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Monooxygenase-like Oxidation of Hydrocarbons by H_2O_2 Catalyzed by Manganese Porphyrins and Imidazole: Selection of the Best Catalytic System and Nature of the Active Oxygen Species

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Abstract: Fe and Mn porphyrins alone are almost unable to catalyze cyclooctene epoxidation or cyclooctane hydroxylation by H_2O_2. In the presence of imidazole, Mn(III) porphyrins, and particularly Mn(TDCPP)Cl, are much better catalysts than Fe porphyrins for oxygen-atom transfer from H_2O_2 to hydrocarbons. From a study of various Mn porphyrin catalysts and nitrogen base cocatalysts, the most efficient system that has been selected involves Mn(TDCPP)Cl in the presence of 10–20 equiv of imidazole. This system leads to high yields of alkene epoxidation (90–100% in less than 1 h at room temperature). Epoxidation of 1,2-dialkylethylenes is stereospecific and corresponds to a syn addition of an oxygen atom to the double bond. This system also leads to the oxidation by H_2O_2 of various alkanes such as cyclohexane, cyclooctane, adamantane, ethylbenzene, or tetralin, with formation of the corresponding alcohols and ketones in yields between 40 and 80%. The Mn(TDCPP)Cl–imidazole–PhIO and Mn(TDCPP)Cl–imidazole–H_2O_2 systems exhibit the following: (i) identical stereospecificities for the epoxidation of stilbene and hex-2-ene, (ii) identical regioselectivities for the epoxidation of isoprene and limonene as well as for the hydroxylation of *n*-heptane, and (iii) almost identical chemoselectivities for the oxidation of cyclohexene and of mixtures of cyclooctane and cyclooctene. This indicates that very similar, if not identical, high-valent Mn-oxo intermediates are the active oxygenating species in both systems. Thus, thanks to the presence of imidazole, it is possible to perform efficient biomimetic monooxygenations of hydrocarbons by using the Mn(TDCPP)Cl catalyst and H_2O_2 instead of PhIO as the oxygen-atom donor.

As cytochrome P-450, simple Fe- or Mn(porphyrin)Cl complexes were found to act as good catalysts for the transfer of oxygen atoms from iodosylarenes,[1] tertiary amine oxides,[2] or hypochlorite[3] to hydrocarbons with formation of epoxides from alkenes and alcohols from alkanes. The active oxygen intermediates formed in these reactions are thought to be $[(\text{porphyrin})^{+\bullet}\text{Fe}^{IV}{=}\text{O}]$[4] and $[(\text{porphyrin})\text{Mn}^{V}{=}\text{O}]$[5] species. The problem is more complex when one wants to use compounds containing an O–O bond such as alkylhydroperoxides or H_2O_2 as oxygen-atom donors. In fact, contrary to cytochrome P-450, these Fe- or Mn(porphyrin)Cl complexes were poor catalysts for the transfer of an oxygen atom of alkylhydroperoxides to hydrocarbons with the intermediate formation of high-valent metal-oxo species. In the case of Mn(III) porphyrins, alkylhydroperoxides react very slowly with the Mn(III) center.[6] Although Fe(porphyrin)Cl complexes lead to fast decomposition of alkylhydroperoxides, yields of alkene epoxidation are low.[6b,7] Alkanes are oxidized with good yields to the corresponding alcohols and ketones by cumylhydroperoxide in the presence of Fe- or Mn-porphyrin catalysts.[6a,7,8] However, the active intermediates formed in such systems do not contain the metal but seem to be the cumyloxy or cumylperoxy radicals derived from an homolytic cleavage of the O–O or O–H bond of the starting alkylhydroperoxide.[7,8] Two mechanisms have been proposed to explain the different nature of the oxidizing species involved in hydrocarbon oxidation when either PhIO or alkylhydroperoxides are used in the presence of Fe(porphyrin)Cl. In the first mechanism, it was proposed that Fe(porphyrin)Cl complexes led to a homolytic cleavage of the O–O bond of alkylhydroperoxides with formation of an alkoxy radical as the active species instead of the expected $[(\text{porphyrin})^{+\bullet}\text{Fe}^{IV}{=}\text{O}]$ intermediate (eq 1).[7,9] In the second one, a heterolytic cleavage of the O–O bond with formation of the $[(\text{porphyrin})^{+\bullet}\text{Fe}^{IV}{=}\text{O}]$ species was proposed (eq 2).[10]

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$$\mathrm{(P)Fe^{III} + ROOH \rightarrow (P)Fe^{IV}{-}OH + RO^{\bullet}} \qquad (1)$$

$$\mathrm{(P)Fe^{III} + ROOH \xrightarrow{-ROH} [(P)^{+\bullet}Fe^{IV}{=}O] \xrightarrow{ROOH} (P)Fe^{IV}{-}OH + ROO^{\bullet}} \qquad (2)$$

Here, the lack of efficient transfer of its oxygen atom to alkenes was explained by a faster reaction of the iron-oxo species with the alkylhydroperoxide than with the alkene.[10b] This fast reaction would explain the formation of ROO$^\bullet$ and then RO$^\bullet$ in such systems as well as the formation of ROOR and O_2. In the particular case of H_2O_2, similar reactions (eq 3 and 4) would explain the propensity of Fe(III) porphyrins to dismutate H_2O_2[10b,11] as well as the poor ability of Fe(porphyrin)Cl–H_2O_2 systems for hydrocarbon monooxygenation.[12]

$$\mathrm{(P)Fe^{III} + H_2O_2 \xrightarrow{-H_2O} [(P)Fe^{V}{=}O] \leftrightarrow [(P)^{+\bullet}Fe^{IV}{=}O]} \qquad (3)$$

$$\mathrm{[(P)Fe^{V}{=}O] + H_2O_2 \rightarrow O_2 + H_2O + (P)Fe^{III}} \qquad (4)$$

However, several studies have recently shown that the ability of Fe or Mn porphyrins to catalyze alkene epoxidation by alkylhydroperoxides is dramatically improved by the use of imidazole as cocatalyst. For instance, under conditions for which cumylhydroperoxide (CumOOH) is unable to epoxidize 2-methylhept-2-ene in the presence of Fe(TPP)Cl, it leads to 17% of epoxidation upon addition of imidazole.[6b] Addition of catalytic amounts of imidazole to the Mn(TPP)Cl–CumOOH system renders it able to epoxidize cyclooctene, *cis*-stilbene, and 2-methylhept-2-ene with yields between 20 and 50%.[6b] Similarly, the reactive alkene tetramethylethylene is epoxidized in 60% yield with Mn(TPP)Cl and *t*BuOOH in the presence of imidazole.[13] These results point to two important improvements of the Fe(porphyrin)Cl–ROOH or Mn(porphyrin)Cl–ROOH systems upon addition of imidazole: (i) a large increase in the rate of ROOH reaction with Mn(III) porphyrins[14] and (ii) a very important increase in oxygen-atom transfer to alkenes.

This paper describes the oxidation of hydrocarbons by H_2O_2 catalyzed by Mn porphyrins in the presence of a nitrogen base.[15] The following factors have been studied: (i) the nature of the porphyrin ring and of the nitrogen base, (ii) the nature of the alkenes or alkanes that are oxidized and the stereochemistry of the epoxidations, and (iii) the nature of the oxidizing active species in comparison to that involved in Mn–porphyrins–PhIO systems.

Results

Reactions of H_2O_2 in the Presence of Hydrocarbons and Fe or Mn Porphyrins. In order to investigate the oxidizing properties of H_2O_2 in the presence of catalytic amounts of Fe or Mn porphyrins, a mixture of cyclooctane and cyclooctene was first used. This could allow one to detect not only the possible intermediate formation of high-valent metal-oxo species similar to those formed when PhIO was used instead of H_2O_2 which are particularly good epoxidizing intermediates[1] but also the possible involvement of free radicals derived from H_2O_2 which could lead to alkane hydroxylation. Effectively, cumylhydroperoxide in the presence of these metalloporphyrins has shown a poor ability to epoxidize alkenes but reacted well with alkanes with formation of alcohols and ketones.[6a,7]

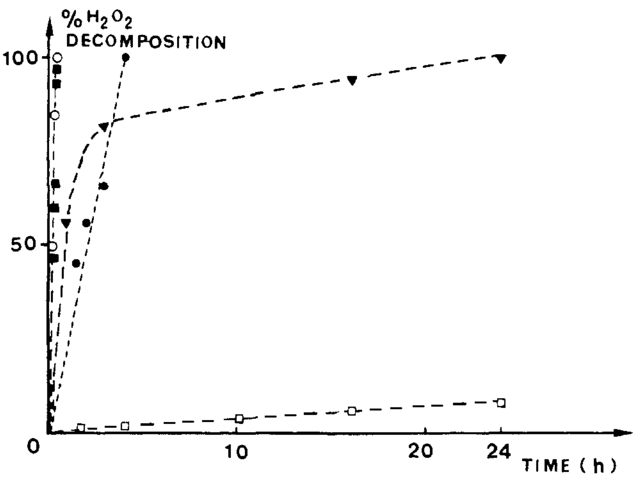

Figure 1. Effects of Fe or Mn porphyrins and imidazole (Im) on the rate of decomposition of H_2O_2 in the presence of cyclooctene and cyclooctane. Conditions: cyclooctane, cyclooctene, H_2O_2 in CH_3CN/CH_2Cl_2 (1:1), respectively, 2, 0.5, and 0.12 M (mixture M) in the presence or absence of 4 mM Fe (or Mn)(porphyrin)Cl and 40 mM imidazole at 20 °C. (○), M + Mn(TDCPP)Cl + Im; (■), M + Fe(TDCPP)Cl + Im; (▼), M + Fe(TPP)Cl; (●), M + Fe(TDCPP)Cl; (□), M + Mn(TDCPP)Cl. The curves obtained with M + Mn(TPP)Cl, with M + Im, and with M alone were almost superimposable to the (□) curve.

Table I. Oxidation of a Cyclooctane–Cyclooctene Mixture by H_2O_2 Catalyzed by Mn or Fe Porphyrins in the Presence or Absence of Imidazole (Im)

catalyst	cocatalyst	cyclooctene oxide yield (%)	cyclo-octanol	cyclo-octanone	total yield[a]
Fe(TDCPP)Cl		2	nd	nd	2
Fe(TDCPP)BF_4		1	2	1	5
Fe(TPP)Cl		1	nd	nd	1
Mn(TDCPP)Cl		2	tr	tr	2
Mn(TDCPP)BF_4		1	1	tr	2
Mn(TPP)Cl		1	tr	tr	1
Fe(TDCPP)Cl	Im	17	tr	tr	17
Mn(TDCPP)Cl	Im	72	10	2	86
	Im	1	tr	tr	1

[a] % yields based on starting H_2O_2 after 24 h in CH_3CN/CH_2Cl_2 (1:1) under anaerobic conditions with M(P)(X), H_2O_2, Im, cyclooctene, and cyclooctane in a 1:30:10:125:500 molar ratio. Total yields assuming 1.1 and 2 mol of H_2O_2 necessary for the formation of 1, 1, and 2 mol of cyclooctene oxide, cyclooctanol, and cyclooctanone, respectively: tr, traces; nd, not detected.

In the absence of a metalloporphyrin catalyst, H_2O_2 remained almost unchanged after 10 h when exposed to cyclooctene and cyclooctane in a 1:1 CH_2Cl_2/CH_3CN mixture (Figure 1). In the presence of catalytic amounts of Fe(TPP)Cl or Fe(TDCPP)Cl, H_2O_2 was almost completely decomposed within 4 h. The decrease of the rate of H_2O_2 decomposition after 1 h in the particular case of Fe(TPP)Cl was due to a progressive oxidative destruction of the catalyst. Mn(TPP)Cl or Mn(TDCPP)Cl did not catalyze H_2O_2 decomposition in these conditions (Figure 1). However, despite the fast decomposition of H_2O_2 in the presence of Fe(TPP)Cl or Fe(TDCPP)Cl (Figure 1), extremely low yields of cyclooctene-oxide, cyclooctanol, and cyclooctanone were observed (Table I). In fact whatever the nature of the metal (Fe or Mn), of the porphyrin (TPP or TDCPP) and of the axial ligand or counterion (Cl or BF_4), the Fe- or Mn–porphyrin–H_2O_2 systems were extremely inefficient for the transfer of an oxygen atom to cyclooctene or cyclooctane (Table I). In the case of Mn porphyrins, this result should be due to a very slow decomposition of H_2O_2 (Figure 1), whereas, in the case of Fe porphyrins, it could be due to the high tendency of these complexes to catalyze H_2O_2 dismutation.[10b,11] When the same reactions were performed in the presence of imidazole, a very fast decomposition of H_2O_2 occurred (Figure 1) with Mn(TDCPP)Cl as well as with Fe(TDCPP)Cl. Quite remarkably, in these conditions a 17% yield of

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Table II. Influence of the Nature of the Porphyrin Catalyst on the Oxidation of Cyclooctene (C) or Styrene (S) by H_2O_2 in the Presence of Imidazole[a]

		conditions A		conditions B	
catalyst	alkene	epoxide yield (%)	catalyst destructn (%)	epoxide yield (%)	catalyst destructn (%)
Mn(TPP)Cl	C	46	50	44	100
	S	30	50	45[b]	100
Mn(TMP)Cl	C	45	<5	75	50
	S	40	<5	80[c]	50
Mn(TFPP)Cl	C	58	<5	74	<5
	S	43	<5	72[c]	<5
Mn(TDCPP)Cl	C	97	<5	91[d]	<5
	S	93	<5	93[c]	<5

[a] Condition A: using an excess of alkene (versus H_2O_2): addition of H_2O_2 (30% in H_2O, 20 equiv relative to catalyst) to an alkene/imidazole/Mn(P)Cl mixture (800:10:1) in CH_2Cl_2/CH_3CN (1:1) under anaerobic conditions. Final concentration of Mn(P)Cl = 3 mM. Yields based on starting H_2O_2 after 2 h at room temperature (yields unchanged after 24 h). Condition B: using an excess of H_2O_2 (versus alkene): progressive addition of 5 equiv (relative to alkene) of H_2O_2 (30% in H_2O, diluted 10 times in CH_3CN) and imidazole (20 equiv relative to Mn) over 0.75 h at room temperature to an alkene/imidazole/Mn(P)Cl mixture (40:4:1) in CH_2Cl_2/CH_3CN (1:1) under aerobic conditions. Final concentration of M(P)Cl = 3 mM. Yields based on starting alkene after 2 h (yields were almost identical under anaerobic conditions). [b] PhCHO (8%) and $PhCH_2CHO$ (1%) were also formed. [c] PhCHO (1%); $PhCH_2CHO$ (1%). [d] 2 equiv of H_2O_2 used instead of 5.

cyclooctene oxide was obtained with Fe(TDCPP)Cl and a 72% yield of cyclooctene oxide and a 10% yield of cyclooctanol were observed with Mn(TDCPP)Cl (Table I). It is noteworthy that, with the latter catalyst, a total 86% yield based on starting H_2O_2 was obtained for the oxidation of cyclooctene + cyclooctane, whereas this yield was only 2% in the absence of imidazole.

Epoxidation of Alkenes by H_2O_2 Catalyzed by Mn Porphyrins and Imidazole: Effects of the Porphyrin Structure. The most efficient epoxidation system, i.e., Mn–porphyrin–H_2O_2–imidazole (Table I), was then used in the following to study the importance of the structure of the porphyrin ligand in the epoxidation of cyclooctene and styrene. In the presence of excess alkene (Table II, condition A: Mn/H_2O_2/imidazole/alkene = 1:20:10:800), the epoxide yields based on starting H_2O_2 varied from about 40% with Mn(TPP)Cl to about 100% with Mn(TDCPP)Cl. The capacity of the Mn catalysts to transfer an oxygen atom to the double bond increased for both alkenes in the following order: TPP, TMP < TFPP < TDCPP. Under conditions A, one half of the Mn(TPP)Cl was destroyed at the end of the reaction, whereas the three other Mn catalysts were found almost unchanged (Table II).

The high efficiency of Mn(TDCPP)Cl to catalyze alkene epoxidation by H_2O_2 allowed one to hope to find conditions for complete conversion of alkenes to their epoxide. Accordingly, upon progressive addition of 5 equiv of H_2O_2 (relative to the alkene) to a mixture containing cyclooctene or styrene, Mn(TDCPP)Cl, and imidazole (40:1:24 ratio, condition B of Table II), these alkenes were almost totally converted into the corresponding epoxide in yields of more than 90%. Under these conditions, the efficiency of the epoxidizing system increased in the following order: TPP < TMP, TFPP < TDCPP. More of Mn(TPP)Cl and Mn(TMP)Cl catalysts were destroyed under condition B than under condition A in which the presence of an alkene in excess protected the porphyrin ligand from oxidative degradation (Table II). However, the Mn(TFPP)Cl and Mn(TDCPP)Cl catalysts, which are more resistant to oxidative degradation,[16,17] were unchanged at the end of the reactions.

The results of alkene conversions collected in Table II were obtained with 5 equiv of H_2O_2 per molecule of alkene. However, in the case of cyclooctene, an 80% epoxide yield was already obtained after addition of 1 equiv of H_2O_2, and the maximum yield was already reached after addition of 2 equiv of H_2O_2 per alkene molecule (Figure 2). In fact, at this stage, cyclooctene was almost completely consumed.

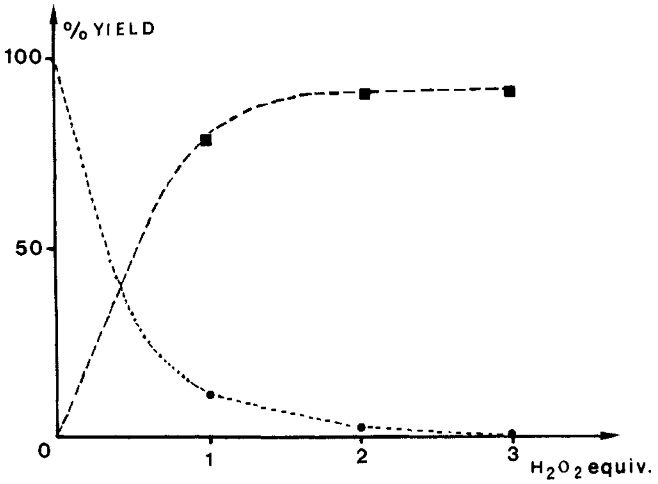

Figure 2. Conversion of cyclooctene to its epoxide, catalyzed by Mn(TDCPP)Cl and imidazole and by progressive addition of H_2O_2: (●), % cyclooctene conversion; (■), epoxide yield (condition B of Table II); cyclooctene conversion and epoxide yield measured after each addition of 1 molar equiv of H_2O_2 (relative to alkene).

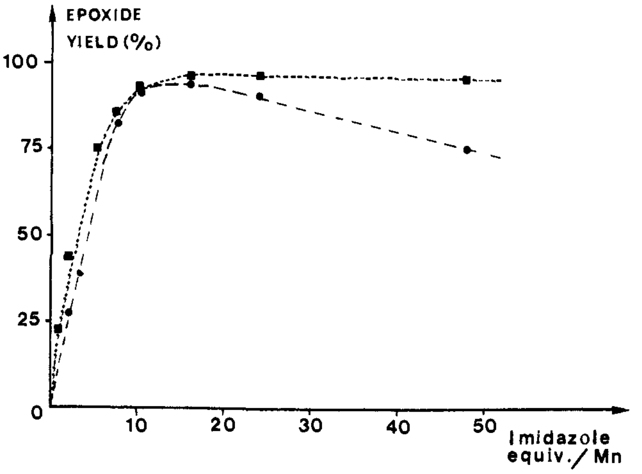

Figure 3. Influence of the imidazole/Mn(TDCPP)Cl ratio on cyclooctene epoxidation by H_2O_2. Conditions: progressive addition of H_2O_2 over 1 h at room temperature to a cyclooctene/Im/Mn(TDCPP)Cl (40:x:1) mixture in CH_3CN/CH_2Cl_2 (1:1). Mn(TDCPP)Cl = 3 mM molar H_2O_2/cyclooctene ratio of 5 (■) or 2 (●). Yields measured after 2 h were found unchanged after 24 h.

Epoxidation of Cyclooctene by H_2O_2 Catalyzed by Mn Porphyrins: Effects of Nitrogen Bases as Cocatalysts. As mentioned above (Table I), in the absence of imidazole, the Mn(TDCPP)Cl–H_2O_2 system was almost unable to epoxidize cyclooctene. Figure 3 shows that the cyclooctene epoxide yields, obtained with a 2-fold excess of H_2O_2 versus alkene, increased progressively when the reactions were performed with an imidazole/Mn ratio increasing from 0 to 10. The yield was maximum when this ratio varied between 10 and 25 and decreased significantly for imidazole/Mn ratios higher than 25. It was likely that this decrease was due to a competition between cyclooctene and imidazole itself for the oxidizing equivalents of H_2O_2. Accordingly, (i) by using a larger excess of H_2O_2 versus alkene (H_2O_2/cyclooctene = 5), the epoxide yield remained maximum even with an imidazole/Mn ratio of 50, as these conditions provided enough H_2O_2 to convert cyclooctene even if a part of H_2O_2 was used to oxidize imidazole; (ii) under extreme conditions using a very large excess of imidazole (Mn/H_2O_2/imidazole/cyclooctene = 1:200:200:40), one observed a 30% consumption of imidazole (estimated by GLC) and a low

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Table III. Influence of the Nature of the Nitrogen Base Cocatalyst (B) on the Epoxidation of Cyclooctene by H_2O_2 and Mn(TDCPP)Cl[a]

	yield of epoxide (%)		H_2O_2 consumed (%)	
cocatalyst	after 1 h	after 24 h	after 1 h	after 24 h
Im	91	91	100	100
2-CH_3-Im	94	94	100	100
4-CH_3-Im	90	90	100	100
1-CH_3-Im	51	85	59	100
benzimidazole[b]	9	45	21	66
1,2,4-triazole	8	20	25	63
pyridine	30	73	52	100
2,6-di-*t*-Bu-pyridine	1	5	16	33
Et_3N	51	51	100	100
i-$PrNH_2$	42	42	100	100
$(C_6H_{11})_2NH$	39	39	100	100

[a] Progressive addition of 2 equiv (relative to alkene) of H_2O_2 (30% in H_2O, diluted 10 times in CH_3CN) over 0.5 h, at room temperature, to a cyclooctene/imidazole/Mn(TDCPP)Cl mixture (40:10:1) in CH_2Cl_2/CH_3CN (1:1) under aerobic conditions. Final concentration of Mn(TDCPP)Cl = 3 mM. Yield based on starting cyclooctene. [b] In this case, a partial precipitation of the catalyst was observed.

Table IV. Epoxidation of Alkenes by H_2O_2 Catalyzed by Mn(TDCPP)Cl in the Presence of Imidazole[a]

alkene	epoxide yield (%)
2-methylhept-2-ene	99
cyclooctene	91
cyclohexene	91[b]
styrene	93[c]
non-1-ene	90
cis-hex-2-ene	76 cis/trans (>98):(<2)
trans-hex-2-ene	40 cis/trans (<2):(>98)
cis-stilbene	94[d] cis/trans (97:3)
trans-stilbene	2 cis/trans (0:100)

[a] Condition B of Table II. [b] Cyclohex-2-en-1-ol (1%), cyclohex-2-en-1-one (1%). [c] PhCHO (1%), $PhCH_2CHO$ (1%). [d] $PhCH_2COPh$ (2%).

yield of cyclooctene epoxide (40%). However, under conditions really useful for catalytic epoxidation and where imidazole was used as a cocatalyst, i.e., by using either an excess of alkene (Mn/H_2O_2/imidazole/cyclooctene = 1:40:10 to 25:800) or H_2O_2 in excess (Mn/H_2O_2/imidazole/cyclooctene = 1:80:10 to 25:40, conditions used in part for Figure 3), imidazole was recovered unchanged at the end of the reaction.

Other nitrogen bases can be used as catalysts for cyclooctene epoxidation by H_2O_2 in the presence of Mn(TDCPP)Cl. Under identical conditions (Mn/H_2O_2/cocatalyst/cyclooctene = 1:80:10:40), they exhibited three different types of behavior (Table III). Those of the first group which includes imidazole, 2-methylimidazole, and 4-methylimidazole gave a fast reaction with very high epoxidation yields (higher than 90% within less than 1 h). Those of the second group, which includes amines such as triethylamine, dicyclohexylamine, and isopropylamine, also led to a fast decomposition of H_2O_2 but to lower epoxide yields (between 40 and 50%). We have not studied the fate of these amines in the reaction medium, but it is likely that they were oxidized under the used conditions. The third group contains nitrogenous bases which led to lower rates of H_2O_2 consumption. This was the case of 1-methylimidazole or pyridine which led only to a 50% consumption after 1 h but to its total consumption after 24 h with final epoxide yields around 80%. Benzimidazole, 1,2,4-triazole, and 2,6-di-*tert*-butylpyridine gave even lower rates of H_2O_2 consumption and low epoxide yields even after 24 h. Thus, imidazole, 2-methylimidazole, and 4-methylimidazole appeared clearly as the best cocatalysts, and the former was used in the following experiments with an imidazole/Mn ratio between 10 and 25.

Epoxidation of Various Alkenes by the H_2O_2/Mn(TDCPP)Cl/Imidazole System: Stereochemistry of the Reaction. The Mn(TDCPP)Cl–imidazole–H_2O_2 system led to the epoxidation of various alkenes (Table IV) with good to excellent yields (76–99%). As indicated previously (Figure 2), complete conversion of cyclooctene to its epoxide was already obtained with 2 equiv of H_2O_2. This was not the case for all alkenes, and 4–5 equiv of H_2O_2 were necessary especially in the case of less reactive alkenes such as non-1-ene. Trans 1,2-disubstituted alkenes such as *trans*-stilbene and *trans*-hex-2-ene were the only alkenes tested which gave low epoxidation yields. Such a marked difference between the epoxidation yields of cis and trans 1,2-disubstituted alkenes has already been reported for Fe or Mn porphyrins and PhIO as the oxygen atom donor.[1e,f,q] The excellent yield observed for cyclohexene epoxidation with formation of only very small amounts of allylic oxidation products as well as the high yield obtained for non-1-ene, a relatively electron-poor alkene, illustrates the efficiency of the Mn(TDCPP)Cl–H_2O_2–imidazole system for alkene epoxidation. Epoxidation of *cis*- and *trans*-hex-2-ene was stereospecific (Table IV) and corresponded to a syn addition of an oxygen atom to the double bond. In the case of stilbenes, *trans*-stilbene led only to the *trans*-epoxide and *cis*-stilbene to a 97:3 mixture of *cis*- and *trans*-epoxides.

Oxidation of Alkanes by H_2O_2 in the Presence of Mn(TDCPP)Cl and Imidazole. Alkanes such as cyclohexane or cyclooctane were oxidized by H_2O_2 in the presence of Mn(TDCPP)Cl to significant amounts of the corresponding alcohol and ketone only in the presence of imidazole (Table V). When a large excess of alkane was used (conditions A of Table V), the total yield of cyclohexane oxidation based on starting H_2O_2 (assuming that 1 and 2 H_2O_2 mol were used, respectively, for alcohol and ketone formation) was 52%. This yield represents the proportion of the oxidizing equivalents from starting H_2O_2 that were transferred to cyclohexane, the rest having been presumably consumed through H_2O_2 dismutation. Accordingly, under extreme conditions using

Table V. Hydroxylation of Alkanes by H_2O_2 Catalyzed by Mn(TDCPP)Cl in the Presence of Imidazole

	condition A[a]					condition B[a]			
alkane	alcohols (%)		ketones (%)		total yield[b] (%)	alkene conversn (%)	alcohols (%)	ketones (%)	ol + one (%)
cyclohexane	cyclohexanol	40	cyclohexanone	6	52	54	30	10	40
without Im							1	0.5	1.5
without Mn(P)Cl							1	1	2
cyclooctane	cyclooctanol	43	cyclooctanone	9	61		33	12	45
adamantane[c]	adamantan-1-ol	40	adamantan-2-one	1	56	95	63	3	85
	adamantan-2-ol	14					19		
ethylbenzene	1-phenylethanol	23	acetophenone	11	45	65	28	38	66
indan	indan-1-ol	48	indan-1-one	2.5	53	80	50	11	61
tetralin	1-tetralol	52	1-tetralone	5	62	80	52	20	72

[a] Condition A of Table II but with the Mn(TDCPP)Cl/H_2O_2/Im/alkane ratio of 1:40:24:700. Condition B of Table II except that, for alkanes, anaerobic conditions were always used because of an observed slight effect of O_2 on the alcohol/ketone ratio. Yields measured after 2 h (unchanged after 24 h). [b] Yields based on starting H_2O_2 assuming that 1 and 2 H_2O_2 moles are, respectively, used for alcohol and ketone formation. [c] For adamantane, condition B of Table II were used but with the solvent mixture C_6H_6/CH_3CN (1:2) and final concentration of Mn(TDCPP)Cl = 2.2 mM; condition A slightly different from those of Table II because of the relative insolubility of adamantane (Mn(TDCPP)Cl/H_2O_2/Im/adamantane = 1:40:24:150) in CH_2Cl_2/CH_3CN (4:1); concentration of Mn(TDCPP)Cl: 2 mM.

Table VI. Regioselectivity of Isoprene Epoxidation by H_2O_2 or PhIO Catalyzed by Manganese Porphyrins[a]

oxidant	catalyst	imidazole	total yield (%)	1,2-epoxide/ 3,4-epoxide
PhIO	Mn(TPP)Cl	-	70	1.7
PhIO	Mn(TPP)Cl	+	41	1.2
H_2O_2	Mn(TPP)Cl	+	40	1.2
PhIO	Mn(TDCPP)Cl	+	70	2.4
H_2O_2	Mn(TDCPP)Cl	+	70	2.4

[a] Addition of H_2O_2 or PhIO (40 equiv relative to catalyst), over 1 h at 20 °C to an isoprene/imidazole/Mn(P)Cl mixture (160:24:1) in CD_3CN–CCl_4 (1:1), Mn(P)Cl = 4 mM; the total yields and the epoxide ratio were quantified by ^1H NMR measurements on the crude mixture.

low alkane concentrations and large excess of H_2O_2, gas evolution was observed. This is in agreement with O_2 evolution coming from H_2O_2 dismutation which has been reported during reactions of H_2O_2 with Mn and Fe porphyrins.[10b,11]

Depending upon the nature of the starting alkane, between 45% to 62% of the oxidizing equivalents of H_2O_2 were used for alkane oxidation. This is to be compared to the quasi-quantitative yield observed for cyclooctene epoxidation under identical conditions (Table II). Under conditions used for converting alkanes (conditions B of Table V, Mn/imidazole/H_2O_2/alkane = 1:24:200:40) a 54% conversion of cyclohexane was obtained with 30% and 10% yields of cyclohexanol and cyclohexanone, respectively (based on starting cyclohexane, 55% and 18% based on consumed cyclohexane). Other alkanes such as cyclooctane, ethylbenzene, indan, and tetralin gave yields of alcohols and ketones between 45% and 72%. Adamantane was almost totally transformed under these conditions leading to adamantan-1-ol as the major product (63%) as well as to adamantan-2-ol (19%) and adamantan-2-one (3%). Figure 4 shows the variation in the yields of the oxidation products derived from adamantane upon gradual addition of 1–5 equiv of H_2O_2 to adamantane under similar conditions. Actually, adamantane was completely consumed after addition of 5 equiv of H_2O_2.

Nature of the Active Oxygen Species in the Mn(porphyrin)–H_2O_2–Imidazole System: Comparison with the Mn(porphyrin)–PhIO–Imidazole System. It has been shown that the species formed upon reaction of Fe(III) porphyrins with PhIO was a high-valent $[(\text{porphyrin}^{+\bullet})Fe^{IV}{=}O]$ complex.[4] It is now generally admitted that this species is the active oxygen complex directly responsible for monooxygenation of hydrocarbons by Fe(III)–porphyrin–ArIO systems.[1] In the case of the Mn(III)–porphyrin–ArIO systems, various complexes derived from reactions between Mn(III) porphyrins and iodosoarenes have been isolated and characterized.[5b,5c,18] However, the nature of the active oxygen complex, which is able to transfer its oxygen atom to hydrocarbons, although not completely established, is generally considered to be a high-valent Mn-oxo complex, at least formally, a $Mn^V{=}O$ species.[5] Such a $Mn^V{=}O$ species could be formed in the Mn(TDCPP)Cl–H_2O_2–imidazole system, but, a priori, other active species like $^\bullet OH$, $^\bullet OOH$, or Mn^{III}–OOH could also be involved. In order to characterize the oxidizing species in the Mn(TDCPP)Cl–H_2O_2–imidazole system, we have compared its chemoselectivity, regioselectivity, and stereospecificity toward several substrates with those of the Mn(TDCPP)Cl–PhIO–imidazole system under identical conditions.

Regioselectivity of Isoprene Epoxidation. It has been shown that the ratio of the two epoxides (1,2-epoxide/3,4-epoxide) formed upon oxidation of isoprene by PhIO or ClO^- catalyzed by Mn porphyrins was dependent on the nature of the porphyrin and on the presence of a nitrogen base which could act as a Mn ligand.[19,20a] Effectively, Table VI shows that, with PhIO as oxidant, this ratio decreased from 1.7 to 1.2 when imidazole was added to Mn(TPP)Cl. It also shows that this ratio markedly increased when Mn(TDCPP)Cl was used instead of Mn(TPP)Cl. Since it has been previously shown that a very bulky Mn porphyrin gave a ratio almost identical with Mn(TPP)OAc,[20a] this important increase observed with Mn(TDCPP)Cl should be mainly due to electronic factors. Anyway it is remarkable that, with both Mn porphyrins, the ratios obtained by using either PhIO or H_2O_2 as the oxidizing agents were identical.

Scheme I

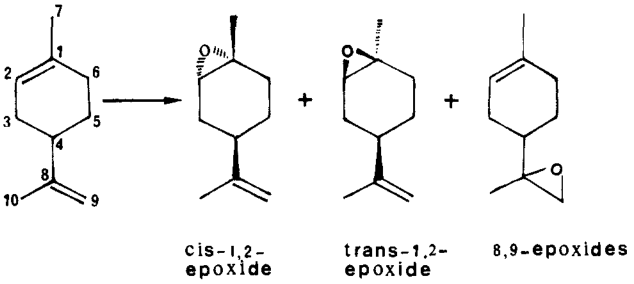
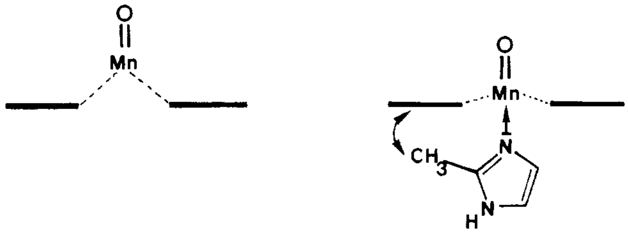


Chart I



Regioselectivity of (+)-Limonene Epoxidation. The major products described in the oxidation of limonene by PhIO or ClO^- catalyzed by Mn porphyrins were two *cis*- and *trans*-epoxides derived from epoxidation of the electron-rich trisubstituted double bond in 1,2-position and the two diastereoisomers derived from epoxidation of the more accessible but less electron-rich double bond in 8,9-position[1f,19,20a] (Scheme I). The ratio between the 1,2- and 8,9-epoxides was found to be greatly dependent on the presence of an imidazole cocatalyst, on the nature of this cocatalyst, and on the porphyrin structure (Table VII). It varied from 7.5 for the less hindered Mn(TPP)Cl catalyst in the absence of imidazole to 0.4 for Mn(TDCPP)Cl in the presence of 2-methylimidazole. The control of the regioselectivity of limonene epoxidation by using hindered metalloporphyrins with lower access of the metal-oxo species to the more electron-rich but more hindered 1,2-double bond has been already reported.[1f,20a] The results of Table VII show that the use of a Mn axial ligand, such as an imidazole, also allows one to modulate this regioselectivity by favoring epoxidation of the less reactive but more accessible 8,9-double bond of limonene. This imidazole effect could be interpreted if one admits that the active oxygen complex is a hexacoordinated Mn-oxo complex with an imidazole ligand in trans position with respect to the oxo ligand (Chart I). This imidazole binding would restrict the displacement of Mn from the mean plane of the porphyrin toward the oxo ligand and thus limit the access of limonene to the Mn=O entity. Binding of 2-methylimidazole to Mn would more severely restrict displacement of Mn toward the strong oxo ligand because of steric repulsion between the 2-methyl substituent and the porphyrin ring. It is thus likely that in a 2-methylimidazole–$Mn^V{=}O$ complex, should it exist, the Mn=O species would be less accessible than in the imidazole–$Mn^V{=}O$ complex.[20b] This could be an explanation for the lower 1,2-epoxide/8,9-epoxide ratio obtained with 2-methylimidazole compared to that obtained with imidazole or 1-methylimidazole (Table VII). Quite remarkably, the 0.4 ratio obtained with Mn(TDCPP)Cl in the presence of 2-methylimidazole was more in favor of the 8,9-epoxide than that obtained with the very bulky Mn[tetra(2,4,6-triphenyl)phenylporphyrin] in the presence of an N-substituted imidazole.[20a] It is noteworthy that the highest cis:trans ratio measured for the isomers of the

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Table VII. Regioselectivity of (+)-Limonene Epoxidation by H_2O_2 or PhIO Catalyzed by Manganese Porphyrins[a,b]

oxidant	catalyst	nitrogen base (B)	total epoxide yield (%)	1,2-epoxide/ 8,9 epoxide	1,2-epoxide cis/trans
PhIO	Mn(TPP)Cl		54	7.5	1.4
PhIO	Mn(TDCPP)Cl		71	1	1.4
PhIO	Mn(TDCPP)Cl	Im	65	0.7	1.4
H_2O_2	Mn(TDCPP)Cl	Im	75	0.7	1.4
PhIO	Mn(TDCPP)Cl	1-CH_3-Im	70	0.8	1.5
H_2O_2	Mn(TDCPP)Cl	1-CH_3-Im	65	0.9	1.5
PhIO	Mn(TDCPP)Cl	2-CH_3-Im	62	0.4	1.8
H_2O_2	Mn(TDCPP)Cl	2-CH_3-Im	63	0.5	1.8

[a] Yields based on starting H_2O_2 or PhIO. Conditions: limonene/oxidant/B/Mn(P)Cl 200:10:14:1 in CH_2Cl_2/CH_3CN (1:2); Mn(P)Cl = 3 mM. [b] The two 8,9-epoxide diastereoisomers were formed in nearly the same amount for all the studied reactions.

Table VIII. Stereospecificity, Chemoselectivity, and Regioselectivity of the H_2O_2–Mn(TDCPP)Cl–Imidazole System: Comparison with the PhIO–Mn(TDCPP)Cl–Imidazole System[a,b]

		products		
substrate	oxidant	epoxide yield (%) (cis/trans ratio)	alcohols (%)	ketones (%)
cis-stilbene	PhIO	96 (97:3)[f]		
	H_2O_2	95 (97:3)		
trans-stilbene	PhIO	2 (0:100)		
	H_2O_2	2 (0:100)		
cyclohexene	PhIO	97	1[c]	1[d]
	H_2O_2	97	1[c]	1[d]
cyclooctene + cyclooctane	PhIO[b]	57	9	1
	H_2O_2[b]	72	10	2

substrate	oxidant	% regioisomers (ol + one)[e]			
n-heptane	PhIO	4	65	27	3
	H_2O_2	4	64	28	3

[a] Yields based on starting oxidant. Conditions A of Table II with either H_2O_2 or PhIO. [b] Yields based on starting oxidant, conditions as in Table I. [c] Cyclohex-2-en-1-ol. [d] Cyclohex-2-en-1-one. [e] Total yields, based on the oxidants, of heptan-1-ol, -2-ol, -3-ol, -4-ol, -2-one, -3-one, and -4-one were 31% with PhIO and 11.5% with H_2O_2. Proportions given in the table are for oxidation (ol + one) in positions 1, 2, 3, and 4 left to right, respectively. [f] With PhIO but in the absence of imidazole, the cis/trans ratio of stilbene oxides is 95:5.

1,2-epoxide was also obtained with 2-methylimidazole. This would be in agreement with a more hindered approach of the Mn=O species to the double bond plane on the side cis to the isopropenyl group.

Whatever may be the cause of variation of the epoxide ratio, it is noteworthy that identical ratios were always obtained when either PhIO or H_2O_2 was used with a given Mn porphyrin and imidazole cocatalyst. Moreover, the ratios of the cis and trans 1,2-epoxide isomers were also almost identical when either PhIO or H_2O_2 was used under identical conditions.

Regioselectivity of the Hydroxylation of *n*-Heptane. Oxidation of linear alkanes such as *n*-heptane by PhIO in the presence of different Mn porphyrins has been reported to give alcohols and ketones with a regioselectivity very dependent on the nature of the porphyrin.[1s,7,8] With Mn(TDCPP)Cl in the presence of imidazole, *n*-heptane was mainly oxidized on position 2 with a proportion of the regioisomers very different from that which could be expected on a statistical basis (Table VIII). Under identical conditions, H_2O_2 gave a regioselectivity of *n*-heptane oxidation identical with that obtained with PhIO.

Stereospecificity of Stilbene Epoxidation and Chemoselectivity of Oxidations of Cyclohexene or of Cyclooctene/Cyclooctane Mixtures. As indicated previously (Table IV), the Mn(TDCPP)Cl–H_2O_2–imidazole system oxidized *trans*-stilbene into the corresponding *trans*-epoxide with low yields and *cis*-stilbene to a 97:3 mixture of the corresponding *cis*- and *trans*-epoxides. Table VIII shows that, under similar conditions but with PhIO instead of H_2O_2, almost identical results concerning the stereospecificity of the reactions were obtained. It also shows that cyclohexene was epoxidized in good yield by the PhIO- as well as by the H_2O_2-dependent systems. With both systems, only minor amounts of the allylic oxidation products cyclohex-2-en-1-ol and cyclohex-2-en-1-one were formed. Finally, very similar results were obtained for the two systems in the oxidation of a 4:1 mixture of cyclooctane and cyclooctene. Both of them showed a marked preference for cyclooctene epoxidation but gave significant amounts of the products of cyclooctane oxidation, cyclooctanol, and cyclooctanone, in similar ratios.

Discussion

In the presence of imidazole, the Mn(porphyrin)Cl–PhIO and Mn(porphyrin)Cl–H_2O_2 systems exhibit (i) almost identical chemoselectivities for the oxidation of cyclohexene and of mixtures of cyclooctane and cyclooctene, (ii) identical stereospecificities for the epoxidation of stilbenes, and (iii) identical regioselectivities for the hydroxylation of *n*-heptane and for the epoxidation of isoprene and limonene. These systems also exhibit almost identical regioselectivities for the hydroxylation of adamantane with a large preference for tertiary C–H bond hydroxylation (Table V, ref 1n). Globally these results suggest that both systems involve a *common active species* which, according to the literature data reported on Mn(porphyrin)–PhIO systems,[5] could be a $Mn^V{=}O$ species.[22] In both systems, the nature of the porphyrin ligand and the presence and nature of an imidazole base exert a strong influence on the observed regioselectivities (see for instance Tables VI and VII). This is in agreement with an oxidizing species linked to Mn and containing the imidazole, such as a hexacoordinate intermediate imidazole–$Mn^V{=}O$ complex.

Thus, in the presence of imidazole, Mn porphyrins decompose H_2O_2 and transfer more or less efficiently one oxygen atom to alkenes or alkanes presumably via a high valent Mn=O intermediate. The efficiency of this transfer depends on the nature of the porphyrin and of the hydrocarbon substrate. With a reactive substrate such as cyclooctene or styrene in excess, epoxidation yields varied from about 40% with Mn(TPP)Cl to about 100% with Mn(TDCPP)Cl (Table II). By using the active catalyst Mn(TDCPP)Cl, monooxygenation yields based on H_2O_2 were almost quantitative with cyclooctene (Table II, condition A) but lower for alkanes (around 50% for cyclohexane or ethylbenzene) (Table V, condition A). It has been shown that Mn(III) porphyrins in the presence of imidazole are very prone to catalyze the dismutation of H_2O_2 into O_2 and H_2O.[11c] It is thus very likely that the variations in the monooxygenation yields are due to competition between the hydrocarbon substrate and H_2O_2 itself for reaction with the $Mn^V{=}O$ intermediate (eq 5 and 6).

$$[\mathrm{Mn}^{(V)}{=}\mathrm{O}]\ \begin{cases} \xrightarrow{+\mathrm{RH}} \mathrm{ROH} + \mathrm{Mn(III)} & (5)\\ \xrightarrow{+\mathrm{H_2O_2}} \mathrm{O_2} + \mathrm{H_2O} + \mathrm{Mn(III)} & (6)\end{cases}$$

Electron-rich alkenes would react more rapidly than alkanes with the electrophilic $Mn^V{=}O$ intermediate explaining the

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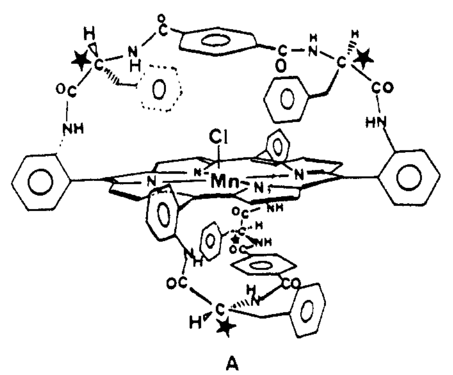
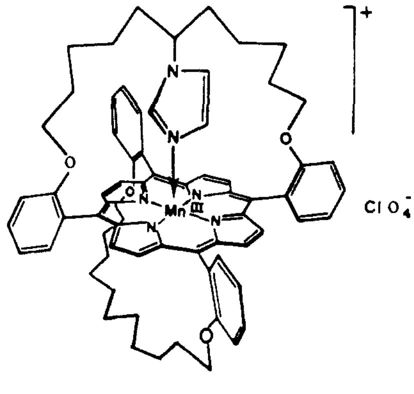
(22) The relative importance of the involvement of Mn(IV)- and Mn(V)-oxo species in Mn-porphyrin-catalyzed oxidations of hydrocarbons was recently discussed (ref 5f).

Chart II



A



B

quantitative epoxidation yields observed with the former and the more important consumption of H_2O_2 by dismutation and lower monooxygenation yields with the latter. Equations 5 and 6 also explain the much lower yields observed with trans disubstituted alkenes than with their cis isomers (Table IV), since it was previously reported that [(tetraarylporphyrin)Fe^V (or Mn)=O] species exhibited a very low reactivity toward *trans*-1,2-dialkyl-(or diaryl)ethylenes because of a hindered approach of the double bond to the porphyrin plane.[1q] The poor reactivity of these alkenes for [(tetraarylporphyrin)Mn^V=O] intermediates should favor H_2O_2 dismutation leading to low epoxide yields.

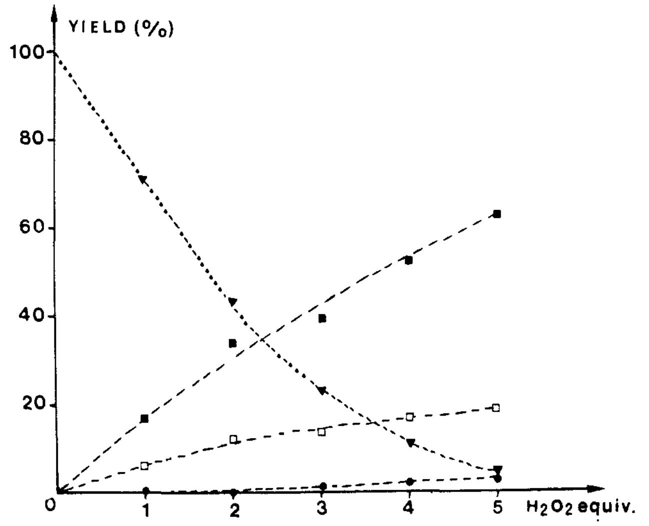


Figure 4. Conversion of adamantane to the corresponding alcohols and ketone by progressive addition of H_2O_2: (▼), % adamantane conversion; yields of adamantan-1-ol (■), adamantan-2-ol (□), and adamantan-2-one (●). Condition B of Table V.

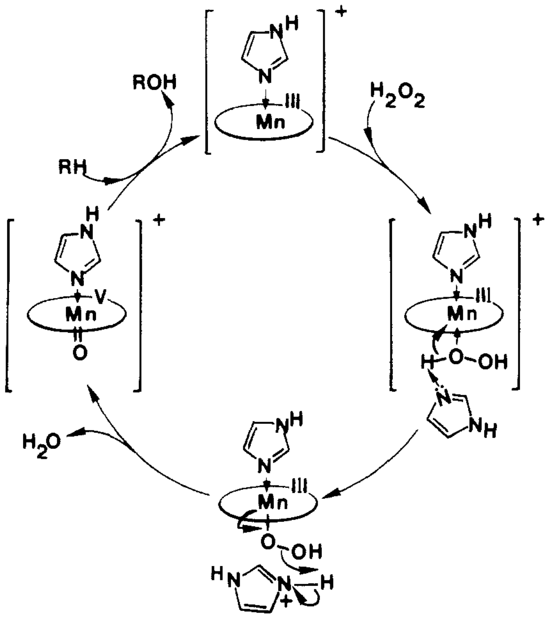


Figure 5. Tentative catalytic cycle for hydrocarbon oxidation by H_2O_2 catalyzed by Mn porphyrins and imidazole.

Fe porphyrins are able to catalyze the decomposition of H_2O_2 even in the absence of imidazole (Figure 1) but give low yields of hydrocarbon monooxygenation (Table I). Moreover Mn porphyrins, in the presence of nitrogen bases such as pyridine or triethylamine, also catalyze the decomposition of H_2O_2 but with lower yields of oxygen transfer to hydrocarbons (Table III). It is likely that, in these systems, dismutation of H_2O_2 is more favored. Further experiments will be required to understand why imidazole and some of its derivatives such as 2-methylimidazole make the Mn(TDCPP)Cl–H_2O_2 system so efficient for the transfer of one oxygen atom to alkenes or alkanes. It has been previously reported that imidazole was necessary both as a Mn ligand and as a base catalyst for efficient alkene epoxidation by H_2O_2 catalyzed by Mn porphyrins.[23] The necessary role of imidazole as a Mn ligand was shown by experiments using the chiral basket-handle Mn porphyrin A (Chart II). For steric reasons due to the close proximity of the handles to the porphyrin plane,[24] Fe(III) or Mn(III) complexes of this porphyrin were unable to bind pyridine or imidazole even in excess. Despite this steric hindrance, complex A catalyzed the epoxidation of styrene by PhIO (50% yield after 1 h) showing that its Mn(III) was able to interact with PhIO to form a high-valent Mn=O complex and that there was enough space for styrene to react with this species. However, A failed to catalyze styrene epoxidation by H_2O_2 under identical conditions and in the presence or absence of imidazole in excess (imidazole: A = 30). Thus, in the imidazole–catalyst A system in which imidazole could only act as a base but not as a Mn ligand, no epoxidation occurred even after 24 h. The necessary role of imidazole as a base was shown by experiments using the Mn(III) porphyrin catalyst B which contained an imidazole bound to the metal.[25] With this catalyst alone, no epoxidation of 2-methylhept-2-ene by H_2O_2 could be observed after 3 h (B/H_2O_2/alkene = 1:5:50), whereas the addition of 10 equiv of imidazole (relative to B) to the reaction mixture led to the immediate formation of the epoxide (43% in 15 min). The use of the two catalysts A and B illustrated well the two necessary roles of imidazole for an efficient transfer of an oxygen atom of H_2O_2 to hydrocarbons. Moreover the importance of imidazole as a base catalyst to favor the formation of Mn^V=O from Mn(III) and H_2O_2 has been already shown.[11c] Its role as an axial Mn ligand could be important (i) to favor the heterolytic cleavage of H_2O_2 (leading to Mn^V=O and H_2O) over a possible homolytic cleavage (leading to •OH) and (or) (ii) to favor hydrocarbon

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monooxygenation over H_2O_2 dismutation at the level of an imidazole–Mn^V=O intermediate (eq 5 and 6). These two roles of imidazole as a Mn ligand and as a base catalyst are illustrated in Figure 5 which shows a possible catalytic cycle for hydrocarbon monooxygenation by H_2O_2 in the presence of imidazole and a Mn porphyrin. This tentative catalytic cycle is in agreement with the aforementioned data on hydrocarbon oxidation by H_2O_2 and with literature data on reactions of H_2O_2 with Mn(III) porphyrins in the presence of imidazole.[11c] The lower rates of cyclooctene epoxidation found with other bases such as pyridine (Table III) could be due to their weaker ligand affinity for Mn(III) porphyrins[11c,21] and (or) to their lower capacity to catalyze the deprotonation of H_2O_2. The lower rates observed with 1-methylimidazole compared to imidazole or 2-methylimidazole (Table III) could be due to the possible deprotonation of imidazole bound to Mn by another imidazole molecule which should result in an increase of electron density of the metal and an easier heterolytic cleavage of the O–O bond of H_2O_2. Such a mechanism has been previously indicated to explain the effect of imidazole on the rates of *t*-BuOOH decomposition by Mn porphyrins.[14] This mechanism is naturally possible for imidazole or 2-methylimidazole but cannot occur in the case of 1-methylimidazole.

Another possible role of imidazole in such systems would be suggested by a recent paper on the reaction of *t*-BuOOH with Mn porphyrins in the presence of imidazole,[13] with kinetic evidence in favor of the intermediate formation of an equivalent of imidazole *N*-oxide.

Further investigations will be necessary to determine the various roles played by imidazole in oxidations by H_2O_2 catalyzed by Mn porphyrins. Whatever these roles may be, the aforementioned results show that the selected Mn(TDCPP)Cl–imidazole catalytic system led to very efficient biomimetic epoxidation of alkenes and hydroxylation of alkanes by using H_2O_2 instead of PhIO as an oxygen-atom donor.

Experimental Section

Physical Measurements. UV–vis spectra were recorded on an Aminco DW 2A spectrophotometer. Fast atom bombardment mass spectra (FAB MS) of metalloporphyrins were obtained on a VG 70-250 double-focussing instrument at the Institut Gustave Roussy, Villejuif. Mass-gas chromatography coupling analyses were performed on a Ribermag apparatus at the Ecole Normale Supérieure, Paris. Gas-chromatographic analysis was done with an Intersmat I.G. 120 FL chromatograph equipped with a hydrogen flame ionization detector. The glass column (length 3 m, internal diameter 3 mm) was packed with 5% FFAP on chromosorb (WAW 80/100 mesh) for aliphatic epoxides, with 5% OV210 on chromosorb for styrene oxide and with Carbowax 20M 5% for stilbene oxide. Imidazole consumption was quantitated by GLC (5% FFAP column) with an internal standard (C_6H_5I) and a calibration curve. The limonene oxidation products were studied on a Girdel (N°-11828) apparatus equipped with a SE-32 capillary column (50 m × 0.32 mm). The products formed were analyzed by comparison of their retention time with authentic samples and by mass-gas chromatography coupling analysis. Yields were determined by using internal standard methods. ^{1}H NMR spectra were recorded at 20 °C in $CDCl_3$ on a Brucker WM 250 spectrometer operating at 250 MHz.

Materials. Acetonitrile and dichloromethane, HPLC grade (S.D.S., Vitry, France), were used as received. Hydrogen peroxide (H_2O_2, 30% in H_2O, Prolabo) was stored at 5 °C and titrated every month.[26] All alkene or alkane substrates were purchased in their highest commercial purity, stored at 5 °C, and purified just before use. Styrene oxide was commercial reagent from Rhône Poulenc; cyclohexene oxide, cyclooctene oxide, and (+)-1,2-limonene oxide were purchased from Janssen and *trans*-stilbene oxide from Aldrich.

The other epoxides were prepared with 3-chloroperbenzoic acid by a standard procedure[27] and purified on a silica gel column. (+)-8,9-Limonene oxide was synthesized by the peroxybenzimidic acid method,[28] purified by gas chromatography, and identified by ^{1}H NMR.[29] *trans*-1,2-Limonene oxide was prepared according to[29a] by hydrolysis of the commercial 1,2-epoxide (ratio cis:trans = 50:50), tosylation of the resulting diol, and cyclization by methanolic KOH.

Alcohols, ketones, deoxybenzoin, diphenylacetaldehyde, phenylacetaldehyde, and benzaldehyde were bought in their highest commercial purity and used as received. Nitrogenous bases were purchased from Janssen and used without purification except for 1-methylimidazole, isopropylamine, dicyclohexylamine, and pyridine which was distilled over KOH and kept over molecular sieves.

Porphyrins. 5,10,15,20-Tetraphenylporphyrin (H_2TPP) was synthesized according to the method of Adler et al.[30] *meso*-tetraphenylchlorin was removed by treatment with dicyanodichloroquinone (DDQ) according to the method of Smith et al.[31] 5,10,15,20-Tetrakis(pentafluorophenyl)porphyrin (H_2TFPP) was prepared as previously reported.[32] 5,10,15,20-Tetrakis(2′,4′,6′-trimethylphenyl)porphyrin (H_2TMP) and 5,10,15,20-tetrakis(2′,6′-dichlorophenyl)porphyrin (H_2TDCPP) were obtained the first time by reaction of pyrrole (freshly distilled) with the corresponding arylaldehydes with dry $Zn(OAc)_2$ as template in dry 2,4,6-trimethylpyridine in a sealed steel tube at 220 °C.[33] More recently the improved synthesis of Lindsey et al. was used[34] with modifications similar to those published in the literature.[35] Metallation was performed by conventional methods.[36,37]

Iodosylbenzene was prepared by hydrolysis of iodobenzene dichloride with aqueous sodium hydroxide[38] carefully dried under reduced pressure and kept at 5 °C.

Hydrogen peroxide titration was done according to the photocolorimetric method of P. Bonet-Maury.[26] For reactions whose results are on Figure 1 and Table III, the H_2O_2 concentrations were measured on 0.1 mL withdrawn from the reaction mixture. To this aliquot was added 0.1 mL of CH_2Cl_2, 0.2 mL of H_2SO_4 1 N, and 2 drops of the stock titanium solution. This mixture was diluted with water (final volume 3 mL), and the porphyrin was extracted with 1 mL of CH_2Cl_2. Then, the H_2O_2 content of the H_2O phase was measured as described previously.[26]

Oxidation Procedure and Product Analyses. All alkene or alkane substrates were purified just prior to use by passage through a column of basic alumina (activity I) and checked by gas chromatography to ensure that no oxidation products were present before reaction. Most reactions were carried out in a 5-mL tube equipped with a serum cap and a stirring bar. Metalloporphyrins and imidazole were dissolved in a CH_2Cl_2/CH_3CN (1:1) solvent mixture. The coordination of imidazole was checked by visible spectroscopy in the Soret part of the spectra.[39,14] The hydrocarbon substrate was then added. For reactions done under argon, the reaction mixture was purged by a three thaw–freeze cycle. Hydrogen peroxide was added by using a microsyringe. GLC analysis was performed on aliquots withdrawn directly from the reaction mixture. Yields were determined, unless noted, by GLC with internal standard methods. No reaction occurred in the absence of the catalysts (porphyrin or nitrogen base) in reactions performed with similar temperature and time of reactions for every substrate. All reactions were done at ambient temperature.

Two main types of procedure were used to study the oxidations by H_2O_2. The first one concerned the oxidation of hydrocarbons used in excess in order to determine the maximum yield of oxygen-atom transfer to different substrates based on starting H_2O_2 or the regioselectivity or chemoselectivity of the reactions. In this case, a large excess of substrates was used to avoid as much as possible dismutation of H_2O_2 and overoxidation of primary monooxygenation products such as epoxides or alcohols. These reactions were done under anaerobic conditions.

The second type of procedure was used in order to convert the hydrocarbons in their oxidation products. For this purpose, excess of H_2O_2 was used, and most reactions were performed under aerobic conditions for alkenes since we found that the presence of O_2 had no significant influence on the results. In contrast, oxidation of alkanes were done

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under anaerobic conditions since we found that, at least for some of them, the presence of O_2 led to slight changes in the alcohol–ketone ratio.

Typical Procedure for Oxidations Using an Excess of Hydrocarbon Relative to the Oxidant (Condition A of Table II). H_2O_2 (40 μmol, 30% in H_2O, 0.004 mL) was added once under argon to a deaerated CH_2Cl_2/CH_3CN solution (0.25 mL:0.25 mL) of Mn porphyrin (2 μmol) and imidazole (20 μmol, 1.36 mg) containing hydrocarbon (1.6 mmol) and the internal standard. Reaction was followed by GLC. It was achieved in less than half an hour for alkene epoxidation and in about 1 h for alkane hydroxylation. The same procedure, with minor variations, was used for the reactions described in Tables I and V–VIII.

Typical Procedure for Oxidations Using an Excess of Oxidant Relative to the Substrate (Condition B of Tables II, IV, and V). A solution of 400 μmol of H_2O_2 (H_2O_2 30% in H_2O, 0.04 mL) and imidazole (40 μmol, 2.7 mg) in CH_3CN (0.36 mL) was progressively added by 20-μL portions in 0.75 h to a solution of the metalloporphyrin catalyst (2 μmol) in CH_2Cl_2 (0.13 mL)–CH_3CN (0.13 mL) containing imidazole (8 μmol, 0.54 mg) and the hydrocarbon substrate (80 μmol). After 1 h the internal standard was added, and the reaction mixture was analyzed by GLC. Aliquots of the solution (0.01 mL) were taken, diluted 300 times in CH_2Cl_2, and then analyzed by UV–vis spectroscopy to follow the evolution of the catalyst.

For reactions whose results were given in Table III, this typical procedure was slightly different as imidazole or the other nitrogen bases were added once at the beginning of the reaction. Moreover, different substrate/H_2O_2/nitrogen base ratios were used.

Reaction of Hydrogen Peroxide with *cis*-Stilbene Catalyzed by Mn(TDCPP)(Cl) in the Presence of Imidazole. Hydrogen peroxide (H_2O_2 30%, 0.04 mL, 400 μmol) and imidazole (40 μmol, 2.7 mg) in CH_3CN (0.36 mL) was slowly added (0.75 h) to a solution of *cis*-stilbene (80 μmol, 14.4 mg), Mn(TDCPP)(Cl) (2 μmol, 1.9 mg), and imidazole (8 μmol, 0.54 mg) in CH_2Cl_2 (0.13 mL)–CH_3CN (0.13 mL). After complete addition, the mixture was stirred for 0.25 h. Iodobenzene (80 μmol) was added as the internal standard. Analysis by GLC showed the presence of *cis*-stilbene oxide in 92% yield based on starting *cis*-stilbene, 2% of *trans*-stilbene oxide, and 2% of deoxybenzoin.

Solvents of the reaction mixture were removed under reduced pressure. Pentane (10 mL) was added to precipitate Mn(TDCPP)(Cl). The mixture was passed through a plug of glass wool, and the pentane was removed under reduced pressure. Analysis by ^{1}H NMR spectroscopy ($CDCl_3$) showed the presence of *cis*-stilbene oxide (s, $\delta = 4.25$ ppm), a trace of *trans*-stilbene oxide (s, $\delta = 3.85$ ppm), and of deoxybenzoin (s, $\delta = 4.2$ ppm). These ^{1}H NMR results completely confirmed the yield determination made by GLC.

Reaction of Hydrogen Peroxide (or Iodosylbenzene) with (+)-Limonene Catalyzed by Mn Porphyrins and Imidazole. Oxidant (20 μmol, H_2O_2 30% in H_2O:0.002 mL or PhIO:4.4 mg) was added to a solution of (+)-limonene (400 μmol, 54.5 mg), imidazole if present (28 μmol), and metalloporphyrin catalyst (2 μmol) in 0.2 mL of CH_2Cl_2 and 0.4 mL of CH_3CN, and the reaction mixture was stirred for 1 h at room temperature.

The ratios of regioisomers and stereoisomers were determined on the crude mixture by GLC with a 50 m, SE-32 capillary column, (in these conditions both stereoisomers for each monoepoxide were separated). Pure samples of 8,9-[28] and 1,2-monoepoxides and of *trans*-1,2-monoepoxide[29] were prepared for GLC calibration. In order to confirm the GLC measurements, a ^{1}H NMR analysis of the mixture of 1,2- and 8,9-monoepoxides was performed after separation of the monoepoxides from the crude mixture on a silica gel column (eluent/CH_2Cl_2). The 1,2-epoxides/8,9-epoxides ratio and the ratio of the cis and trans isomers of the 1,2-epoxide were determined from the signal intensities of the protons in α-position of the epoxide oxygen atom. These signals were observed at 2.98 and 3.04 ppm, respectively, for the trans and cis isomers of the 1,2-epoxide and at 2.64 and 2.56 ppm for the stereoisomers of the 8,9-epoxide.

Reaction of Hydrogen Peroxide (or Iodosylbenzene) with Isoprene Catalyzed by Mn Porphyrins and Imidazole. Oxidant (96 μmol, H_2O_2 30% in H_2O:0.0096 mL or PhIO:21 mg) was added to a solution of isoprene (384 μmol, 0.038 mL), imidazole if present (58 μmol, 4 mg), and metalloporphyrin catalyst (2.4 μmol) in 0.275 mL of CD_3CN and 0.275 mL of CCl_4. The reaction mixture was stirred for 1 h at room temperature. After addition of the internal standard ($(CH_3)_3SiOSi(CH_3)_3$), the crude mixture was analyzed by ^{1}H NMR. Yields were measured by integration of the signal at 1.40 ppm (CH_3 of the 1,2-epoxide) and at 1.57 ppm (CH_3 of the 3,4-epoxide).

Registry No. Fe(TDCPP)Cl, 91042-27-2; Fe(TDCPP)BF_4, 117226-86-5; Fe(TPP)Cl, 16456-81-8; Mn(TDCPP)Cl, 91463-17-1; Mn(TDCPP)BF_4, 117226-88-7; Mn(TPP)Cl, 32195-55-4; Im, 288-32-4; C, 931-88-4; S, 100-42-5; Mn(TMP)Cl, 85939-49-7; Mn(TFPP)Cl, 79968-43-7; 2-CH_3-Im, 693-98-1; 4-CH_3-Im, 822-36-6; 1-CH_3-Im, 616-47-7; H_2O_2, 7722-84-1; Et_3N, 121-44-8; *i*-$PrNH_2$, 75-31-0; $(C_6H_{11})_2NH$, 101-83-7; PhCHO, 100-52-7; $PhCH_2CHO$, 122-78-1; $PhCH_2COPh$, 451-40-1; PhIO, 536-80-1; cyclooctene epoxide, 286-62-4; styrene epoxide, 96-09-3; benzimidazole, 51-17-2; 1,2,4-triazole, 288-88-0; pyridine, 110-86-1; 2,6-di-*tert*-butylpyridine, 585-48-8; 2-methylhept-2-ene, 627-97-4; 2-methylhept-2-ene epoxide, 3776-34-9; cyclohexene, 110-83-8; cyclohexene epoxide, 286-20-4; non-1-ene, 124-11-8; non-1-ene epoxide, 28114-20-7; *cis*-hex-2-ene, 7688-21-3; *cis*-hex-2-ene epoxide, 6124-90-9; *trans*-hex-2-ene epoxide, 6124-91-0; *trans*-hex-2-ene, 4050-45-7; *cis*-stilbene, 645-49-8; *trans*-stilbene, 103-30-0; *cis*-stilbene epoxide, 1689-71-0; *trans*-stilbene epoxide, 1439-07-2; cyclohex-2-en-1-ol, 822-67-3; cyclohex-2-en-1-one, 930-68-7; cyclohexane, 110-82-7; cyclohexanol, 108-93-0; cyclohexanone, 108-94-1; cyclooctane, 292-64-8; cyclooctanol, 696-71-9; cyclooctanone, 502-49-8; adamantane, 281-23-2; adamantan-1-ol, 768-95-6; adamantan-2-ol, 700-57-2; adamantan-2-one, 700-58-3; ethylbenzene, 100-41-4; 1-phenylethanol, 98-85-1; acetophenone, 98-86-2; indan, 496-11-7; indan-1-ol, 6351-10-6; indan-1-one, 83-33-0; tetralin, 119-64-2; 1-tetralol, 529-33-9; 1-tetralone, 529-34-0; isoprene, 78-79-5; isoprene 1,2-epoxide, 1838-94-4; isoprene 3,4-epoxide, 7437-61-8; (+)-limonene, 5989-27-5; *cis*-limonene 1,2-epoxide, 4680-24-4; *trans*-limonene 1,2-epoxide, 6909-30-4; *cis*-limonene 8,9-epoxide, 28098-68-2; *trans*-limonene 8,9-epoxide, 28098-67-1; heptane, 142-82-5; heptan-1-ol, 111-70-6; heptan-2-ol, 543-49-7; heptan-3-ol, 589-82-2; heptan-4-ol, 589-55-9; heptan-2-one, 110-43-0; heptan-3-one, 106-35-4; heptan-4-one, 123-19-3.