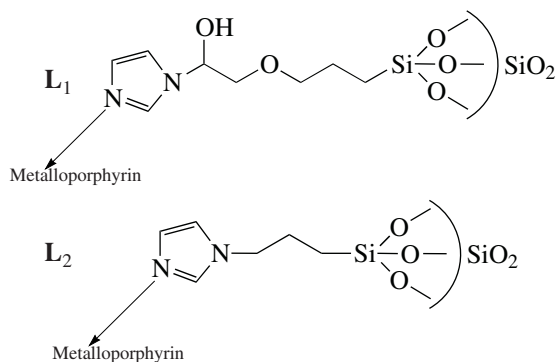
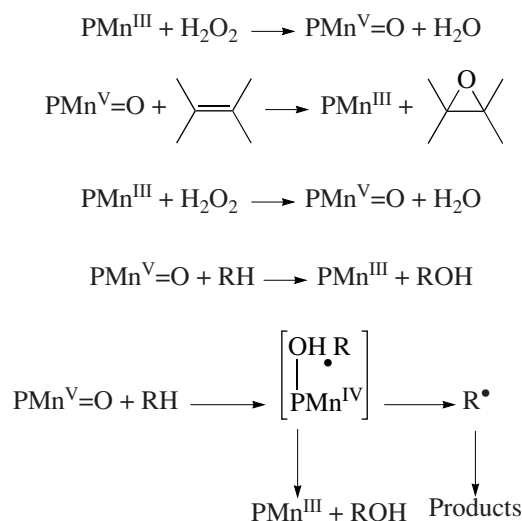
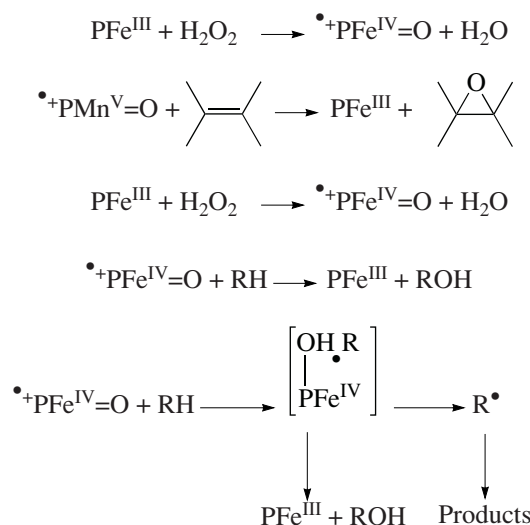


Fig. 2. Complexes of *meso*-tetrakis(3,5-di-*tert*-butyl-4-hydroxyphenyl)porphyrin (R).



Scheme 2.



Scheme 3.

rins, the C=N band shifts toward longer wavelengths (1630–1620 cm⁻¹); here, as in compounds of **L**₁, this shift indicates the coordination between the metal ion and nitrogen atom.

ACTIVITY OF METALLOPORPHYRINS IN THE OXIDATION OF ALKANES AND ALKENES BY HYDROGEN PEROXIDE

Iron and manganese tetraarylporphyrins express their catalytic properties in alkane oxidation and alkene epoxidation [10, 11]. The effect of iron and manganese *meso*-tetraarylporphyrins, either immobilized or non-immobilized, on the oxidation of hydrocarbons by hydrogen peroxide was studied previously. The compounds described in the literature had a catalytic effect [8, 12–14].

The alkene-oxidation mechanism and the general schemes of alkene epoxidation and alkane hydroxyla-

tion in the presence of iron and manganese porphyrins were discussed in detail [12]. The action of manganese porphyrin was represented by the following stages (Scheme 2). For manganese porphyrins, the oxo complex with the metal in the oxidation state +5 (PMn^V=O) is a characteristic catalytic species. Such species are biomimetics of monooxygenases: they transfer oxygen atoms to substrate molecules.

For iron porphyrin, another intermediate is characteristic, namely, the radical cation form of the ligand in iron porphyrin with the oxidation state +4 (Scheme 3). We studied the influence of unsupported metalloporphyrins **2** and **3** and silica-gel-immobilized porphyrins **4–7** on the oxidation of alkenes and alkanes by hydrogen peroxide.

Table 1 displays data on epoxide formation during the oxidation of cyclooctene by hydrogen peroxide in the presence of silica-gel-immobilized metalloporphyrins **4–7** and unsupported metalloporphyrins **2** and **3**.

It is known that manganese *meso*-chlorotetraphenylporphyrin is catalytically active in such systems [8]. For manganese porphyrin containing 2,6-di-*tert*-butylphenol groups (compound **3**), the catalytic effect is virtually unexpressed regardless of whether porphyrin is immobilized or not. Iron porphyrins **2**, **4**, and **5** virtually do not affect the generation of cyclooctene epoxides during oxidation by H₂O₂.

Table 2 displays data on the oxidation of cyclohexene by H₂O₂ in the presence of supported metalloporphyrins **4–7**. The reaction produces cyclohexene epoxides and cyclohexan-2-ene.

Manganese porphyrin containing 2,6-di-*tert*-butylphenol groups (compound **6**) immobilized on silica gel via a long spacer **L**₁ is catalytically active, but its catalytic activity is lower than that of its phenyl analogue [14]; the processes are not selective. In the pres-

Table 1. Epoxide yields in the oxidation of cyclooctene by H₂O₂ in the presence of metalloporphyrins immobilized on silica gels via various spacers (compounds **4–7**) and unsupported metalloporphyrins (compounds **2** and **3**)*

Porphyrin	Epoxides, %	TOF × 10 ⁻²
R ₄ PFeCl (2)	>1	0.86
R ₄ PMnCl (3)	2	4.68
R ₄ PFeCIL ₁ (4)	1	0.08
R ₄ PFeCIL ₂ (5)	>1	0.04
R ₄ PMnCIL ₁ (6)	>1	0.04
R ₄ PMnCIL ₂ (7)	2	0.16

* The reaction time with immobilized metal porphyrins is 24 h; with unsupported, 1 h. For the process parameters, see text.

Table 2. Product yields and selectivities in the oxidation of cyclohexane by H₂O₂ in the presence of metalloporphyrins immobilized via various spacers (compounds 4–7)

Porphyrin	Epoxide, %	Ketone, %	Overall product yield, %	Epoxide selectivity, %	Ketone selectivity, %
R ₄ PFeClL ₁ (4)	0	9	9	0	100
R ₄ PFeClL ₂ (5)	>1	8	9	5.6	94.4
R ₄ PMnClL ₁ (6)	6	13	18	30.5	69.5
R ₄ PMnClL ₂ (7)	2	5	7	32.0	68.0

* The reaction time with immobilized metalloporphyrins is 24 h. For the process parameters, see Experimental.

Table 3. Product yields in the oxidation of cyclohexane by H₂O₂ in the presence of metal porphyrins 2–7

Porphyrin	Cyclohexanol, %	Cyclohexanone, %	TOF × 10 ⁻⁴ (alcohol)	TOF × 10 ⁻⁴ (ketone)
R ₄ PFeCl (2)	>1	>1	22.0	28.0
R ₄ PMnCl (3)	>1	0	24.0	0
R ₄ PFeClL ₁ (4)	>1	>1	5.0	3.8
R ₄ PFeClL ₂ (5)	>1	>1	5.4	1.3
R ₄ PMnClL ₁ (6)	1	0	8.0	0
R ₄ PMnClL ₂ (7)	>1	1	3.0	11.5

* The reaction time with immobilized metalloporphyrins is 24 h; with unsupported, 1 h. For the process parameters, see Experimental.

Table 4. Product yields and process selectivities in the oxidation of hexane by H₂O₂ in the presence of metal porphyrins immobilized via a long spacer L₁ (compounds 4 and 6)

Porphyrin	Alcohol, %	Ketone, %	Overall product yield, %	Alcohol selectivity, %	Ketone selectivity, %
R ₄ PFeClL ₁ (4)	6	3	9	67.2	32.8
R ₄ PMnClL ₁ (6)	7	4	11	67.3	32.7

* The reaction time with immobilized metal porphyrins is 24 h.

ence of iron porphyrins 4 and 5, which are immobilized on supports via long (L₁) and short (L₂) spacers, respectively, cyclohexan-2-ene is generated with near-100% selectivity, but product yields are insignificant.

Table 3 displays data on the oxidation of cyclohexane by H₂O₂ in the presence of metalloporphyrins 2–7. Cyclohexanol and cyclohexanone are produced by the reaction.

All porphyrin additives only insignificantly affect the generation of oxidation products. However, it is important that all nonimmobilized metalloporphyrins have higher catalytic properties than their immobilized analogues. These results are consistent with [15]; apparently, they are due to the inhibition of the axial positions of metalloporphyrins in their coordination to the imidazole groups of the spacer.

Table 4 displays the data obtained from the oxidation of hexane with H₂O₂ in the presence of metalloporphyrins immobilized via long spacer L₁ (compounds 4 and 6). Oxidation products are hexan-2-ol and hexan-2-one.

From the above, we deduce that the catalytic activity of porphyrins is controlled by several factors: the nature of the metal, the existence of antioxidant phenol groups immobilized on a support, and the nature of the binding group of the support. The interpretation of our experimental data should apparently include the generation of various intermediates by phenol-substituted porphyrins. From tentative data, we can presume that the antioxidant phenol group is involved in the main process route via the inter- or intramolecular electron and proton transfer.

Thus, presumably, 2,6-di-*tert*-butylphenol substituents dramatically decrease the catalytic activity of manganese and iron porphyrins.

EXPERIMENTAL

Electronic absorption spectra were recorded on a Cari-219 Varian (Jasco) UV/Vis/NIR spectrophotometer. IR absorption spectra were recorded as KBr disks on an IKAR Fourier-transform spectrophotometer,

Spectrum GX Perkin-Elmer FT-IR system. Thermogravimetric analysis (TGA) was carried out on a Shimadzu DTG-60 instrument. Chromatographic analysis was carried out on a Shimadzu GC-17A instrument (a gas chromatograph coupled with GCMS-QP5000 mass spectrometer). Thin-layer chromatography was performed on Silufol UV-254 plates. Column chromatography was carried out using alumina (neutral) and silica gel (40/100).

Porphyrins **1**, **2**, and **3** were synthesized as described previously [3–5]; purification was carried out by column chromatography on silica gel with 80% CHCl₃ + 20% hexane eluent.

Modifying silica gel with (3-glycidyloxypropyl)trimethoxysilane (L₁) was carried out as described in [6]. To a solution of imidazole (3 mmol, 0.204 g) in toluene (50 mL), (3-glycidyloxypropyl)trimethoxysilane (3 mmol, 0.663 mL) was added. The mixture was refluxed for 24 h at 80°C. Then, SiO₂ (1.5 g) and ethanol (5 mL) were added to the mixture and stirred at 80°C for 24 h. The mixture was cooled; the precipitate was filtered, repeatedly washed with ethanol and acetone, and dried in vacuo. Yield: 1.6 g. The organic content as determined by TGA was 20%. IR spectrum (ν, cm⁻¹): 1510 (C–O), 1631 (C=N), 3400 (O–H).

Modifying silica gel with (3-chloropropyl)trimethoxysilane (L₂) was carried out as described in [7]. To a solution of imidazole (3 mmol, 0.204 g) in toluene (50 mL), (3-chloropropyl)trimethoxysilane (3 mmol, 0.552 mL) was added. The mixture was refluxed for 24 h at 80°C. Then, SiO₂ (1.5 g) and ethanol (5 mL) were added to the mixture and stirred at 80°C for 24 h. The mixture was cooled; the precipitate was filtered, repeatedly washed with ethanol and acetone, and dried in vacuo. Yield: 1.58 g. The organic content as determined by TGA was 8.5%. IR spectrum (ν, cm⁻¹): 1631 (C=N).

Immobilization of metalloporphyrins 2 and 3 on silica gel (R₄PFeL₁, R₄PFeL₂, R₄PMnL₁, and R₄PMnL₂). To a solution of metalloporphyrin (R₄PFeCl or R₄PMnCl) in CH₂Cl₂, L₁ or L₂ was added. The reaction was carried out for 24 h with continuous stirring. The reaction mixture was filtered and repeatedly washed with CH₂Cl₂ and dried for 3 h at 60°C.

Oxidation of alkanes and alkenes by hydrogen peroxide [8]. The catalytic oxidation of cyclohexene, cyclooctene, cyclohexane, and hexane by hydrogen peroxide was carried out in glass reactors at a high stir-

ring speed, which released diffuse limitations, at a fixed temperature of the reaction medium (20°C). The solvent used were CH₃CN and CH₂Cl₂. The products were analyzed by GLC and mass spectrometry. The reaction was carried out as follows. Into a glass reactor, metalloporphyrin (1 μmol), either immobilized or nonimmobilized, was placed; then, CH₃CN (650 μL) and CH₂Cl₂ (350 μL) were added. Then, the cocatalyst CH₃COONH₄ (0.77 mg, 0.01 mmol) and the support (0.8 mmol) were added in sequence. Next, a reference was added: a 0.1 M solution of acetophenone in acetonitrile (23.2 μL). An oxidizing agent, namely a 0.1 M solution of hydrogen peroxide in acetonitrile (20 μL), was the last added. When immobilized metalloporphyrins were used, the reaction lasted 24 h; with unsupported metalloporphyrins, the reaction time was 1 h.

REFERENCES

1. Keppler, B., *Metal Complexes in Cancer Chemotherapy*, New York, 1993.
2. Milaeva, E. and Shpakovsky, D., *Macromol. Symp.*, 2003, vol. 204, p. 191.
3. Milgrom, L.R., *Tetrahedron*, 1983, vol. 39, p. 3895.
4. Milgrom, L.R., Jones, C.C., and Harriman, A., *J. Chem. Soc., Perkin Trans.*, 1988, vol. 1, p. 71.
5. Jones, R.D., Summerville, D.A., and Basolo, F., *J. Am. Chem. Soc.*, 1978, vol. 100, p. 4416.
6. Armatas, G.S., Salmas, C.E., Louloudi, M., et al., *Langmuir*, 2003, vol. 19, p. 3128.
7. Louloudi, M., Mitopoulou, K., Evaggelou, E., et al., *J. Mol. Catal. A: Chem.*, 2003, vol. 198, p. 231.
8. Martinez-Lorente, M.A., Battioni, P., Kleemiss, W., et al., *J. Mol. Catal. A: Chem.*, 1996, vol. 113, p. 343.
9. Edwards, L., Dolphin, D.H., Gouterman, M., and Adler, A.D., *J. Mol. Spectrosc.*, 1971, vol. 38, no. 1, p. 16.
10. Battioni, P., Renaud, J.P., Bartoli, J.F., et al., *J. Am. Chem. Soc.*, 1988, vol. 110, p. 8462.
11. Baciochi, E., Boshi, T., Galli, C., et al., *Tetrahedron*, 1997, vol. 53, no. 12, p. 4497.
12. *Metalloporphyrins in Catalytic Oxidation*, New York, 1994.
13. Doro, F.G., Lindsay, Smith, J.R., Ferreira, A.G., et al., *J. Mol. Catal. A: Chem.*, 2000, vol. 164, p. 97.
14. Vinhado, F.S., Prado-Manso, C.M.C., Sacco, H.C., and Iamamoto, Y., *Mol. Catal. A: Chem.*, 2001, vol. 174, p. 279.