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Epoxidation and Hydroxylation Reactions Catalyzed by the Manganese and Iron Complexes of 5,10,15,20-tetrakis(2,6-dimethoxyphenyl)porphyrin.

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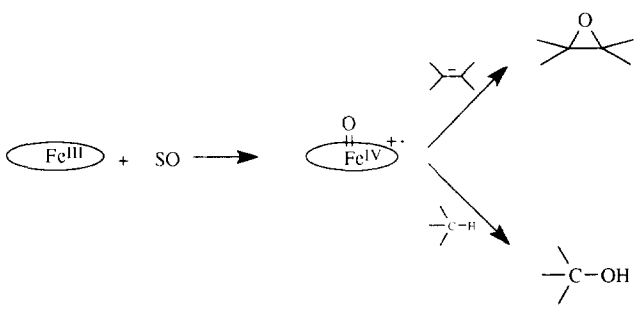
Abstract: Manganese(III) and iron(III) complexes of 5,10,15,20-tetrakis-(2,6-dimethoxyphenyl)porphyrin (H_2TDMeOPP) were tested as catalysts in the epoxidation of alkenes and in the hydroxylation of adamantane with H_2O_2 (in the presence of imidazole) or PhIO as oxidants. The behavior of the two catalysts is compared with that of the corresponding manganese(III) and iron(III) complexes of 5,10,15,20-tetrakis-(2,6-dichlorophenyl)porphyrin and 5,10,15,20-tetraphenylporphyrin, and the observed differences ascribed to the electron donating effect of the methoxy groups.

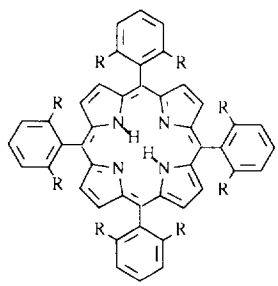
During the last fifteen years an ever growing attention has been devoted to the catalytic properties of Fe(III) and Mn(III) tetraphenylporphyrins in oxygenation reactions, such as the epoxidation of alkenes and the hydroxylation of alkanes.[1] In these reactions an oxygen donor (SO in Scheme 1), e.g. H_2O_2, iodosylbenzene, ClO^-, peracids or hydroperoxides, converts the metalloporphyrin into a metallo oxo-complex, which is the actual oxidizing species.



Scheme 1

One of the currently investigated features of these reactions concerns the relationship between the structure of the porphyrin ring and the catalytic properties of the metalloporphyrin. Most of these studies have been focused on porphyrins containing electron withdrawing substituents on the pyrrole and/or *meso*-phenyl rings, as

they appear to be the most efficient catalytic systems.[2] Less information is instead available on the catalytic properties of metalloporphyrins substituted in the phenyl ring by electron-donating substituents. In this paper we now report on the epoxidation and hydroxylation reactions catalyzed by the iron and manganese complexes of a porphyrin substituted in the 2 and 6 positions of the phenyl rings by the strong electron donating OCH_3 group, namely, the 5,10,15,20-tetrakis-(2,6-dimethoxyphenyl)porphyrin (H_2TDMeOPP) (Chart 1). This porphyrin attracted our attention also because it can be easily prepared in a relatively large scale and purified by simple crystallization[3].



H_2TDMeOPP: R = OCH_3
H_2TDCPP: R = Cl
H_2TPP: R = H

Chart 1

Results and discussion

The manganese and iron complexes of H_2TDMeOPP, Mn^{III}TDMeOPPCl and Fe^{III}TDMeOPPCl, respectively, have been prepared and their catalytic efficiency in the epoxidation reaction of cyclooctene has been studied with H_2O_2 or PhIO as the oxygen donors. With the former oxygen donor, the solvent was a CH_2Cl_2-MeCN mixture; with the latter it was neat CH_2Cl_2. The reactions of the Mn porphyrin/H_2O_2 system were always carried out in the presence of imidazole (25-fold in excess with respect to the porphyrin). The presence of imidazole was necessary to favour the heterolytic cleavage of the O-O bond of H_2O_2 and to stabilize the P-Mn(V)=O complex. Variable substrate : oxidant : catalyst ratios were used, and the results are reported in Table 1. They are accompanied by the results of the same reactions induced by the unsubstituted tetraphenylporphyrins (Mn^{III}TPPCl) and (Fe^{III}TPPCl), and also by the Mn(III) and Fe(III) complexes of tetrakis-(2,6-dichlorophenyl)porphyrin (i.e. Mn^{III}TDCPPCl and Fe^{III}TDCPPCl), which are among the most efficient and most widely used catalysts.[4]

It can be noted that with H_2O_2 as the oxygen donor, Mn^{III}TDMeOPPCl results to be a very efficient catalyst, with a yield of epoxide which becomes quantitative when a 10-fold excess of H_2O_2 with respect to the substrate is used (entry 2). Interestingly, Mn^{III}TDMeOPPCl appears to be a more efficient catalyst than both Mn^{III}TDCPPCl and Mn^{III}TPPCl (entry 1 *vs.* entries 3 and 4).

Mn^{III}TDMeOPPCl remains a very efficient catalyst also when PhIO is the oxygen donor. In this case the yield of epoxide is comparable with that obtained with Mn^{III}TDCPPCl, but higher than that observed with Mn^{III}TPPCl (entry 8 *vs.* entries 9 and 10). It is also worth noting that the new manganese dimethoxyphenylporphyrin is a very efficient catalyst even with an oxidant/substrate molar ratio as low as 2 (entry 7).

Table 1. Epoxidation of Cyclooctene[a]

Entry	Ox.	Porphyrin	Ox./Subs./Por.	Yield(%)[b]	Bleaching(%)[c]	Turnover[g]
1	H_2O_2	MnTDMeOPPCl	200/40/1	78		31
2			400/40/1	100		40
3		MnTDCPPCl	200/40/1	36[d,e]		-
4		MnTPPCl	200/40/1	15		6
5		FeTDMeOPPCl	200/40/1	15		6
6		FeTDCPPCl	200/40/1	21		8
7	PhIO	MnTDMeOPPCl	100/50/1	80		40
8			20/400/1	87[f]	3.1	17
9		MnTDCPPCl	20/400/1	87[f]	2.6	17
10		MnTPPCl	20/400/1	73[f]	10	15
11		FeTDMeOPPCl	100/50/1	77		39
12			20/400/1	50[f]	28	10
13		FeTDCPPCl	20/400/1	77[f]	1.0	15
14		FeTPPCl	20/400/1	62[f]	20	12

a) The reactions were performed in MeCN-CH_2Cl_2 with H_2O_2, while in CH_2Cl_2 with PhIO.
b) Yields are referred to the substrate (evaluated by GLC).
c) The bleaching of the porphyrin was evaluated by the decrease in Soret absorbance.
d) The substrate was completely converted, but overoxidation of cyclooctene oxide occurs.
e) Ref. 4a reports that the epoxide is obtained in 91% yield.
f) Yield referred toward the oxidant.
g) Calculated as number of oxidative cycles per molecule of catalyst

The corresponding iron complex, Fe^{III}TDMeOPPCl, is a less valuable epoxidation catalyst than the corresponding manganese complex. The decrease in the catalytic efficiency is larger when H_2O_2 is the oxidant (compare entry 1 with entry 5) than in the reactions promoted by PhIO (compare entry 8 with entry 12). Fe^{III}TDMeOPPCl is also slightly less efficient than both Fe^{III}TDCPPCl and Fe^{III}TPPCl.
The stability of the metalloporphyrins was tested in some oxidations promoted by PhIO by determining the decrease in the Soret absorbance. Interestingly, it turned out that the stability of Mn^{III}TDMeOPPCl is very close to that of Mn^{III}TDCPPCl and significantly higher than that of Mn^{III}TPPCl. Fe^{III}TDMeOPPCl is instead much less stable than Fe^{III}TDCPPCl.

To acquire information on the stereochemical behaviour of these porphyrins, the epoxidations of *cis*-stilbene catalyzed by Fe^{III}TDMeOPPCl or by Mn^{III}TDMeOPPCl was investigated. The *cis*-epoxide was the *only* product from reaction with Fe^{III}TDMeOPPCl and PhIO, in line with previous results concerning epoxidations catalyzed by other Fe(III)porphyrins.[5] The *cis*-epoxide was the *main* product (9:1 *cis*:*trans*) in the reaction of *cis*-stilbene catalysed by Mn^{III}TDMeOPPCl and H_2O_2 in the presence of imidazole. The observed stereoselectivity is certainly good but somewhat smaller than that (*cis*:*trans*-epoxide, *ca* 30:1) observed with Mn^{III}TDCPPCl under comparable conditions.[4a] Very interestingly, Mn^{III}TDMeOPPCl exibited a good stereoselectivity (*cis*:*trans*-epoxide, 5.4:1) also in the absence of imidazole (PhIO, oxygen donor), which contrasts with the behaviour of Mn^{III}TPPCl under the same conditions, where more *trans* than *cis*-epoxide was produced.[6]

Poor stereoselectivity in epoxidation reactions induced by manganese porphyrins has recently been associated to the contamination of Mn(V)=O porphyrins by Mn(IV)=O porphyrins, which are endowed with a much lower stereoselectivity since react by a free-radical mechanism.[7] Thus, the much higher stereoselectivity observed with Mn^{III}TDMeOPP than with Mn^{III}TPPCl, *in the absence of imidazole*, would seem to indicate a higher tendency of the former porphyrin to form the Mn(V)=O complex as the epoxidizing species. The presence of the electron donating methoxy groups in the *meso*-phenyl rings might have a role in this respect (*vide infra*).

Finally, a few experiments have been carried out to investigate the behaviour of Mn^{III}TDMeOPP and Fe^{III}TDMeOPP as catalysts for the hydroxylation of alkanes. The results are reported in Table 2 for adamantane as the substrate. With H_2O_2 as the oxidant, the reaction catalyzed by Mn^{III}TDMeOPPCl gives oxidation products (1- and 2-adamantanol and 2-adamantanone) with a overall yield of 27%, which compares unfavorably with that (85%) observed when Mn^{III}TDCPPCl is the catalyst.[5a] However, the former reaction turns out to be somewhat more selective, the 3°-CH/2°-CH reactivity ratio being 15, whereas it is 9 for the latter. When PhIO is the oxidant, the yield of oxidation products remains low (*ca* 30%) both with Mn^{III}TDMeOPPCl and with Fe^{III}TDMeOPPCl, which accordingly appears to be a less efficient hydroxylation catalyst than Fe^{III}TPPCl.

Table 2. Hydroxylation of Adamantane

Oxidant	Porphyrin	Ox/Subs/Por	Reaction time (h)	Yields (%)			Tn[b]
				1-AdOH,	2-AdOH,	2-Ad=O	
H_2O_2	MnTDMeOPPCl	400/40/1	2	22	3	2	12
	MnTDCPPCl	200/40/1	1	63	19	3	35
PhIO	MnTDMeOPPCl	200/100/4	2	30	-	6	11
		200/100/2	2	18	1.4	2	12
	FeTDMeOPPCl	200/100/2	2	30	3.3	2	19
		6/33/1	1	8[a]	1	-	3
	FeTPPCl	6/33/1	1	20[a]	3	-	8

a) Yield referred toward the oxidant
b) Turnover number, calculated as number of oxidative cycles per molecule of catalyst

Summing up, the results presented here clearly indicate that, while a 2,6-disubstitution in the phenyl ring by electron donating substituents like OCH_3 decreases the catalytic properties of a metallo porphyrin in hydroxylation reactions, it does not interfere with the epoxidation of alkenes. In fact, the catalytic efficiency as well as the stereoselectivity of the epoxidations promoted by Mn^{III}TDMeOPPCl and Fe^{III}TDMeOPPCl are comparable to or even higher than those induced by the iron and manganese complexes of H_2TPP and H_2TDCPP in the corresponding reactions.

It should be clarified that in both Mn^{III}TDMeOPPCl and Fe^{III}TDMeOPPCl the presence of the 2,6-dimethoxy groups is bound to increase the electron density of the *meso*-phenyl rings by a resonance effect. These electron-rich phenyl rings are however perpendicular to the porphyrin system, so that they are expected to increase the electron density of the porphyrin itself only by an inductive effect. This is confirmed by the observation that the oxidation potential of Fe^{III}TDMeOPPCl (1.03 V *vs.* SCE)[8] is lower than that of Fe^{III}TPPCl (1.20 V *vs.* SCE; 1.11 V vs. Ag^+/Ag),[8,9] and to an even greater extent lower than that of Fe^{III}TDCPPCl (1.33 V *vs.* Ag^+/Ag).[9] Such an increase of electron density might have a plurality of effects. In the first place, it should make the catalyst somewhat less robust, which is indeed observed. In the second place, the free radical character of oxygen in the metallo oxo-complex is expected to decrease,[10] thus making this species less active in hydrogen atom abstraction reactions. Finally, it has been recently suggested that electron donating group at the *meso* positions can have a favorable effect on the formation of the metallo-oxo complex.[11] Thus, we suggest that our results derive from a balance of the above factors. The decresed robustness of Mn^{III}TDMeOPPCl and Fe^{III}TDMeOPPCl, together with a diminished free radical character of the metallo-oxo oxygen, are probably responsible for the lower efficiency of these catalysts in the hydroxylation reaction with respect to other less electron-rich porphyrins. On the other hand, epoxidation of alkenes is a less energy-demanding process than alkane hydroxylation. Thus, the diminished robustness of Mn^{III}TDMeOPPCl and Fe^{III}TDMeOPPCl is no longer a problem in this reaction, wheras the above mentioned favorable effect of the *meso* electron-donating groups on the formation of the metallo-oxo complex could come into play. It follows

that both porhyrins, and particularly Mn^{III}TDMeOPPCl, result to be efficient and highly stereoselective catalysts for the epoxidation of alkenes.

While these interesting and in some respect *unexpected* properties of the metallo complexes of H_2TDMeOPP (particularly that of Mn) need to be further investigated, they are made more valuable by the fact that, as already mentioned, this porphyrin can be easily prepared in a relatively large scale; it is therefore a convenient starting material for further functionalization, *e.g.* at the ß-positions of the pyrrole rings, which might hopefully lead to still more efficient and robust catalytic systems. Work in this direction is under way in our laboratories.

Experimental

Materials. Acetonitrile (HPLC grade; Carlo Erba) and benzene (Fluka) were used as received. Dry CH_2Cl_2 was obtained by refluxing and distilling over P_2O_5. Iodosylbenzene was prepared by hydrolysis of iodobenzene diacetate (Aldrich),[12] stored at -20 °C and titrated every 3 months. H_2O_2 (30% in water; Carlo Erba) was stored at 5 °C and titrated every 2 months. Cyclooctene and adamantane (Fluka) were used without further purification. Cyclooctene oxide, 1-adamantanol, 2-adamantanol and 2-adamantanone were purchased from Fluka.

Porphyrins. Manganese and iron complexes of 5,10,15,20-tetraphenylporphyrin (MnTPPCl, FeTPPCl) were purchased from Aldrich and used as received. 5,10,15,20-tetrakis(2',6'-dimethoxyphenyl)porphyrin (H_2TDMeOPP) and 5,10,15,20-tetrakis(2',6'-dichlorophenyl) porphyrin (H_2TDCPP) were prepared following literature procedures.[4,13] Metallation was performed by conventional methods.[14,15]

Oxidation of cyclooctene with H_2O_2. A solution of H_2O_2 (30% in H_2O, 800 µmol or 1600 µmol) and imidazole (84 µmol) in CH_3CN (0.72 cm^3) was added in 0.08 cm^3 portions (50 min overall) to a solution of the metalloporphyrin (4 µmol), imidazole (16 µmol) and cyclooctene (160 µmol) in 0.52 cm^3 of a 1:1 CH_2Cl_2-CH_3CN mixed solvent. The reaction mixture was stirred for 2 h at room temperature and then the internal standard (pentadecane) was added. The analysis of the products was performed by GLC and GC-MS. In order to follow the degradation of the catalyst, 0.01 cm^3 of the reaction mixture were diluted 300 times in CH_2Cl_2 and then analyzed by UV-Vis spectroscopy.

Oxidation of cyclooctene with PhIO. Iodosylbenzene (20 µmol) was added to a solution of the metalloporphyrin (1 µmol) and cyclooctene (400 µmol) in CH_2Cl_2 (1 cm^3). The reaction mixture was stirred for 0.5 h at room temperature and then quenched by addition of an aqueous solution of $Na_2S_2O_5$ (2cm^3, $5\cdot10^{-2}$M) under stirring. The internal standard (pentadecane) was added and the organic layer dried over Na_2SO_4 and analysed by GLC and GC-MS. Degradation of the catalyst was measured as described above.

Oxidation of *cis*-stilbene with H_2O_2. A solution of H_2O_2 (30% in H_2O, 1600 µmol) and imidazole (84 µmol) in CH_3CN (0.72 cm^3) was added in 0.08 cm^3 portions (50 min overall) to a solution of the metalloporphyrin (4 µmol), imidazole (16 µmol) and *cis*-stilbene (160 µmol) in 0.52 cm^3 of a 1:1 CH_2Cl_2-CH_3CN mixed solvent. The reaction mixture was stirred for 2 h at room temperature and then the internal standard (acetophenone) was added. Methanol (5 cm^3) was added after partial removing of the solvent. The analysis was performed by HPLC and ^{1}H-NMR.

Oxidation of *cis*-stilbene with PhIO. Iodosylbenzene (20 µmol) was added to a solution of Mn^{III}TDMeOPPCl (4 µmol) and *cis*-stilbene (200 µmol), in the absence or in the presence of imidazole (40 µmol), in dichloromethane (1 cm^3). The reaction mixture was stirred for 5 min at room temperature and then quenched by addition of an aqueous solution of $Na_2S_2O_5$ (2 cm^3, $5\cdot10^{-2}$M) under stirring. The internal standard (acetophenone) was added. Methanol (5 cm^3) was added after partial removing of the solvent. The mixture was analysed by HPLC.

Oxidation of adamantane with H_2O_2. A solution of H_2O_2 (1.6 mmol) and imidazole (84 µmol) in CH_3CN (0.72 cm^3) was added in 0.05 ml portions (1.25 h overall) to a solution of the metalloporphyrin (4 µmol), imidazole (16 µmol) and adamantane (160 µmol) in 1.8 cm^3 of a 1:2 C_6H_6-CH_3CN mixed solvent. The reaction mixture was stirred for 2 h at room temperature and then the internal standard added. The analysis was performed by GLC and GC-MS.

Oxidation of adamantane with an excess of PhIO. Iodosylbenzene (100 μmol) was added to a solution of the metalloporphyrin (2 or 4 μmol) and adamantane (100 μmol) in CH_2Cl_2 (0.5 cm^3). The reaction mixture was stirred for 1 h at room temperature and then other PhIO (100 μmol) was added. The stirring was continued for an additional hour and then the reaction was quenched by addition of an aqueous solution of $Na_2S_2O_5$ (2 cm^3, $5 \cdot 10^{-2}$M) under stirring. The internal standard was added and the organic layer dried over Na_2SO_4 and analysed by GLC and GC-MS.

Oxidation of adamantane with an excess of substrate. The oxidant (50 μmol) was added to a solution of the metalloporphyrin (8 μmol) and adamantane (1.6 mmol) in CH_2Cl_2 (3 cm^3). The reaction mixture was stirred for 1 h at room temperature and then quenched by addition of an aqueous solution of $Na_2S_2O_5$ (2 cm^3, $5 \cdot 10^{-2}$M) under stirring. The internal standard was added and the organic layer dried over Na_2SO_4 and analyzed by GLC and GC-MS.

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