

Comparative study of catalytic activity of some biomimetic models of cytochrome P450 in oxidation of olefins with tetra-*n*-butylammonium periodate: Electron-rich Mn-porphyrins versus the electron-deficient ones

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ABSTRACT

Oxidation of a wide range of cyclic and acyclic olefins with tetra-*n*-butylammonium periodate shows different orders of catalytic activity for a series of electron-rich and electron-deficient Mn-porphyrins in oxidation of various alkenes. While the Mn(III) complex of *meso*-tetra(4-thiomethoxyphenyl)porphyrin, MnT(4-SCH₃P)P(OAc), has the highest activity among the series, the β tetra-brominated derivative shows the lowest catalytic efficiency for the oxidation of the used olefins with the exception of *cis*- and *trans*-stilbene. The results clearly show that the electron-withdrawing effects of *meso*- and β-substituents may increase or decrease the catalytic activity of Mn-porphyrins in the case of different olefins.

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In recent years, different biomimetic approaches to cytochrome P450 activity have been achieved with metalloporphyrins and various oxidants [1]. Synthetic manganese(III) porphyrins have been used as catalysts for oxidation of organic compounds by various oxygen donors. High catalytic activities have been observed, mainly with catalysts bearing electron-withdrawing substituents at the periphery of the porphyrin ring [2]. The introduction of bulky substituents at the *ortho* positions of *meso*-tetraarylporphyrins and peripheral substitution of the aromatic macrocycle with electron-withdrawing groups are among the main strategies utilized to improve the stability of metalloporphyrin-based catalysts [3]. Although the oxidative degradation of catalyst is an important factor influencing the catalytic efficiency of the metalloporphyrins, there are many reports showing higher or comparable catalytic activity of the electron-rich Mn-porphyrins (Mn-pors) compared with electron-deficient ones [2d,4]. In the present work, the oxidation of a wide range of olefins with tetra-*n*-butylammonium periodate (TBAP) catalyzed by a series of electron-rich and electron-deficient Mn(III) *meso*-tetraarylporphyrins (Fig. 1) has been studied in a comparative manner. It should be noted that MnT(4-OCH₃P)P(OAc) and MnT(4-NO₂P)P(OAc) have been previously utilized by Mohajer et al. in oxidation of styrene and α-methyl styrene [4b]. For a systematic study, in the present work the catalytic activity of these metalloporphyrins for oxidation of different olefins, their stability towards oxidative degradation and the nature of active intermediate have been studied and

compared with the other metalloporphyrins. Indeed, the results of this work indicate that the dependence of catalytic activity of Mn-pors on the electronic effects of the peripheral substituents at the *meso* and β positions change when going from an olefin to another one so that the electron-rich Mn-pors may have similar, higher or lower catalytic activities compared to the electron-rich ones.

Meso-tetra(4-methoxyphenyl)porphyrin, H₂T(4-OCH₃P)P [5a], *meso*-tetra(4-thiomethoxyphenyl)porphyrin, H₂T(4-SCH₃P)P [5a,b], *meso*-tetra(4-nitrophenyl)porphyrin, H₂T(4-NO₂P)P [5c,d] and *meso*-tetra(2-nitrophenyl)porphyrin, H₂T(2-NO₂P)P [5a,b] (Fig. 1) and β-tetrabromo-*meso*-tetra(4-thiomethoxyphenyl)porphyrin [5e], H₂T(4-SCH₃P)PBr₄, were synthesized, characterized, purified and metallated [5f] according to the literature methods (see S1) [5f].

The changes in the UV–vis spectra of a solution of MnT(4-NO₂P)P(OAc) in dichloromethane in the presence of ImH and cyclohexene after the addition of TBAP have been shown in Fig. 2. The rate of degradation of metalloporphyrin is significant at the first 10 min of reaction but decreases after this point so that the absorption due to the Soret band of MnT(4-NO₂P)P(OAc) remains nearly unchanged up to about 90 min.

The extent of degradation of Mn-pors has been measured on the basis of the change in the absorbance at the λ_{max} of the metalloporphyrins (Table 1) and increases in the order MnT(2-NO₂P)P(OAc) ≪ MnT(4-SCH₃P)P(OAc) ~ MnT(4-SCH₃P)PBr₄(OAc) < MnT(4-OCH₃P)P(OAc) < MnT(4-NO₂P)P(OAc). It is observed that with the exception of MnT(2-NO₂P)P(OAc), there is no clear correlation between the stability of the catalysts and the electronic properties of the groups at the periphery of porphyrins. Interestingly, MnT(4-

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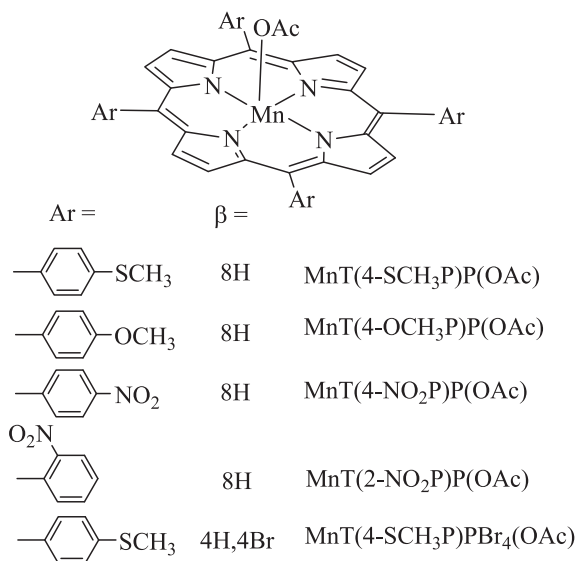


Fig. 1. The Mn-pors used in this study.

NO₂P)P(OAc) is less stable than MnT(4-OCH₃P)P(OAc), in spite of the presence of electron-withdrawing —NO₂ groups in the former compared with the electron-donor substituents (—OCH₃) of the latter [6]. The positions with highest electron densities i.e. the α and *meso* ones are expected to be involved in oxidative degradation of metalloporphyrins [7]. The introduction of four NO₂ groups at the *para*-positions of the Mn(III) complex of *meso*-tetraphenylporphyrin, Mn(TPP)(OAc), is expected to decrease the total electron density on the porphyrin core of MnT(4-NO₂P)P(OAc) with respect to that of Mn(TPP)(OAc). Although there is no proper explanation for this observation but apparently, the electron-withdrawing effects of the *para*-NO₂ groups cause an increase in the electron densities at the α and *meso* positions by resonance structures leading to readily oxidative degradation of MnT(4-NO₂P)P(OAc). On the other hand, the competitive oxidation of *cis*- and *trans*-stilbene with TBAP catalyzed by MnT(4-NO₂P)P(OAc) strongly suggests the exclusive involvement of a high valent Mn-oxo species as the active oxidant (*vide infra*). The greater oxidizing ability of a high valent Mn-oxo species as the main active intermediate in the case of MnT(4-NO₂P)P(OAc) relative to Mn(III)(porphyrin)(ImH)(IO₄)/Mn-Oxo species for the other Mn-pors may also explain the enhanced oxidative degradation of MnT(4-NO₂P)P(OAc) with respect to the other Mn-pors [8].

The β tetra-brominated counterpart of MnT(4-SCH₃P)P(OAc), MnT(4-SCH₃P)PBr₄(OAc) has the same stability as the non-brominated

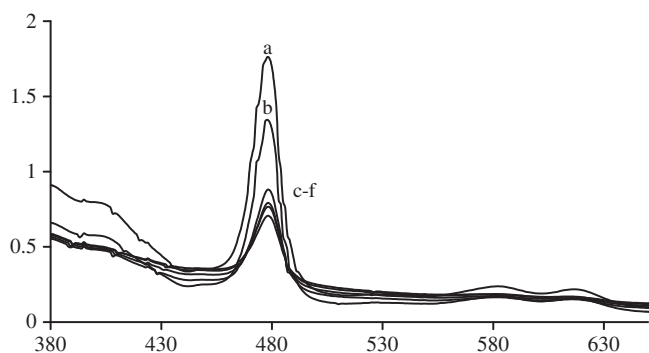


Fig. 2. The changes in the UV-vis spectra of a solution of Mn(4-NO₂P)P(OAc)/ImH/cyclohexene in 1:10:83 molar ratios (a, λ_{\max} = 479 nm) in dichloromethane (a), in the interval time of 5, 10, 30, 60 and 90 min after the addition of TBAP (b–f).

Table 1

Degradation of the Mn-pors in the presence of cyclohexene, ImH and TBAP in dichloromethane at room temperature.^a

Mn-pors	Degradation (%) ^b	Time (min)
MnT(4-SCH ₃ P)P(OAc)	31.5	90
MnT(4-OCH ₃ P)P(OAc)	40.0	90
MnT(4-NO ₂ P)P(OAc)	47.0	90
MnT(2-NO ₂ P)P(OAc)	8.5	90
MnT(4-SCH ₃ P)PBr ₄ (OAc)	33.5	90

^a The molar ratios of catalyst:ImH:cyclohexene:oxidant are 1:10:83:167 (see S1).

^b On the basis of the absorbance changes (ΔA) at the λ_{\max} of the metalloporphyrins ($\Delta A/A$).

compound suggesting that the substitution of β positions of MnT(4-SCH₃P)P(OAc) with four bromine atoms has little or no effect on its stability towards oxidative degradation.

Competitive epoxidation of *cis*- and *trans*-stilbene with various oxidants has been used as an indirect method to elucidate the nature of active oxidant in oxidation of olefins catalyzed by metalloporphyrins [4b,9]. The results of catalytic oxidation of *cis*- and *trans*-stilbene with TBAP have been summarized in Table 2. The ratios of *cis/trans* stilbene oxide are in the range of 1.6 to 4.7 for the used Mn-pors. A ratio of ca. 1 strongly suggests [9] that a high valent Mn-oxo species is involved in the reaction catalyzed by MnT(4-NO₂P)P(OAc). In the case of the other Mn-pors the observed ratios of *cis/trans*-stilbene oxide (3.1 to 4.7) show the presence of an equilibrium between a six coordinate Mn(III) (porphyrin)(ImH)(IO₄) and the corresponding high valent Mn-oxo species as the active oxidizing species [4a]. However, the steric hindrance due to the presence of bulky —2-NO₂ groups at *ortho* positions are also involved in the observed *cis/trans*-stilbene oxide ratio in the reaction catalyzed by MnT(2-NO₂P)P(OAc).

The results of oxidation of different olefins (see S1) were shown in Tables S1 to S7 and Table 3. Accordingly, the following patterns of catalytic activity have been found for the Mn-pors in oxidation of various alkenes:

The order of catalytic activity of Mn-pors for oxidation of cyclohexene is as follows: MnT(4-SCH₃P)P(OAc) > MnT(2-NO₂P)P(OAc) ~ MnT(4-OCH₃P)P(OAc) > MnT(4-NO₂P)P(OAc) \gg MnT(4-SCH₃P)PBr₄(OAc) (Table S1). The product selectivity is similar for the Mn-pors, but the catalytic efficiency of MnT(4-SCH₃P)P(OAc) is larger than the others. MnT(4-SCH₃P)PBr₄(OAc) shows the lowest catalytic activity of the series. Interestingly, MnT(2-NO₂P)P(OAc) and MnT(4-OCH₃P)P(OAc) show very similar activities for the oxidation of cyclohexene, in spite of the significantly enhanced oxidative stability of the former compared with the latter (Table 1). This observation cannot be simply attributed to the steric hindrance of *ortho* —NO₂ groups of MnT(2-NO₂P)P(OAc), since in the case of more bulky olefins such as styrene and *trans*-stilbene the two catalysts show similar activities (*vide infra*).

In oxidation of styrene the catalytic activity decreases in the order MnT(4-SCH₃P)P(OAc) ~ MnT(2-NO₂P)P(OAc) > MnT(4-OCH₃P)P(OAc) > MnT(4-SCH₃P)PBr₄(OAc) ~ MnT(4-NO₂P)P(OAc) (Table S2). The order of catalytic activity for the first three Mn-pors is nearly the same as

Table 2

Competitive oxidation of *cis*- and *trans*-stilbene with TBAP in dichloromethane catalyzed by various Mn-pors.^{a,b}

Mn-pors	<i>Cis</i> -epoxide (%)	<i>Trans</i> -epoxide (%)	<i>cis/trans</i>
MnT(4-SCH ₃ P)P(OAc)	10.2	3.2	3.2
MnT(4-OCH ₃ P)P(OAc)	9.4	3.0	3.1
MnT(4-NO ₂ P)P(OAc)	5.6	3.5	1.6
MnT(2-NO ₂ P)P(OAc)	10.2	2.5	4.1
MnT(4-SCH ₃ P)PBr ₄ (OAc)	10.6	2.2	4.7

^a The molar ratios for alkene:oxidant:ImH:catalyst are:(500,500):167:10:1 (see S1).

^b Analyzed by ¹H NMR for a reaction time of 4 h.

Table 3
Oxidation of *cis*-stilbene with TBAP in dichloromethane catalyzed by various Mn-pors.^a

Mn-pors	Conversion (%) ^b	Selectivity (%)	<i>Cis-trans</i> rearrangement
MnT(4-SCH ₃ P)P(OAc)	58.0	86.5 ^c , 13.5 ^d	13.5
MnT(4-OCH ₃ P)P(OAc)	51.0	84.2 ^c , 15.8 ^d	15.8
MnT(4-NO ₂ P)P(OAc)	21.2	97.0 ^c , 3.0 ^d	3.3
MnT(2-NO ₂ P)P(OAc)	23.0	95.5 ^c , 4.5 ^d	4.5
MnT(4-SCH ₃ P)PBr ₄ (OAc)	46.2	75.0 ^c , 25.0 ^d	24.0

^a The molar ratios for Mn-por:imidazole:alkene:oxidant are 1:10:83:167.

^b Analyzed by ¹H NMR.

^c *Cis*-stilbene oxide and

^d *trans*-stilbene oxide.

described for cyclohexene. However, very similar activity has been observed for MnT(4-SCH₃P)PBr₄(OAc) and MnT(4-NO₂P)P(OAc).

The following order of catalytic efficiency was observed in the case of α -Methylstyrene: MnT(4-SCH₃P)P(OAc) > MnT(4-OCH₃P)P(OAc) ~ MnT(2-NO₂P)P(OAc) > MnT(4-NO₂P)P(OAc) ~ MnT(4-SCH₃P)PBr₄(OAc) (Table S3). The change in the position of MnT(2-NO₂P)P(OAc) in the series compared with that in the case of styrene seems to be due to the increased steric hindrance at the double bond of α -methylstyrene. It should be noted that the substitution of bulky substituents at the *ortho* position of aryl groups limits the range of porphyrin-aryl group dihedral angle [10] and leads to an increase in the steric hindrance at the reaction center of the active oxidant [4a]. In comparison with styrene, there is no difference between the efficiency of MnT(4-SCH₃P)P(OAc) and (4-OCH₃P)P(OAc) for the oxidation of α -methylstyrene.

Oxidation of indene resulted in the following order: MnT(4-SCH₃P)P(OAc) \geq MnT(4-OCH₃P)P(OAc) ~ MnT(2-NO₂P)P(OAc) \gg MnT(4-NO₂P)P(OAc) ~ MnT(4-SCH₃P)PBr₄(OAc) (Table S4). The catalytic activity of MnT(4-SCH₃P)P(OAc), MnT(4-OCH₃P)P(OAc) and MnT(2-NO₂P)P(OAc) for the oxidation of indene is nearly the same. The position of MnT(4-OCH₃P)P(OAc) in the series of catalytic activity is in contrast to that observed in the case of cyclohexene, styrene and 3-chloro-2-methyl-1-propene. However, it seems that the substituent dependence of the catalytic activity of the Mn-pors for the oxidation of indene is less than that observed in the case of other olefins.

The order observed in oxidation of 1-hexene is as follows: MnT(4-SCH₃P)P(OAc) ~ MnT(2-NO₂P)P(OAc) \gg MnT(4-NO₂P)P(OAc) ~ MnT(4-OCH₃P)P(OAc) > MnT(4-SCH₃P)PBr₄(OAc) (Table S5). In oxidation of the terminal olefin, 1-hexene, MnT(4-SCH₃P)P(OAc) and MnT(2-NO₂P)P(OAc) show similar catalytic activities. However, these two Mn-pors are about 2.5 times more efficient than the other ones in this reaction (see Table S5).

Catalytic efficiency of Mn-pors in oxidation of 3-chloro-2-methyl-1-propene follows the following order: MnT(4-SCH₃P)P(OAc) \geq MnT(2-NO₂P)P(OAc) > MnT(4-OCH₃P)P(OAc) > MnT(4-NO₂P)P(OAc) ~ MnT(4-SCH₃P)PBr₄(OAc) (Table S6). The order is as that observed in the case of 1-hexene, but here MnT(4-OCH₃P)P(OAc) is about 2 times more efficient than MnT(4-NO₂P)P(OAc).

Relative catalytic activity of Mn-pors for oxidation of *trans*-stilbene is as follows: MnT(4-SCH₃P)P(OAc) \geq MnT(4-SCH₃P)PBr₄(OAc) ~ MnT(2-NO₂P)P(OAc) > MnT(4-OCH₃P)P(OAc) ~ MnT(4-NO₂P)P(OAc) (Table S7). The activity of Mn-pors for the oxidation of *trans*-stilbene follows a pattern different from that observed for the other olefins. Here the efficiency of MnT(4-SCH₃P)PBr₄(OAc) is very similar to MnT(4-SCH₃P)P(OAc) and MnT(2-NO₂P)P(OAc).

Oxidation of *cis*-stilbene, on the other hand, gives the following order of activity for Mn-pors: MnT(4-SCH₃P)P(OAc) > MnT(4-OCH₃P)P(OAc) > MnT(4-SCH₃P)PBr₄(OAc) \gg MnT(2-NO₂P)P(OAc) ~ MnT(4-NO₂P)P(OAc) (Table 3). Oxidation of *cis*-stilbene with TBAP in the presence of the Mn-pors gives the *cis*-epoxide as the major product and *trans*-epoxide as the minor one. Interestingly, MnT(2-NO₂P)P(OAc) and MnT(4-NO₂P)P(OAc) show the lowest catalytic activity and

cis to *trans* isomerisation among the Mn-pors. The low degree of isomerisation observed in the presence of MnT(2-NO₂P)P(OAc) may be attributed to the steric hindrance caused by the introduction of bulky groups at the *ortho* position of aryl substituents which prevent the rotation around the C—C bond in the intermediate [9]. However, in the case of MnT(4-NO₂P)P(OAc), the electronic effects rather than the steric ones seem to be involved in the observed low extent of *cis-trans* isomerisation.

It is observed that the relative catalytic activity of a series of electron-rich and electron-deficient Mn-pors cannot be simply explained in oxidation of different olefins. In other words, the observed pattern of catalytic activity of the used Mn-pors in oxidation of a given olefin cannot be generalized to the rest. In contrast to the previous reports on the oxidation of olefins with TBAP catalyzed by electron-rich and electron-deficient Mn-pors [7,9], the results of this study indicate that the relative catalytic activity of the two classes of Mn-pors changes when going from an olefin to another one.

In summary, in spite of the complex order of catalytic activity for a series of electron-rich and electron-deficient Mn-pors in oxidation of various alkenes, MnT(4-SCH₃P)P(OAc) shows the highest catalytic activity for the oxidation of a wide range of cyclic and acyclic olefins. While the substitution of β positions of MnT(4-SCH₃P)P(OAc) with four bromine atoms has little or no effect on the oxidative stability of this Mn-porphyrin, the efficiency of the catalyst has been significantly decreased for the oxidation of olefins. However, the observed order of catalytic activity for the used Mn-pors in the oxidation of various olefins cannot be simply explained by the steric and electronic effects of the substituents attached to the periphery of porphyrins as well the olefin double bond. While MnT(2-NO₂P)P(OAc) is the most stable catalyst of the series, MnT(4-NO₂P)P(OAc) shows unusual instability towards oxidation with the active oxidant.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at doi:10.1016/j.inoche.2011.03.057.

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