Study of catalytic activity of nitro substituted ironporphyrins

Marilda das Dores Assis *, Andréa Junqueira Botelho de Melo, Osvaldo Antonio Serra, Yassuko Iamamoto

Departamento de Química, FFCLRP USP, Av Bandeirantes 3900, CEP14040-901 Ribeirão Preto, SP, Brazil

Abstract

ortho-Nitrophenyl meso-substituted ironporphyrins (FeP) and their corresponding μ-oxo dimers were studied as catalyst in the oxidation of cyclohexane by iodosylbenzene (PhIO). The cyclohexanol yield versus FeP concentration plot indicate the nature of active species. For (FeTNPP)Cl and (FeDNPP)Cl the active species is $Fe^{IV}(O)P^{+\cdot}$ (**1**). For unhindered (FeMNPP)Cl, the involvement of PFe^{IV}–O–$Fe^{IV}(O)P^{+\cdot}$ (**2**) explains the results. The catalytic activity of dimeric species (FeMNPP)$_2$O and (FeDNPP)$_2$O were surprisingly high, being as good as the monomeric ones. There is evidence of species **2** for these dimer catalysts. The oxidation reaction conditions were studied. We observed that the concentration of the catalyst, stirring method, ratio of iodosylbenzene/catalyst and presence of air can affect the cyclohexanol yields. (FeMNPP)Cl and (FeMNPP)$_2$O as catalysts can be seen as good P-450 model systems due to their stability, efficiency and selectivity toward cyclohexanol. The electron withdrawing effect of the substituents on the meso-phenyl rings of the porphyrin overwhelms the steric one in the catalytic activity, since only one *ortho*-nitro group is almost as efficient as the tetra-*ortho*-nitro substituted FeP. This work contributes to the understanding of the catalytic activities of unhindered ironporphyrins.

Keywords: Biomimetic catalyst; Cyclohexane; Cytochrome P-450 model; Ironporphyrin; Nitro substituted ironporphyrin; Oxidation

1. Introduction

The catalytic oxidation of organic compounds by molecular oxygen plays an important role in the transformation of hydrocarbon from coal, oil and natural gas into valuable chemical and fuel products. Despite the great amount of work devoted to this problem, it is far from being completely solved. There are many variables that hinder the creation of selective processes. The difficulty usually lies in the prevention of different parallel oxidation reactions which lead to a variety of by-products [1].

Enzymes in reactions are well known to have the characteristic of promoting high rates, selectivity and stereospecificity; which is difficult to achieve in simple chemical systems [2]. In the past twenty years, a great deal of work has been done to elucidate the mechanism of these enzymatic systems. A possible approach to solve these problems is to use synthetic systems as models for enzymatic activity [3]. The discovery that cytochromes P-450 are capable of catalyzing epoxidation and hydroxylation of saturated hydrocarbons has stimulated the search for simple ironporphyrin (FeP) systems which can mimic these reactions [2].

* Corresponding author. Fax. (+55-16)6338151, E-mail: MDDASSIS@BRUSP.ANSP.BR

Recent studies with P-450 model systems have used iron tetraarylporphyrins with *ortho*-substituents on the aryl ring in order to prevent ironporphyrin aggregation. These sterically hindered ironporphyrins afford higher stability with respect to oxidative degradation and generally render higher reactive and stable monomer ferryl radical $Fe^{IV}(O)P^{+ \cdot}$ (**1**) species than unhindered ones, such as the corresponding iron tetraphenylporphyrin, (FeTPP)Cl [4,5]. *Ortho*-nitrophenyl substituted ironporphyrins have been shown to be an unusual catalyst. Shilov et al. [6] reported interesting results with iron(III) tetra-*ortho*-nitrophenylporphyrin chloride, (FeTNPP)Cl, for lower alkane hydroxylation. At the same time we have done preliminary studies on the catalytic efficiency of the iron(III) mono-*ortho*-nitrophenyl, triphenylporphyrin bromide, (FeMNTPP)Br, and the corresponding μ-oxo dimer stable species [7]. We observed high yields for cyclohexane hydroxylation, with only one *ortho*-nitro group substituent in the porphyrin ring. The predominant active species in the reaction of (FeMNTPP)Br with iodosylbenzene (PhIO) were determined by EPR and UV–Vis spectroscopies as the dimeric radical, PFe^{IV}–O–$Fe^{IV}(O)P^{+ \cdot}$ (**2**) [8]. The formation of these species overwhelms the ferryl radical, **1**. We observed that mono-*ortho*-nitrophenyl substituted FeP have a strong tendency to dimerize. The role

of one *ortho*-nitro group in the dimer formation can be explained by two major factors: the electron withdrawing effect associated with the tendency to dimerize through π–π stacking interactions in analogy to what occurs with (2,3,7,8,12,13,17,18-octaethyl-5-nitroporphyrinate)zinc(II) [9].

Catalytic activity of dimeric species $(FeP)_2O$ has not been extensively studied. In this paper we report the catalytic activity of the μ-oxo dimer species of ironporphyrins compared to the monomer species of Fig. 1, the *ortho*-nitro group effect in the cyclohexane oxidation, percentage of FeP recuperation after catalyzed reactions and the systematic and detailed study of the oxidation reaction conditions.

2. Experimental

2.1. Materials

All the materials were of commercial reagent grade unless otherwise stated. Dichloromethane was distilled and stored on 4 Å molecular sieves. *N,N*-dimethylformamide (DMF) was stirred over KOH at room temperature overnight, decanted and then distilled at reduced pressure. Cyclohexane purity was determined by gas chromatographic analysis.

2.1.1. Iodosylbenzene (PhIO)

PhIO was obtained through the hydrolysis of iodosylbenzene diacetate [10]. Samples were stored in freezer and the purity was checked every six months by iodometric assay.

2.1.2. Porphyrins and ironporphyrins

The synthesis and purification of the mono-*ortho*-nitrophenyl, triphenylporphyrin (MNPP) was described previously [8]. The *cis* and *trans* mixture of di-*ortho*-nitrophenyl, diphenylporphyrin (DNPP) was obtained in the same way and eluted from the purification column as the third band. The tetra-*ortho*-nitrophenylporphyrin (TNPP) was purchased from Midcentury. The iron insertion in these porphyrins was done using
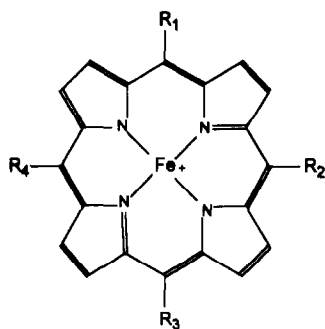
(FeMNPP)Cl $R_1 = R_2 = R_3 = Ph$ $R_4 = oNO_2Ph$

(FeDNPP)Cl (cis and trans) $R_1 = R_2 = Ph$ $R_3 = R_4 = oNO_2Ph$

(FeTNPP)Cl $R_1 = R_2 = R_3 = R_4 = oNO_2Ph$

Fig. 1. Structure of ironporphyrins.

DMF method [11]. For mono and di-*ortho*-nitro substituted FeP, the purification with neutral alumina resulted in the μ-oxo dimers, $(FeMNPP)_2O$ and $(FeDNPP)_2O$, respectively. The corresponding monomers were obtained by bubbling HCl gas through solutions of the dimers. The monomer and dimer species were characterized by UV–Vis and IR spectra in accord with previous work [8].

2.2. Oxidation reactions

The reactions were carried out in a 2 ml vial with an open top screw cap containing a silicone Teflon faced septum. In a standard reaction the vial containing the FeP (ca. 0.30 mg) and iodosylbenzene (ca. 0.50 mg) was under argon atmosphere and in an adapted dark chamber. While the mixture was being stirred at 0°C, with ultrasound (ultrasound laboratory cleaner Minison–Thornton, 40 W, 50–60 Hz), the dichloromethane (160 μl) and cyclohexane (90 μl) were added and the mixture reaction was stirred for 30 min. After the desired time, a saturated aqueous solution of sodium bisulfite (20 μl) was added to the reaction mixture, in order to quench further oxidation, and the vial was then removed from the ultrasound bath.

2.2.1. Product analysis

The product was analysed by gas-chromatography using n-octanol as internal standard. Yields were based on iodosylbenzene. Gas chromatographic analysis were performed on a CG 37-002 gas chromatograph. Nitrogen was used as the carrier gas with an hydrogen flame ionization detector. The stainless steel column (length, 1.8 m; internal diameter, 3 mm) was packed with 10% Carbowax 20M on Chromosorb WHP. The products obtained were analyzed by comparison of their retention times with those of authentic samples. All reactions were carried out in the same conditions, but in absence of FeP.

The percentage of FeP recuperation after catalyzed reactions were determined by spectrophotometry, through the absorption intensity of the Soret band. Electronic spectra were recorded on a

Hewlett-Packard 8452, Diode Array UV–Vis spectrophotometer.

3. Results and discussion

Initially, we observed that mono-*ortho*-nitrophenyl substituted ironporphyrin catalyzes the oxygen transfer from iodosylbenzene to cyclohexane, resulting in a high yield of cyclohexanol (Col) and only trace amounts of cyclohexanone. The yield of Col with $(FeTPP)Cl$ as catalyst was half or less, compared with that of $(FeMNPP)Cl$ in the same conditions.

The *ortho*-nitro group effect is shown in Table 1. We can observe that $(FeMNPP)Cl$ and $(FeMNPP)_2O$, which have one *ortho*-nitro group in each porphyrin ring, which as catalysts are as good as $(FeTNPP)Cl$, which gave the highest yields of Col and also had high catalyst recoveries. The effect of the mono-*ortho*-nitro group may act in two ways: (a) it promotes the dimer formation and consequently the catalytic active species in these systems are predominantly dimeric ferryl π-cation radical 2 [8]; (b) electron withdrawing substituents at meso-aryl position may activate the intermediate, increasing the electrophilicity of the metal-oxo entity and promoting its reactivity towards hydrocarbon [12]. Because the nitro

Table 1

Catalytic activity of ironporphyrins in the cyclohexane hydroxylation by PhIO. *ortho*-Nitro substituent effect

Reaction	FeP	COH yield [a], %	Catalyst recovery, %
1	$(FeTPP)Cl$	30	30
2	$(FeTPP)_2O$	21	23
3	$(FeMNPP)Cl$ [b]	70	70
4	$(FeMNPP)_2O$	60	60
5	$(FeDNPP)Cl$ [c]	50	42
6	$(FeDNPP)_2O$	44	65
7	$(FeTNPP)Cl$	74	99

Reactions were carried out under argon, in the dark and yields were based on PhIO, ultrasound stirring for 30 min, [FeP] ca. 1.0×10^{-3} $mol \cdot l^{-1}$ and [PhIO]/[FeP] = 5–10.

[a] Cyclohexanone product was not observed.

[b] [FeP] ca. 5.0×10^{-4} $mol \cdot l^{-1}$.

[c] 15 min of reaction.

group removes electron density from the ring and offers some steric hindrance too, the porphyrin is less susceptible to electrophilic attack and the oxidative destruction of the FeP decreases. Evidence for the latter comes from measuring the extent of FeP recovery after oxidation reaction when compared with (FeTPP)Cl (Table 1).

Generally speaking, the catalytic activity of μ-oxo dimers are only slightly lower than the corresponding monomer catalysts. They are not inactive as was envisaged previously [13]. The dimeric active intermediate species 2 can be formed directly, in addition to the monomer active species 1.

For (FeDNPP)Cl, di-*ortho*-nitro substituted FeP, the monomeric intermediate species 1 is favored due to the steric hindrance of the two nitro substituents. This catalytic species is more susceptible to oxidative destruction despite the electron-withdrawing effect of the two nitro groups, and the recuperation percentage is low when compared with other ironporphyrins. For (Fe-TNPP)Cl, the monomeric intermediate 1 is the catalytic species responsible for the high yield. This species 1 is highly reactive and stable because of the steric and electronic effects of the four *ortho*-nitro groups.

The results in Table 1 represent the best catalytic activity of each ironporphyrin. We observed that the yields of Col decrease about 15–40%, depending on the humidity of the solid FeP. Water normally increases the catalytic activity, except for the tetra-*ortho*-nitro substituted FeP, (Fe-TNPP)Cl. In this case the yield decreases from 74% to 37% when the reaction is carried out under water-saturated argon atmosphere. We observed also a higher Col yield at 15 min than at 30 min of reaction for (FeDNPP)Cl. Now we are investigating this and the role of water in the catalytic sites of FeP and intermediates involved in these oxidation reactions.

3.1. Effect of FeP concentration

It is interesting to observe that the catalytic activity follows different patterns depending on

the active intermediates involved (Figs. 2 and 3). For (FeMNPP)$_2$O, which involves species 2, the yields of Col increase sharply up to about 1.2×10^{-3} mol·l^{-1}, persisting to increase slightly up to 2.5×10^{-3} mol·l^{-1} (Fig. 2). This pattern is similar to the (FeTPP)Cl one reported by Nappa and Tolman [14] when the best concentrations were in the range of 1.0–3.0×10^{-3} mol·l^{-1}. We previously reported that for (FeTPP)Cl there is also the participation of dimeric active species 2 [15]. For (FeMNPP)Cl we observed high yields with diluted solutions. The high catalytic activity may be explained by the presence of the monomer-active species 1 in addition to the dimer active species 2 and the dilution effect combined with the nitro group effect does not favour the bimolecular destruction as observed for (FeTPP)Cl [14]. A decrease in the yield of Col from ca. 70% to ca. 45% on passing from 0.5×10^{-3} to 1.0×10^{-3} mol·l^{-1} is observed in Fig. 2 for (FeMNPP)Cl. For higher concentrations of this FeP, the dimer active species 2 is predominantly responsible for the activity. Therefore, for (FeMNPP)Cl at 2.0×10^{-3} mol·l^{-1}, the effective concentration will be almost half (ca. 1.0×10^{-3} mol·l^{-1}) of the (FeMNPP)$_2$O one and the respective yields at this concentration correspond to the intersection of the two plots in Fig. 2.

For (FeDNPP)$_2$O the dimeric 2 and monomeric 1 intermediates were detected [16] and the
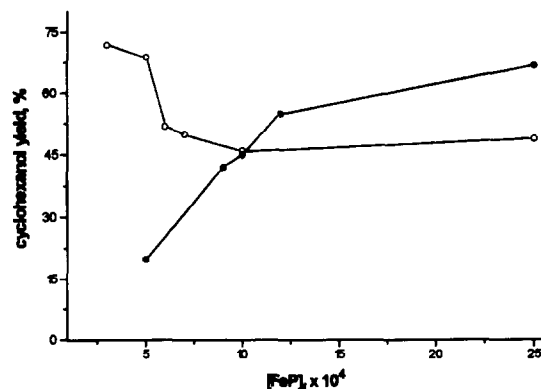

Fig. 2. Catalyst concentration effect. Reactions carried out under argon, in the dark, ultrasound stirring for 30 min, [PhIO]/ ·[FeP] = 5–10 and yields based on PhIO. ● (FeMNPP)$_2$O, ○ (FeMNPP)Cl.
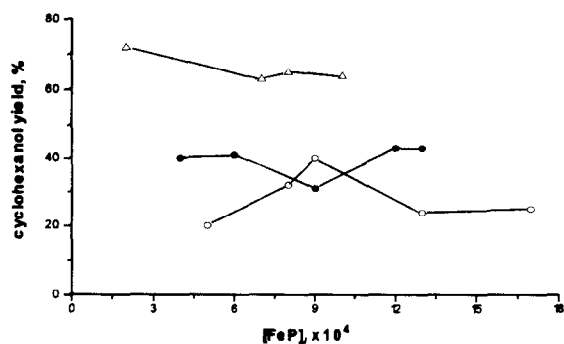
Fig. 3. Catalyst concentration effect. Reactions were carried out under argon, in the dark, ultrasound stirring for 30 min, [PhIO]/ [FeP] = 5–10 and yields based on PhIO. ● (FeDNPP)$_2$O, ○ (FeDNPP)Cl, △ (FeTNPP)Cl.

corresponding plots have an intermediate pattern (Fig. 3). There is a slight decrease in yield when concentration increases, however, higher yields are observed above ca. 1.0×10^{-3} mol·l^{-1} indicating that the dimeric active species 2 participate, as was observed for (FeMNPP)$_2$O. For (Fe-DNPP)Cl only intermediate 1 is active [16]. However, the yield of Col is low at diluted conditions as observed for (FeTPP)Cl [14] due to the destruction of the catalyst (Table 1). The plot confirms the absence of the active intermediate 2.

For (FeTNPP)Cl, which involves only species 1, the yield is almost independent of the catalyst concentration (Fig. 3).

3.2. Optimization of reactions with FeP catalysts

We selected (FeMNPP)$_2$O to study the reaction conditions because we are interested in catalytic activities of dimers, species previously considered inactive. The same effects were observed with other FeP studied in this work unless otherwise stated. A special technique in small scale was developed and the concentration ratio of PhIO and FeP, the stirring method, atmosphere, temperature and light effects were investigated (Table 2).

We observed a significant increase in the Col yield when ultrasound was used as stirring method. Ultrasound is more effective for mixing and homogenization of the reactants, promoting rate enhancements in reactions in which active

radical intermediates are produced chemically, subsequent to the cavitation [17]. The presence of the solid particles of PhIO are responsible for the inhomogeneities and may act as cavitation nuclei. The intermediate dimer radical 2, responsible for the high yield of Col is favored by ultrasound, however without changing the reaction mechanism once the selectivity is not affected. For (FeTNPP)Cl, which does not dimerize, the catalytic activity was less affected by ultrasound.

The presence of dioxygen is responsible for a decrease in Col yield, and cyclohexanone was not detected. The ultrasound effect promotes a radical-forming process which, in presence of dioxygen, could produce cyclohexanone. However, in this condition, an attack at the α-carbon atom is favored, producing cyclohexyloxy radicals. These radicals are in equilibrium with open-chain aldehyde radicals, which are easily oxidized to carboxylic acids [1d][18]. We observed a higher yield of Col in reactions carried out at 0°C when compared to those carried out at room temperature (ca. 25°C). At lower temperature, the porphyrin degradation is lower. With (FeTNPP)Cl, which is resistant to the bimolecular destruction, the yield of Col remained high (71%) at 25°C. The reactions were carried out protected from light, in a dark chamber, to prevent photo-oxidation of the porphyrin ligand followed by fission of the macrocycle and demetalation [19]. However, the presence of light in the absence of oxygen did not affect the yield of Col.

The yield of Col is dependent on the [PhIO]/ [FeP] ratio. For ratios over 10, the Col yields

Table 2
Stirring method, atmosphere, temperature and light effects in the catalytic activity of (FeMNPP)$_2$O in cyclohexane hydroxylation

Agitation	Atmosphere	Temperature, °C	Light	Col yield, %
magnetic	argon	0	no	45
ultrasound	argon	0	no	60
ultrasound	air	0	no	22
ultrasound	argon	25	no	30
ultrasound	argon	0	yes	60

Reactions were carried out for 30 min, [FeP] ca. 1.0×10^{-3} mol·l^{-1}, [PhIO]/[FeP] = 5–10 and the yields were based on PhIO.

Table 3
Influence of the [PhIO]/[FeP] ratios on the cyclohexanol yield (%).

FeP	[PhIO]/[FeP]		
	5–10	20	100
(FeMNPP)Cl	70	46	23
(FeMNPP)$_2$O	60	39	26
(FeDNPP)Cl	50	26	14
(FeDNPP)$_2$O	44	24	17
(FeTNPP)Cl	74	70	46 [a]

Reactions were carried out for 30 min, [FeP] ca. 1.0×10^{-3} mol·l^{-1}, [PhIO]/[FeP] = 5–10 and the yields were based on PhIO.
[a] 5% of cyclohexanone.

decrease (Table 3) because the competitive reactions of PhIO behaving as substrate are favored, leading to PhIO$_2$ and oxidative destruction of FeP [14,20]. Almost complete destruction in the ratio of 100 was observed except for (FeTNPP)Cl, which shows a complete recovery. In this case, the competitive reaction of PhIO to PhIO$_2$ was responsible for the drop in the yield.

Dimerization has been regarded as being unfavorable in model P-450 reactions, because they lead to a catalyst deactivation [5]. However, evidence for almost the same catalytic activity of (FeTPP)$_2$O, when compared to the corresponding monomer has been reported for the epoxidation of cyclohexene, in 43% and 55% yields, respectively [21]. We were surprised by the high catalytic activities for cyclohexane hydroxylation of mono-ortho-nitrophenyl substituted ironporphyrins dimers and we conclude that it is due to the presence of the dimeric radical 2 as active species in these systems.

The high selectivity towards cyclohexanol, relatively high efficiency and stability for (FeMNPP)Cl and (FeMNPP)$_2$O have indicated that they are good P-450 model systems. These results indicate that the electron withdrawing effect of the substituents on the meso-phenyl rings of the porphyrin overwhelms the steric one in the catalytic activity, since only one ortho-nitro group is almost as efficient as that of tetra-ortho-nitro substituted FeP. In this way, this work contributes to the understanding of unhindered ironporphyrin catalytic activities.

Acknowledgements

References

[1] (a) R.A. Sheldon and J.K. Kochi, Metal-Catalyzed Oxidations of Organic Compounds, Academic Press, New York, (1981); (b) A.E. Shilov, Activation of Saturated Hydrocarbons by Transition Metal Complexes, D. Reidel Publishing Company, Dordrecht, (1984); (c) P.E. Ellis, Jr. and J.E. Lyons, Coord. Chem. Rev. 105 (1990) 181; (d) U. Schuchardt, W.A. Carvalho and E.V. Spinacé, Synlett, 10 (1993) 713.

[2] (a) D. Mansuy, P. Battioni and J.P. Battioni, Eur. J. Biochem., 184 (1989) 267; (b) D. Mansuy, Coord. Chem. Rev., 125 (1993) 129; (c) B. Meunier, Chem. Rev., 92 (1992) 1411; (d) M.J. Gunter and T. Turner, Coord. Chem. Rev., 108 (1991) 115.

[3] J.H. Dawson and M. Sono, Chem. Rev., 87 (1987) 1255.

[4] (a) T.G. Traylor, Pure Appl. Chem., 63 (1991) 265; (b) D. Mansuy, Pure Appl. Chem., 62 (1990) 741; (c) P.S.Traylor, D. Dolphin and T.G. Traylor, J. Chem. Soc., Chem. Commun., (1984) 279.

[5] (a) T.C. Bruice, J. Am. Chem. Soc., 110 (1988) 158; (b) A.J. Castellino and T.C. Bruice, J. Am. Chem. Soc., 110 (1988) 7512; (c) S. Tsuchiya and M. Sono, Chem. Lett., 263 (1989); (d) S.Tsuchiya, J. Chem. Soc., Chem. Commun., 716 (1991); (e) T.G. Traylor, K.W. Hill, W.P.Fann, S.Tsuchiya and B.E. Dunlap, J. Am. Chem. Soc., 114 (1992) 1308; (f) T.G. Traylor and S.Tsuchiya, Inorg. Chem. 26 (1987) 1338; (g) J.Renaud, P. Battioni, J.F. Bartoli and D. Mansuy.J. Chem. Soc., Chem. Commun., (1985) 888.

[6] (a) A. Khenkin, O. Koifman, A. Semeikin, A. Shilov and A. Shteinman, Tetrahedron Lett., 26 (1985) 4247; (b) V.S. Belova, A.M. Khenkin and A. Shilov, Kinet. Catal., 28 (1987) 1016.

[7] (a) M.D. Assis, Ph.D. Thesis, University of São Paulo, Brazil, (1988); (b) M.D. Assis, O.A. Serra, Y. Iamamoto, O. Baffa and O.R. Nascimento, Ciênc. Cult. (São Paulo), 38 (1986) 486.

[8] M.D. Assis, O.A. Serra, Y. Iamamoto and O.R. Nascimento, Inorg. Chim. Acta., 187 (1991) 107.

[9] (a) W.S. Caughey, H. Eberspaecher, W.S. Fuchsman and S. McCoy, Ann. NY Acad. Sci., 153 (1969) 722; (b) M.O. Senge, C.W. Eigenbrot, T.D. Brennan, J. Shusta, W.R. Sheid and K.M. Smith, Inorg. Chem., 32 (1993) 3134.

[10] J.G. Sharefkin and H. Saltzman, Org. Synth., 5 (1963) 658.

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

[12] C.K. Chang and F. Ebina, J. Chem. Soc., Chem. Commun., (1981) 778.
[13] (a) M.M. Williamson, C.M. Prosser-McCartha, S. Mukundan, Jr. and C.L. Hill, Inorg. Chem., 27 (1988) 1061 and refs. therein; (b) D. Ostovic and T.C. Bruice, J. Am. Chem. Soc., 111 (1989) 6511.
[14] M.J. Nappa and C.A. Tolman, Inorg. Chem. 24 (1985) 4711.
[15] Y. Iamamoto, M.D. Assis, O. Baffa, S. Nakagaki and O.R. Nascimento, J. Inorg. Biochem., 52 (1993) 191.
[16] A.J.B. Melo, K.J. Ciuffi, O. Baffa Filho, M.D. Assis, Y. Iamamoto and O.R. Nascimento, Encontro em Catálise Homogênea e Heterogênea, IQ-USP, São Paulo, 1993.

[17] (a) P. Riez, D. Berdahl and C.L. Christman, Environmental Health Perspectives, 64 (1985) 233; (b) J.C.S. Barbosa and A.A. Serra, Quím. Nova, 15 (1992) 302.
[18] (a) A.L J. Beckwith and B.P. Hay, J. Am. Chem. Soc., 111 (1989) 2674; (b) ref. 1(a) p. 343.
[19] J.W. Buchler in D. Dolphin (Ed.), The Porphyrins, Academic Press, New York, 1978, Vol. 1, p. 417.
[20] D. Mansuy, N. J. Chim., 9 (1985) 711.
[21] (a) M.J. Gunter and P. Turner, J. Mol. Catal., 66 (1991) 121; (b) J.T. Groves, T.E. Nemo and R.S. Myers, J. Am. Chem. Soc., 101 (1979) 1032.