What do we know About Metalloporphyrin Catalytic Oxidations?

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While oxidation may be considered one of the nasty chemical events we are faced with, it is also an important useful reaction playing a fundamental role in the living processes whose control in 'man made' chemical reactivity is extremely relevant.

Essential to the importance of oxidation on its role into the living processes is the smoothness and delicate control of the phenomenon allowing for its occurrence in a delicate tailored way.

The first approach to mimicking natural oxidation involved the plain replay of the natural enzymatic oxidation using simple metalloporphyrins in the presence of an axial ligand and using the singular mono-oxygen donor iodosyl benzene. Such a simple model demonstrated the feasibility of the artificial approach.

In a second generation of studies, far better catalysts and catalytic conditions were established.

From those, considerable progress was made to the present day. Experimental and theoretical studies on the mechanism of the catalytic oxidations allowed for the development of very promising and useful reactions where the most desirable oxidants can be used to perform efficient and selective reactions providing that specific catalysts, oxidants and reaction conditions are properly selected.

To the common man oxidation is a word of concern, without realising that besides the undesirable phenomena he associates to the word, oxidation is also a basic phenomenon he himself very much depends on. As a source of energy in the diverse spectacular combustion processes, but also in the peaceful chemical events which sustain life, his own life. We, as we are, would not be concerned with oxidation were it not for the importance of those quiet manifestations of oxidative processes.

An admirable characteristic of the spirit of man is that if he starts to understand something, hardly stops to desire penetrating deeper and deeper in the knowledge of the facts. The reward is not only intellectual delight but also the capacity to manipulate nature to our own advantage.

Combustion was a phenomenon known to primitive man. After chemistry has risen from the darkness of phlogiston establishing the importance of oxygen, the relationship between "fire combustions" and respiratory events came to light with the concept of "cold combustions". The story follows, and the desire to understand and mimic the oxidation enzymes and their performance made germinate an ambitious but sound research effort that has produced many important results.

Scheme 1
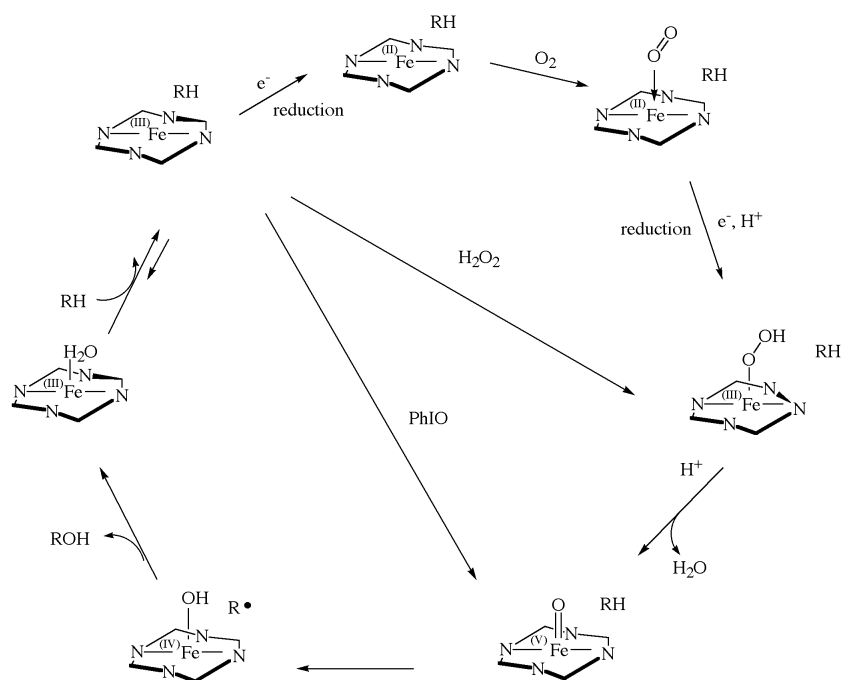
Rewarding, so far, in terms of deep understanding of facts. Practical economical applications are still mainly to be hoped.
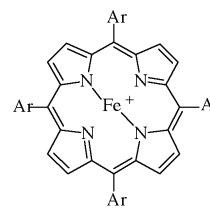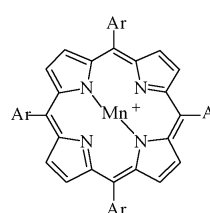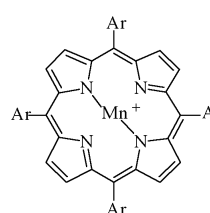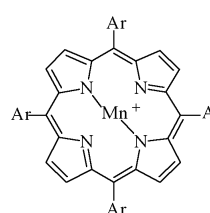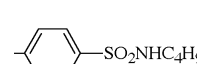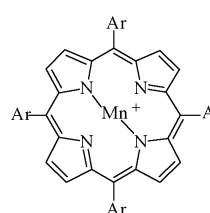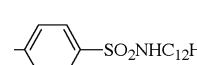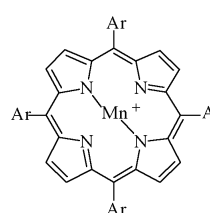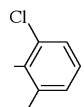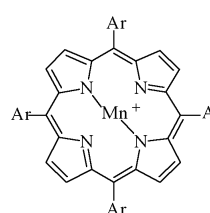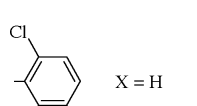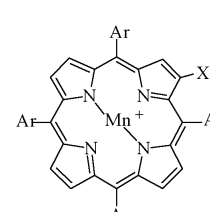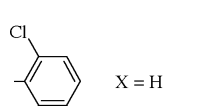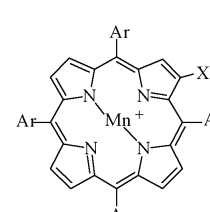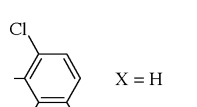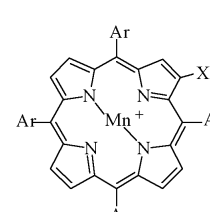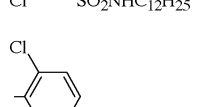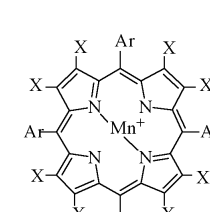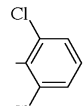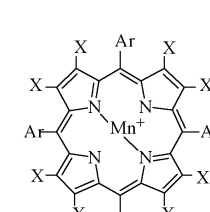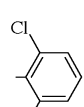
Requirements of chemical production have, as most necessary, oxidative steps for the conversion of abundant, cheap, environment disturbers, limited use, poorly reactive compounds into harmless or preferably useful valuable products. Poor reactivity, that is understood as a lack of chemical-, regio-, and stereo-selectivity between the various bonds of the substrate structure is a difficulty typical of laboratory chemistry methods. On the contrary, enzymatic methods typical of the internal chemistry of living cells have the ability to play the game where those problems are overcome in the most efficient and elegant way. To put this capacity at the service of our own needs has been the object of many efforts with variable success. In the cases where whole cells can be used to perform their chemistry, we do not have much more than a technological manipulation of the art of growing plants and animals, more generally, living things, in order to make use of the chemicals they make. Higher productivities of specific products are attained while the chemical machine is not perturbed. Isolation of the enzymatic system to be used outside of its living environment is an attractive approach possible to apply, however, it has the limitation of having taken the enzyme out of its natural environment. On doing this, the enzyme becomes more vulnerable to degradation and, above all, can not be replaced because the instrument that can build it is no longer there.

Present day knowledge of chemistry gives us access to the details of chemical structure and architecture even of highly complex molecules. It also gives us the capacity to build molecules similar to natural ones or following artificial patterns. It is such a capacity that allows the making of molecular models.

A model is an attractive and elegant approach to the real thing but, under modelling circumstances, we have the risk of not being able to come close enough to the desired analogy. Also the simplification brought by modelling does not necessarily make the structures more stable to the conditions of the catalytic system and certainly does not bear the capacity of replacing "in situ" the damaged catalyst molecules as it occurs inside living cells.

The ultimate aim on oxidizing convenient substrates for the production of required and useful molecules would be using molecular oxygen and a readily obtainable cheap catalyst and catalytic operation conditions. This would allow pure emulation of nature that takes advantage of the natural reactivity locked state of, the earth atmosphere readily available, molecular oxygen. Not a direct easy task to start with. Were it not this reactivity locking of molecular oxygen and only the nasty side of oxidation would be known. Or, to be sure, life systems if they existed would not be what they are. The incorporation of oxygen into the enzyme catalytic cycle involves two reductive steps which brings the dioxygen molecule to the

Table 1
Metalloporphyrins

peroxi-oxidation stage before entering into the steps which lead to the oxidation of the substrate, Scheme 1. The coexistence of reductive and oxidative conditions in the vicinity of the active site is a delicate game easily played by a living enzyme structure, but difficult to make work in an efficient way in an artificial system. Recent works, using artificial ruthenium complexes as catalysts, avoid that type of mechanistic route and allow for oxidations with molecular oxygen without requiring the presence of the specific redutant [1]. These oxidations, catalysed by ruthenium complexes must be considered bioinspired and not biomimetic oxidations. They will not be the object of attention in this presentation. They originated, however, an important area of research that has produced significant results. In any case, the most desirable oxidant should not be to far from the natural one and in that respect hydrogen peroxide is certainly an interesting candidate. As seen in Scheme 1, it corresponds to a form of oxygen in an oxidation state that belongs to the natural cycle of oxygen in the natural enzymatic oxidation processes. From that form the enzyme uses one of the oxygen atoms to attach to the substrate eliminating the other as water. In its oxidation state, hydrogen peroxide is ready to bind to the metal of the model enzyme in its normal oxidation state. So the use of hydrogen peroxide as the oxidant presents a diversity of advantages. While it emulates the final part of the natural enzymatic cycle, it is a "green" oxidant whose only elimination fragment is water. Argue that hydrogen peroxide is expensive, and its use in biomimetic oxidations corresponds simply to take the reductive step out of the catalytic cycle to perform it externaly in a similar way, does not take into account that today's technology for hydrogen peroxide production is very elegant and a fairly efficient and clean bioinspired process.

Our own studies in biomimetic oxidation catalysis have always been guided by some conditions we reckon as essential if we aim at any chance of having a process that may be of some use in terms of preparative applications. Of course the limiting parameters to define the viability of an industrial process span over a broad range, depending on the cost of starting material and the market value of the final product. Waste products, environmental concerns and preservation costs are, more and more, important factors to take into account. In any case the feasibility and cost of the catalyst preparation is of major importance. We always thought that the porphyrin selected to prepare the metallocomplex for any industrially feasible process must be obtained from available cheap starting materials *via* a straightforward synthesis. Simple derivatives obtained through peripheric substitution on the porphyrin macro-cycle or on its substituents were also acceptable. Our contribution in the field includes efficient practical improve-ments to the Rothemund methodology for the synthesis of *meso*-substituted porphyrins [2-4], and for the functionalization of simple porphyrins both on the *meso*-substituents and on the β-carbons [5,6]. Following

those synthetic approaches, various useful porphyrins for the preparation of metallocomplexes to use as catalysts can be prepared in a fairly convenient way for big scale preparations. Structures of some of those porphyrins are shown in Table 1

Without ignoring the highly valuable results which have been brought to the metalloporphyrin catalytic studies using as oxygen donors iodosylbenzene, its fluorinated derivative, or even some amine oxides [7-11], we decided to concentrate our effort selecting the oxidants we reckon as more promising in terms of possible intensive use. For that purpose, in our work, we have mainly used hypo-chlorite and hydrogen peroxide. We certainly would not put aside the chance of exploiting the use of molecular oxygen. Also, we consider the appealing use of oxone, percarbonate, and under some circumstances nitrogen oxide.

While our own interest has been centred on the oxidants mentioned above because we recognise them as those having better perspectives to give practical applicable methods for the preparative scale, we do not discard the importance of so many studies that have been performed using other oxygen donors. By all means the importance of the first studies by Groves [12] using FeTPP, **Fe-1**, as catalyst and iodosylbenzene as the oxidant can never be overemphasised. These studies opened the door for the first successful biomimetic catalysis and corresponded to an elegant way to prove its feasibility. Under very incipient conditions, considering the poor performance of the first attempted catalyst and the absence of knowledge relative to the setting of reaction conditions, it was possible to insert an oxygen atom on the metallocomplex. An oxo-species, similar to the one in the final steps of the natural cycle, was generated. A particular observation made in Groves first work was the need for the presence of an axial ligand to the metal in order to assist the formation of the active oxidative species. In this first work, pyridine was used as axial ligand. Imidazole was also used later for the same purpose [13].

One of the problems raised during biomimetic oxidations is the stability of this axial ligand to oxidation. Actually if it is an amine, like the above mentioned pyridine or imidazole, it is easily oxidized to the corresponding amine oxide or to more extensively degraded forms in the case of imidazole. This makes those ligands potential competitors with the substrate for oxidation. Also having reacted, the compounds can loose the characteristics that make them assist the mechanistic steps of the oxidation catalysis.

One of our first works in the area [14] lead us to study the problem of the stability of the axial ligand in the case of where the catalyst was MnTDCPP, **Mn-5**, and hydrogen peroxide the oxidant. In this particular case the available evidence pointed for the need of the simultaneous presence of a base [13], a role that could be played by any one of the ligands mentioned above . In the case of degradation this

Table 2

Effect of Various Base/Ligand Combinations on the Epoxidation of *cis*-Cyclooctene

Base	Ligand	Time(h)	Yield epoxide (%)
TO[a] (0.74×10^{-4}mol)	TO(0.74×10^{-4}mol)	5	73
$Bu_4N^+OH^-$ (0.1 mol)	TO(1.5×10^{-4}mol)	2	83
		5	98
Na_2CO_3 (3.3 mmol)	TO (1.7×10^{-4}mol)	2	51
		5	74
NaOAc (1.5 mL of MeOH saturated with NaOAC)	AO [b] (1.7×10^{-4}mol)	2	96
$Bu_4N^+OH^-$ (0.1 mol)	Imidazole (18.5×10^{-3}mmol)	2	98
$Bu_4N^+OH^-$ (0.1 mol)	PPh_3O (0.2 mmol)	1	37

[a] TO-Triethylamine *N*-oxide; [b] AO- Diisopropylamine *N*-oxide.

addictive became a consumable of the reaction that was eliminated during its course. In our work we found that a stable base could be used in these hydrogen peroxide catalysed reactions, and also the possibility of using a non-oxidizable ligand. Reactions performed in a single phase through the use as solvent of the mixture dichloromethane/methanol produced epoxides in the presence of various non-oxidizable bases and axial ligands as shown in Table 2 [15]. Between the examples shown, the pair sodium acetate-diisopropylethylamine *N*-oxide, proved to be very efficient.

Following the preceding studies we found that the epoxidation reaction could be performed in an advantageous way using adducts of hydrogen peroxide, of the type $A.xH_2O_2$, a non-aqueous source of the reagent [15]. The results of such work are shown in Table 3. As seen on this Table, using the hydrogen peroxide adduct with sodium carbonate, $NaCO_3.3/2H_2O_2$ fairly efficient epoxidations can be obtained.

Having established a convenient synthetic method for the peripheric perhalogenation of *meso*-arylporphyrins [16,17], we decided to exploit the performance of the manganese complexes of these fully β-halogenated porphyrins which were then claimed [18-21] particularly promising as highly active and stable as oxidation catalysts. For the specific purpose of hydrogen peroxide oxidations using the type of conditions we were exploiting, we came to conclude that some of the then expected advantage of such complexes as oxidation catalysts were

Table 3

Use of H_2O_2 Adducts for Epoxidation of *cis*-Cyclooctene

Adducts	Base	Time (h)	Yield epoxide (%)
(A. H_2O_2)			
Na_2CO_3	$Bu_4N^+OH^-$	2	91
Na_2CO_3	--------	4.5	90
H_2NCONH_2	$Bu_4N^+OH^-$	24	89
Me_3NO	$Bu_4N^+OH^-$	17	22
Ph_3PO	$Bu_4N^+OH^-$	3	21

not fulfilled. As evidenced in Table 4 for **Mn-10**, the stability of the metal complexes of these porphyrins having such a large number of peripheric electron-withdrawing groups is questionable when the oxygen donor is hydrogen peroxide.

Under specific reaction conditions and particularly with iodosylbenzene or iodosylpentafluorobenzene, the polyhaloporphyrins have been reckoned as high performance catalysts particularly for specialy difficult hydroxylations [10]. However, it seems that the high stability claimed for the catalysts in many of the works cited on the last reference can not be taken for granted, particularly if hydrogen peroxide is the oxygen source. This was confirmed even for the case of "Teflon" porphyrin which was claimed by Seno as the apparently most promising [22].

As a consequence of our own results on the attempted use of the catalyst Mn(TDCPPCl$_8$), **Mn-10**, for hydrogen peroxide oxidations, we decided to study the performance of the same catalyst in sodium hypochlorite oxidations [17]. For that we matched the catalytic performance of Mn(TDCPP), **Mn-5**, with that of Mn(TDCPPCl$_8$), **Mn-10**, to find the results which are condensed in Table 5. It has to be emphasised that the catalytic activity of Mn(TDCPP), **Mn-5**, is consistently higher than that of Mn(TDCPPCl$_8$), **Mn-10**, being this last always less selective than former. Interestingly, only for the case of *trans*-stilbene is the β-chlorinated porphyrin active whilst the parent compound is totally inactive although, the reaction is slow and selectivity is poor. Another interesting observation was that in some cases, substantial amounts of chlorinated materials were formed. These originating either from attack by Cl$^-$ on the epoxide or Cl$^+$ on the alkene, particularly in the case of the perchlorinated catalyst. This reveals a chloroperoxidase activity, event that we can associate to the property of this catalyst to loose its activity due to the formation of its derivative Mn-OCl. The inactive form which we have isolated when the catalytic activity has stopped, having a visible Soret absorption band at 448, nm corresponds apparently to this species

Table 4

Oxidations with H_2O_2 (50%) Catalysed by Manganese Complex of β-Octachloro-*meso*-tetrakis-
(2,6-dichlorophenyl)porphyrin (**Mn-10**) in a Monophasic System (CH_2Cl_2/MeOH)

Substrate	Substrate:oxidant molar ratio	Time (min.)	Yield epoxide (%)	Remaining catalyst [a] (%)
cis-Cyclooctene	0.32	2	99	0
cis-Cyclooctene	32	20	1	75
Pinane	0.32	3	28	0
Toluene	0.32	10	2	0
Tridecane	0.32	10	18	0

[a] Estimated from the absorbance of the Soret band.

Having developed efficient conditions for the chlorosulphonation of porphyrins, we decided to prepare a set of sulphonamide metalloporphyrins and make a study of their catalytic performance. Using metalloporphyrin structures **Mn-1** to **Mn-9** [23], a two-phase system previously reported for catalytic epoxidations with hydrogen peroxide was firstly used. Montanary had reported [24] that adding not only the classical ligand, but also benzoic acid, increased the reaction rates of the reactions. Starting with Montanary's original conditions, but taking into account our own observations we were able to prove that it is possible to perform these two phase system oxidations using simply 5% hydrogen peroxide, so allowing the addition of the oxidant in excess and all at once. Metalloporphyrins **Mn-1** to **Mn-4** proved to be weekly stable and poor catalysts. Metalloporphyrins **Mn-6** to **Mn-8** showed some stability and catalytic efficiency, the known catalyst **Mn-5** performed acordingly to its recognised catalytic capacity, but **Mn-9**, the catalyst having a β-sulphonamide group proved to be the most efficient and stable, Table 6.

Becoming convinced that it was worth to further exploit the possibilities of the still not well understood role of the lipophilic acid in the catalytic system we decided to study the performance of metalloporphyrin **Mn-6** as a function of the benzoic acid concentration. Figure 1 represents the percentage of the substrate converted and the remaining catalyst after 10 minutes reaction time as a function of the ratio benzoic acid/metalloporphyrin. Total conversion of the *cis*-cyclooctene to the corresponding epoxide was observed after that period with a minimum ratio of 5:1, while total recovery of the catalyst required a ratio of 20:1.

With this series of experiments we proved that the presence of lipophilic acid in this catalytic system, more than a synergistic effect increasing the rate of reaction, also played the role of stabilising the catalyst.

Taking the benzoic acid/metalloprphyrin ratio 20:1 as convenient working conditions, we studied the performance of our whole set of metalloporphyrins in the epoxidation of *cis*-cyclooctene. Interesting and relevant observations were made under such conditions and they are summarised in Table 7. From these results we obtained

Table 5

Oxidations of Alkenes using NaOCl as Oxygen Donor
and 4Methylpyridine as Axial Ligand

Catalyst	Alkene	Time (h)	Yield epoxide (%)
MnTDCPP(Mn-5)	Styrene	0.3	88
MnTDCPPCl$_8$ (Mn-10)	Styrene	2.5	70
MnTDCPP (Mn-5)	*cis*-Cyclooctene	0.5	95
MnTDCPPCl$_8$ (Mn-10)	*cis*-Cyclooctene	3	80
MnTDCPP (Mn-5)	*cis*-Stilbene	0.3	70
MnTDCPPCl$_8$ (Mn-10)	*cis*-Stilbene	1	50 [a]
MnTDCPP (Mn-5)	Octene-1	1	90
MnTDCPPCl$_8$ (Mn-10)	Octene-1	4	10 [a]

[a] Chlorinated products identified by GC/MS methods.

Table 6

Epoxidation of *cis*-Cyclooctene Catalysed by Manganese Porphyrins using
H_2O_2 (5%) as Oxidant in a Two-phase System: Catalyst/Benzoic acid 1:1

Metalloporphyrin	Time (min.)	Conversion %	Remaining catalyst %[a]
Mn-1	20	1	6
Mn-2	20	2	0
Mn-3	20	2	0
Mn-4	20	4	7
Mn-5	20	74	
Mn-6	40	93	73
	20	41	
Mn-7	40	52	65
	20	45	
Mn-8	40	51	41
	20	52	
Mn-9	40	65	57
	20	97	
	40	100	88

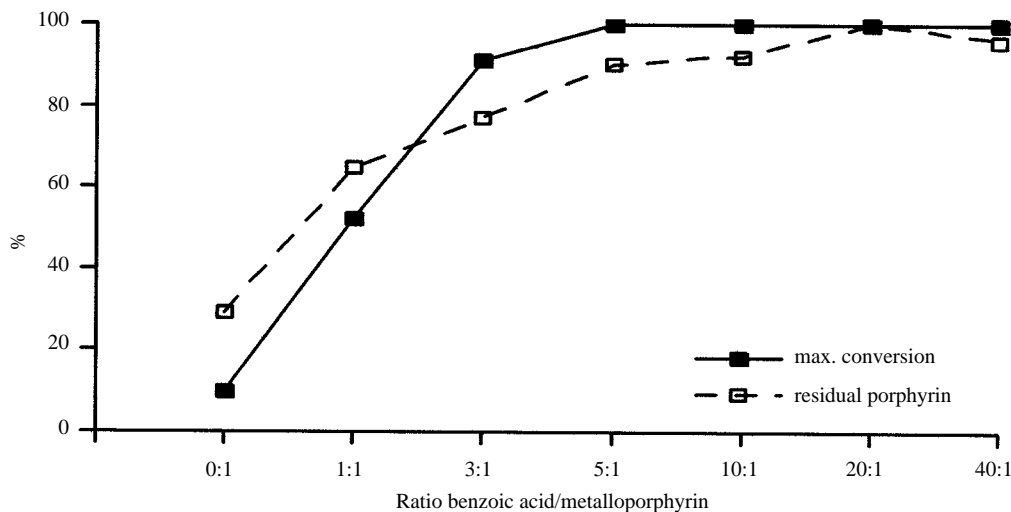[a] Measured relatively to the height of the initial Soret band.

Figure 1. Influence of the ratio benzoic acid/metalloporphyrin on the catalytic activity and stability of the catalyst **Mn-5** in aqueous/organic two phases H_2O_2 oxidation of *cis*-cyclooctene.

clear evidence that the presence of a high concentration of the lipophilic acid, when present in these hydrogen peroxide oxidations, stabilised the catalyst. Perhaps, most significant is the case of the metalloporphyrins **Mn-1**, **Mn-2**, and **Mn-3** which were almost instantaneously destroyed and had showed virtually no catalytic effect when the benzoic acid/metalloporphyrin ratio was 1:1 but can survive the reaction conditions if the ratio is 20:1. However, the catalytic performance is still poor in these cases. Catalyst **Mn-9**, stands as the most efficient of this set of catalysts under study.

Taking into account the good catalytic performance of **Mn-9** for the hydrogen peroxide epoxidation of *cis*-cyclooctene when used in the biphasic system in the presence of a lipophilic acid, we decided to extend the method to other substrates, and explore the performance of other metalloporphyrins bearing different electron withdrawing β- substituents. Alkenes more difficult to oxidise than *cis*-cyclooctene and alkanes were used as substrates. Metalloporphyrins fully halogenated in β-positions, **Mn-10**, and **Mn-11**, and known as hardly stable to hydrogen peroxide oxidation conditions [16,17], were studied. The results obtained for the catalytic epoxidation of *cis*-cyclooctene by **Mn-5, 6, 7, 8, 9** under the two sets of conditions A and B are condensed in Table 8. Catalyst/-ligand/benzoic acid ratio of A is 1:1:1 and B 1:1:20 [25].

Similar epoxidation of styrene, octene-1 and *cis*-stilbene catalysed by the metalloporphyrins **Mn-5, 6, 7, 9** gave the results shown in Table 9, Table 10, and Table 11. Epoxidation is observed in all cases and this occurs with a relatively fast kinetics in the case of conditions B, which are also required to guarantee the stability of the catalyst.

In the case of the more difficult oxidizable octene-1 the amount of residual porphyrin can not be properly determined by our selected method, due to the existence of a masking band, but the catalytic activity does not seem significantly impaired.

Table 7

Epoxidation of *cis*-Cyclooctene Catalysed by Manganese Porphyrins using H_2O_2 (5%) as Oxidant in a Two-phase system: Catalyst/Benzoic acid 1:20

Metalloporphyrin	Time (min.)	Conversion %	Remaining catalyst % [a]
Mn-1	20	3	
	40	5	100
Mn-2	20	4	
	40	6	93
	120	13	63
	24 h	29	0
Mn-3	20	4	
	40	9	60
Mn-4	20	9	
	40	15	78
Mn-5	5	44	
	10	92	100
Mn-6	5	98	
	10	100	100
Mn-7	5	81	
	10	100	100
Mn-8	5	77	
	10	98	98
Mn-9	5	100	99

[a] Measured relatively to the height of the initial Soret band.

Table 8

Epoxidation of *cis*-Cyclooctene Catalysed by Metalloporphyrins **Mn-5** to **Mn-9** using Conditions A [a] and B [b]

Mn-Porphyrin	Conditions	Time (min)	Conversion %	Remaining catalyst % [c]
Mn-5	A	40	93	73
	B	10	92	92
Mn-6	A	40	52	65
	B	5	98	100
Mn-7	A	40	65	57
	B	10	98	98
Mn-8	A	20	98	88
	B	5	100	100
Mn-9	A	40	51	41
	B	10	100	100

[a] Catalyst/axial ligand/benzoic acid 1:1:1; [b] Catalyst/axial ligand/benzoic acid 1:1:20; [c] Measured relatively to the height of the initial Soret band.

In all cases reported in preceding tables catalyst **Mn-9** was the one that produced better results. This being a metalloporphyrin with an electron attracting group in a β-position, we decided to study if the newly developed conditions that we had established would also prove efficient when β-perhalogenated metalloporphyrins were used as catalysts. In the first experiment using conditions B for *cis*-cyclooctene oxidation, it was observed that catalyst **Mn-10** was less efficient than **Mn-5** but did not suffer the type of extensive degradation that we had observed in reactions performed in oxidations in one phase systems [16, 17]. Taking into account observations made during that previous work, we planned a set of experiments

Table 9

Epoxidation of Styrene Catalysed by Metalloporphyrins **Mn-5**, **Mn-6**, **Mn-7** and **Mn-9** using Conditions A [a] and B [b]

Mn-Porphyrin	Conditions	Time (min)	Conversion %	Remaining catalyst % [c]
Mn-5	A	40	70	58
	B	10	100	97
Mn-6	A	40	87	20
	B	10	100	91
Mn-7	A	40	73	90
	B	10	100	91
Mn-9	A	20	98	80
	B	10	100	97

[a] Catalyst/axial ligand/benzoic acid 1:1:1; [b] Catalyst/axial ligand/-benzoic acid 1:1:20; [c] Measured relatively to the height of the initial Soret band.

that proved the need of another adjustment of the ratio catalyst/ligand/benzoic acid. It was also proved to be necessary to adjust the amount of ligand and conditions C, ratio 1:10:40, was set as the most adequate to use catalyst

Mn-10 and **Mn-11**. In Table 11, we can verify that under the established conditions, this metalloporphyrin **Mn-10** can be an efficient catalyst for the hydrogen peroxide epoxidation of *cis*-cyclooctene. We could not establish the real value of the residual catalyst due to difficulty of measuring the Soret's intensity.

The behaviour of our catalysts and catalytic two-phase system in the more demanding oxidation of alkanes, was an important test of their performance. Adamantane, cyclohexane, and cyclododecane were therefore chosen as substrates. Selecting for this set of experiments the more easily available metalloporphyrin **Mn-5**, we found that the most convenient catalyst/ligand/benzoic acid ratio for the oxidation of adamantane was 1:4:40. Under these newly established reaction conditions, the oxidation of the mentioned alkanes was performed in the presence of catalysts **Mn-5, Mn-6**, and **Mn-9**, with the results shown in Table 13. Table 13 also includes the results of adamantane oxidation by the β-perchlorinated and the β-perbrominated metaloporphyrins **Mn-10,** and **Mn-11**.

Table 10

Epoxidation of Octene-1 Catalysed by Metalloporphyrins **Mn-5**, **Mn-6**, **Mn-7** and **Mn-9** using Conditions A [a] and B [b]

Mn-Porphyrin	Conditions	Time (min.)	Conversion %	Remaining catalyst %
Mn-5	A	40	43	c
	B	40	93	c
Mn-6	A	40	70	c
	B	40	98	c
Mn-7	A	40	55	c
	B	40	81	c
Mn-9	A	40	74	c
	B	40	100	c

[a] Catalyst/axial ligand/benzoic acid 1:1:1; [b] Catalyst/axial ligand/-benzoic acid 1:1:20; [c] Not possible to evaluate due to the existence of a band around 450 nm.

Table 11

Epoxidation of *cis*-Stilbene Catalysed by Metalloporphyrins **Mn-5**, **Mn-6**, **Mn-7** and **Mn-9** using Conditions B [a]

Mn-Porphyrin	Time (min)	Conversion %	Remaining catalyst % [b]
Mn-5	40	92	94
Mn-6	40	93	92
Mn-7	40	73	100
Mn-9	20	94	98

[a] Catalyst/axial ligand/benzoic acid 1:1:20; [b] Measured relatively to the height of the initial Soret band.

Table 12

Epoxidation of *cis*-Cyclooctene and Octene-1 Catalysed by Metalloporphyrins **Mn-10** and **Mn-11** using Conditions C [a]

Mn-Porphyrin	Alkene	Time (min)	Conversion %	Remaining catalyst %
Mn-10	*cis*-cyclooctene	5	100	[b]
Mn-11	*cis*-cyclooctene	20	100	[b]
Mn-10	octene-1	40	52	[c]
Mn-11	octene-1	40	40	[c]

[a] Catalyst/axial ligand/benzoic acid 1:10:40; [b] Blue-shift of the Soret band, about 8-10 nm; [b] Not possible to evaluate due to the persistence of a band around 467 nm for **Mn-10** and 481 nm for **Mn-11**.

For these two later cases it proved to be necessary to make another adjustment of conditions. The required ratio catalyst/ligand/benzoic acid to obtain the best results was

Table 13

Oxidation of Cycloalkanes Catalysed by **Mn-5**, **Mn-6**, **Mn-9**, **Mn-10** and **Mn-11**

Mn-Porphyrin	Alkane	Time (min.)	Conversion %	Remaining catalyst % [c]
	adamantane	40	96	93
Mn-5 [a]	cyclohexane	80	51	100
	cyclododecane	80	48	97
	adamantane	40	100	94
Mn-6 [a]	cyclohexane	80	67	97
	cyclododecane	80	64	88
	adamantane	20	100	86
Mn-9 [a]	cyclohexane	80	83	83
	cyclododecane	80	73	99
Mn-10[b]	adamantane	20	97	87
Mn-11[b]	adamantane	40	95	100

[a] Reaction conditions: catalyst:axial ligand:benzoic acid:alkane:H_2O_2 (5%); 1:4:40:200:1300; [b] Reaction conditions: catalyst:axial ligand:benzoic acid:alkane:H_2O_2 (5%); 1:10:60:200:1300; [c] Measured relatively to the height of the initial Soret band.

in this case 1:10:60. In general, the metalloporphyrin **Mn-9** gave the best results in terms of rate of reaction and stability of the catalyst. Interestingly the β-perchlorinated metalloporphyrin **Mn-10** performed almost as efficiently as **Mn-9** in this case, both in terms of rate of catalytic reaction and catalyst stability

Looking at the selectivity of these alkane oxidations it is observed that in the case of adamantane, adamantanol-1 is the dominant product. However, for cyclohexane and cyclododecane significant amounts of alcohol and ketone are always obtained in a ratio that depends of the catalyst and of the substrate as illustrated in Figure 2. The least active catalyst is the most selective and the selectivity is higher for the most reactive substrate.

It was clear that through convenient adjustment of parameters it is possible to increase the catalytic activity of many metalloporphyrins in hydrogen peroxide oxidations while maintaining their stability, using a two-phase system in the presence of a ligand and a lipophilic acid. *meso*-Phenyl-sulphonamide derivatives of the already stable MnTDCPP, **Mn-5** particularly a derivative having one extra β-sulphonamide substituent, **Mn-9**, behaved as the most efficient catalysts.

At this stage of the study of the metalloporphyrins catalysed oxidations by hydrogen peroxide in a biphasic system in the presence of a lipophilic acid as a co-catalyst, we intended to further exploit the influence of the nature of carboxylic acid on these reactions. A selection of carboxylic acids having different structures but covering
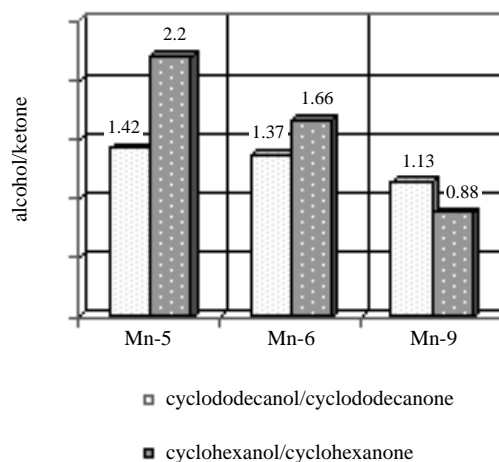

Figure 2. Ratio of alcohol/ketone obtained at the end of the oxidation of cyclododecane and cyclohexane catalysed by Mn-5, Mn-6 and Mn-9.

essentially a range of different acid strengths was made and the experiment of oxidation of *cis*-cyclooctene with hydrogen peroxide was promoted using as catalyst **Mn-5** with a catalyst/ligand/benzoic acid ratio of 1:1:20 [26].
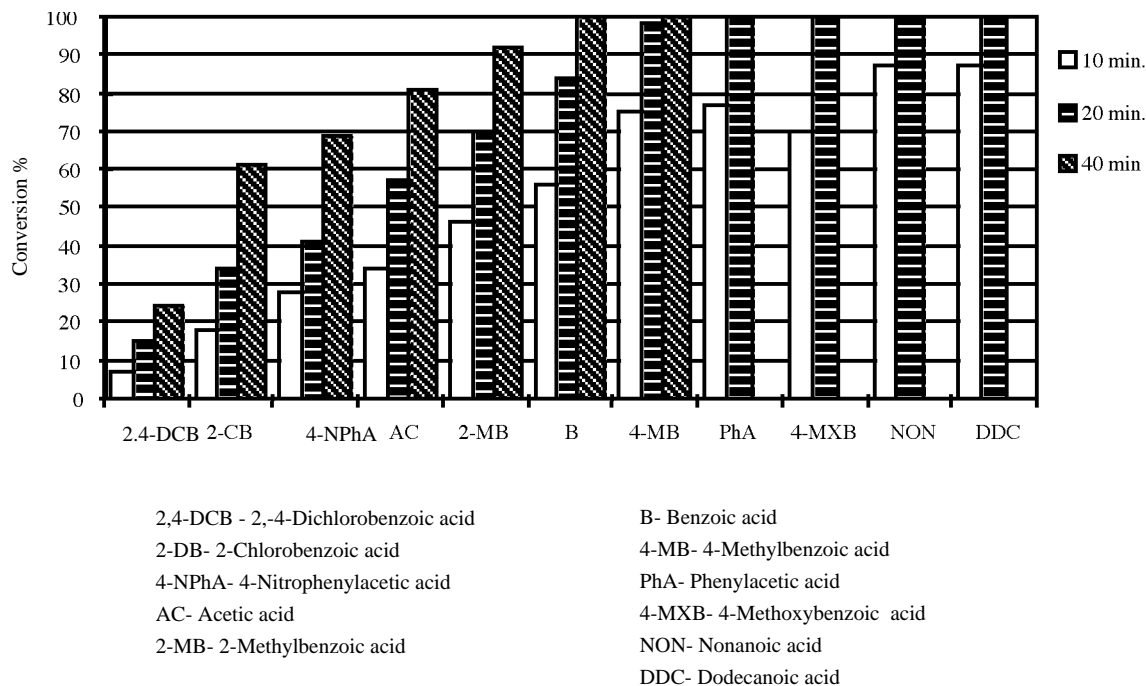
Figure 3. Epoxidation of cis-cyclooctene catalysed by Mn-5 in the presence of several organic acids. Reaction conditions: catalyst: axial ligand: organic acid: alkene: H_2O_2 (5%); 1:1:20:300:1300 (except acetic acid with a 1:40 ratio).

2,4-DCB - 2,-4-Dichlorobenzoic acid
2-DB- 2-Chlorobenzoic acid
4-NPhA- 4-Nitrophenylacetic acid
AC- Acetic acid
2-MB- 2-Methylbenzoic acid

B- Benzoic acid
4-MB- 4-Methylbenzoic acid
PhA- Phenylacetic acid
4-MXB- 4-Methoxybenzoic acid
NON- Nonanoic acid
DDC- Dodecanoic acid
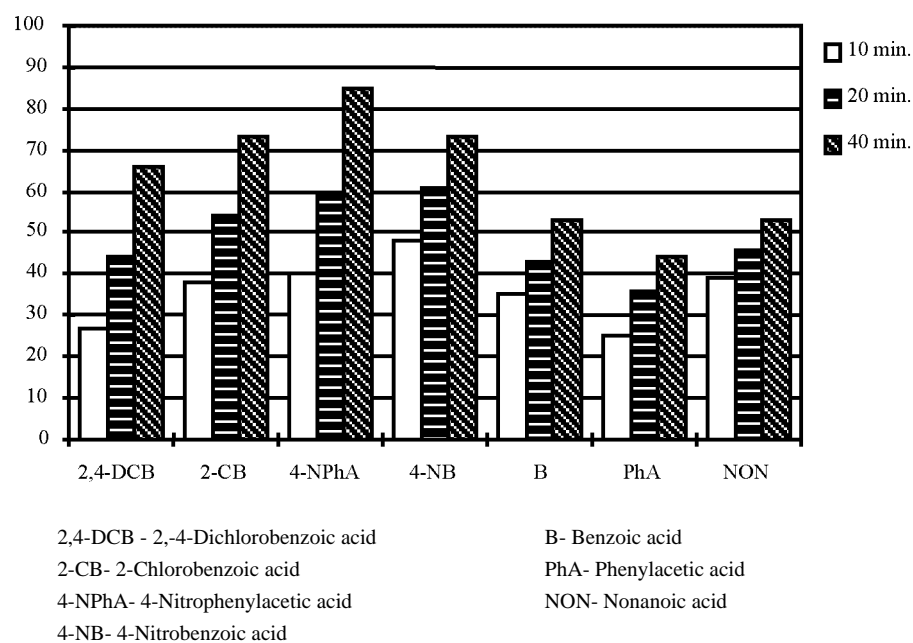

Figure 4. Epoxidation of cis-cyclooctene catalysed by Mn-5 in the presence of several organic acids. Reaction conditions:catalyst: axial ligand: organic acid: alkene: H_2O_2 (5%); 1:1:1:300:1300.

2,4-DCB - 2,-4-Dichlorobenzoic acid
2-CB- 2-Chlorobenzoic acid
4-NPhA- 4-Nitrophenylacetic acid
4-NB- 4-Nitrobenzoic acid

B- Benzoic acid
PhA- Phenylacetic acid
NON- Nonanoic acid

Table 14

Epoxidation of *cis*-Cyclooctene Catalysed by
Manganese Complexes of Porphyrin **Mn-6** using
H_2O_2 (30%) as Oxidant in a One-phase System

Organic acid	Time (min)	Conversion %	Remaining catalyst [a] %
phenylacetic acid	40	0	66
p-nitrophenyl acetic acid	40	0	68
benzoic acid	20	0	81

[a] Measured relatively to the height of the initial Soret band.

Conversion into the epoxide was obtained in all cases with selectivity higher than 90% to epoxide and with the efficiency illustrated in Figure 3. Acids with acid constant higher than benzoic acid originate slower reactions while those having lower constant gave faster reactions.

Interestingly doing similar reactions but using this time a catalyst/ligand/benzoic acid ratio of 1:1:1, it was observed that although the reactions were generally slower than those performed in presence of excess acid, the acids with higher acid constants gave faster reactions than those having lower constants. Noteworthy, the 2,4-dichloro-benzoic and the 4-nitrophenylacetic gave even faster

the same reagents and quantities as used for the biphasic system. The hydrogen peroxide was added as a 30% solution to preserve only one phase. Under such conditions the results obtained were as shown in Table 14 [23]. No oxidation was observed and the catalyst was degraded in a similar extension in the case of a metallo-porphyrin of low stability, such as **Mn-6**. No difference was also found for different carboxylic acids.

All the evidence so far accumulated can be explained on the basis of the interface phenomenon. The lipophilic acid and the metalloporphyrin form an organised structure at the interface between the water phase where the oxidant is dissolved and the organic phase carrying the substrate as schematically shown in Figure 5.

The suggested interface structure can be visualized as an interface membrane allowing the placement of the porphyrin in a favourable position for the efficient approach of the peroxide in a way that the carboxylic group assists the formation of the active oxidising species as schematically indicated in Figure 6.

The approach of the substrate to the active oxidation species is apparently not difficult when it is in the organic phase and also not disfavoured for an approach from the side of the aqueous phase as our most recent results, performing reactions in microemulsion systems, show [27].

The stabilisation of the metalloporphyrin to degradation during the catalytic process can also be understood as a consequence of this organised interface structure. The
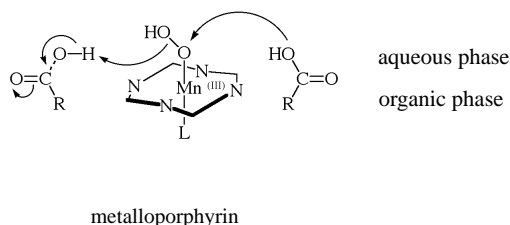

Figure 5. Proposed action of the lipophilic acid at the interface.

reactions under these last conditions than when present in high quantity. The results obtained in this last set of experiments are presented in Figure 4.

Attempting to interpret the overall observations concerning the simultaneous increase of the rates of the oxygen peroxide catalytic oxidations and of the stability of the catalyst in the reactions originated by the presence of high quantities of a lipophilic acid, it is apparent that a surface phenomenon may be responsible. In a first attempt to check this hypothesis, we tried the epoxidation of *cis*-cyclooctene in a single-phase system (dichloromethane/methanol, 1:1) using
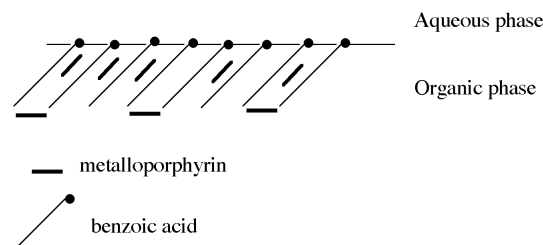

Figure 6. Suggested interface structure.

location of the individual metalloporphyrin units must provide for a convenient separation preserving them from oxidative degradation.

The better performance in terms of catalytic efficiency and stability shown by the metalloporphyrin **Mn-9** can be accounted for to the favourable electron withdrawing effect of the β-sulphonamide group but also favoured by the capacity of this metalloporphyrin to assemble more favourably into the interface organised structure.

As for the nature of the active oxidation species, the interface structure represented in Figure 6 allowed to suggest the easy formation of an high oxidation state metal-oxo species, the ordinarily accepted active species both in the natural enzymes and the synthetic catalysts. However, if this was simply so, to an increased activity of the catalyst should correspond a decrease in stability contrary to what is observed in our experiments. More than that, it was to be expected that the stronger acids should increase the catalyst activation relatively to the weaker ones. This is exactly the opposite of what is observed in the experiments whose results are quoted in Figure 6. The stronger acids promote more efficient catalysis when present in a ratio catalyst/ligand/co-catalyst acid of 1:1:1, but not when the in much larger amounts which allow for them to play a more important role.

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