Tetrahedron Vol 40, No 15, pp 2847 to 2857, 1984
Printed in the U S A

0040-4020/84 $3.00 + 00
Pergamon Press Ltd

REGIOSELECTIVITY OF OLEFIN OXIDATION BY IODOSOBENZENE CATALYZED BY METALLOPORPHYRINS : CONTROL BY THE CATALYST

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(Received in France 31 January 1984)

Abstract - The regioselectivity of the oxidation of three monosubstituted olefins, 6-phenoxyhex-1-ene, hex-1-ene and styrene, by iodosobenzene in the presence of various Fe-, Mn- or Cr-tetraarylporphyrins, was studied. It was found that, besides epoxides, known products from such systems, allylic alcohols and aldehydes were formed, the latter not being derived from the corresponding epoxides. The relative importance of these reactions greatly depends upon both the metal and porphyrin constituents of the catalyst. More particularly, the competition between epoxidation and allylic hydroxylation can be efficiently controlled by non-bonded interactions between the olefin and porphyrin substituents. No hydroxylation of the aromatic rings and no oxidative dealkylation of the ether function was detected.

Cytochrome P-450 dependent monooxygenases catalyze the oxidation by dioxygen of a wide range of substrates including alkanes and olefins[1-3]. These cytochromes are also able to catalyze the transfer of an oxygen atom from oxygen donors such as alkylhydroperoxides[4-6] or iodosobenzene[7,8] to the same substrates.

Simple Fe-[9] or Mn-porphyrins[10] have also been shown to catalyze the transfer of the oxygen atom of iodosobenzene into substrates in very mild conditions, leading to alcohols from alkanes and epoxides from olefins. Epoxidations of olefins upon transfer of the oxygen atom of hypochlorite catalyzed by a Mn-porphyrin have also been reported[11]. Concerning the metalloporphyrin-catalyzed oxidation of olefins, several studies have been devoted to the epoxidation reaction which is generally the major route involved[9, 10]. Electron rich olefins give the highest yields of epoxide with iodosobenzene and Fe-[9f] as well as Mn-porphyrins[10f, 12], indicating that the active oxygen species is electrophilic in nature. Cis-1,2-disubstituted olefins are more easily epoxidized than their trans isomer[9a,f,g], this result having been interpreted by a more difficult approach of trans olefins to the iron-oxo active species due to unfavorable interactions between olefin and porphyrin substituents[9g]. Epoxidation of stilbenes[9a], cis- and trans-4-methylpent-2-ene[9f] by C_6H_5IO and Fe(tetraphenylporphyrin = TPP)(Cl) is stereospecific whereas epoxidation of stilbenes by C_6H_5IO catalyzed by Mn(TPP)(Cl) is not[10b]. Very recently, by using chiral iron porphyrins as catalysts, various substituted styrenes were epoxidized by iodosoarenes with enantiomeric excesses as high as 51 % for p-chlorostyrene oxide[9h].

Chromium porphyrins have also been found to catalyze the epoxidation of cyclohexene, norbornene, styrene, cis- and trans-stilbene and cyclo-octene, but to give low yields of epoxide with cyclohexene and cyclooctene as substrates[13, 9b]. Although several studies have been devoted to epoxidations performed by C_6H_5IO-metalloporphyrin systems, very few data concerning the other oxidations of olefins that compete with epoxidations have been so far reported. The only available data concern the allylic hydroxylation of cyclohexene by iodosoarenes in the presence of iron or chromium porphyrins[13-15], as well as the formation of arylacetaldehydes upon oxidation of styrenes by iodosoarenes and iron porphyrins[9h]. Such reactions also compete with epoxidation during the oxidation of certain olefins by cytochrome P-450[16-18].

In order to understand the oxidation of olefins catalyzed by cytochrome P-450 and to design highly selective metalloporphyrin-based chemical systems for olefin oxidation, it is important to determine the nature of the different routes of olefin oxidation by the metalloporphyrin-iodosobenzene system which mimics quite well the cytochrome P-450-iodosobenzene system and which is presently the best known model system for oxidation by oxygen atom transfer. It is also important to know the factors which determine the relative importance of the different oxidation reactions occuring on the olefin and therefore the chemi- and regioselectivity of the oxidation. The present results are concerned with the oxidation of the monosubstituted olefins hex-1-ene, styrene, and 6-phenoxyhex-1-ene, a polyfunctional compound that we have previously used to study the regioselectivity of the oxidation catalyzed by various cytochrome P-450 forms[19], by iodosobenzene in the presence of several metalloporphyrins. They show that these olefins are not only epoxidized but also hydroxylated on the allylic positions and oxidized to the corresponding aldehydes. The relative importance of these reactions greatly depends upon the nature of the metal and of the porphyrin and can be controlled to a great extent by nonbonded interactions between the olefin and porphyrin substituents.

RESULTS

Oxidation of 6-phenoxyhex-1-ene 1, hex-1-ene and styrene by C_6H_5IO in the presence of Fe(TPP)(Cl)

6-phenoxyhex-1-ene was chosen as the substrate for the study of the regioselectivity of the C_6H_5IO-metalloporphyrin systems for two reasons: (i) it involves not only a double bond and allylic C-H bonds but also three kinds of potentially reactive C-H bonds, one of them being in the α-position of the $-OC_6H_5$ moiety, and an aromatic ring electron-enriched by the O-alkyl group ; (ii) it was found to have a good affinity for microsomal cytochromes P-450 and its oxidation by various cytochromes P-450 was studied earlier[19]. Treatment of compound 1 by C_6H_5IO in the presence of catalytic amounts of Fe(TPP)(Cl) in benzene leads to two major products in nearly equal amounts, the epoxide 2 and the allylic alcohol 3, and as a minor product the aldehyde 4 (Scheme 1). The reaction products were analyzed by g.l.c. (gas-liquid-chromatography) and mass spectrometry, their structure having been established by comparison with authentic samples prepared by chemical techniques. With 10 mM Fe(TPP)(Cl) and a 1:5:100 ratio of the Fe(TPP)(Cl): C_6H_5IO: 1 reactants in benzene, the oxidant is completely consumed in about 0.5 h at 20°C, leading to a nearly quantitative formation of iodobenzene and to products 2, 3 and 4 in respective yields of 40, 48 and 1.4%, based on starting C_6H_5IO (Table 1). The initial rate of the reaction corresponds to 0.45 mole of oxidized product (2 + 3 + 4) formed per mole of catalyst per min.

Scheme 1

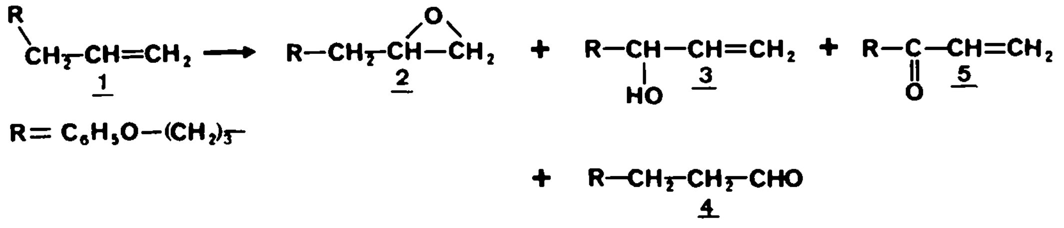


Table 1. Oxidation of olefin 1, styrene and hex-1-ene by iodosobenzene catalyzed by various metallotetraphenylporphyrins(a)

PRODUCTS	Yields(b)		
	Fe(TPP)(Cl)	Mn(TPP)(Cl)	Cr(TPP)(Cl)
2	40 ± 3	45 ± 4	nd(c)
3	48 ± 4	34 ± 2	9 ± 0.8
4	1.4 ± 0.1	2 ± 0.1	nd(c)
5	nd(c)	8 ± 0.6	11 ± 1
Styrene oxide	75 ± 7	86 ± 6	65 ± 5
Phenylacetaldehyde	3 ± 0.3	3 ± 0.3	nd(c)
Hex-1-ene oxide	40 ± 4	29 ± 3	-
Hex-1-en-3-ol	3 ± 0.3	4 ± 0.4	-
Hex-1-en-3-one	nd(c)	3 ± 0.3	-
Hexanal	nd(c)	1 ± 0.1	-

(a) The assays were performed as described in the experimental section. (b) % yields based on C_6H_5IO (c) not detected.

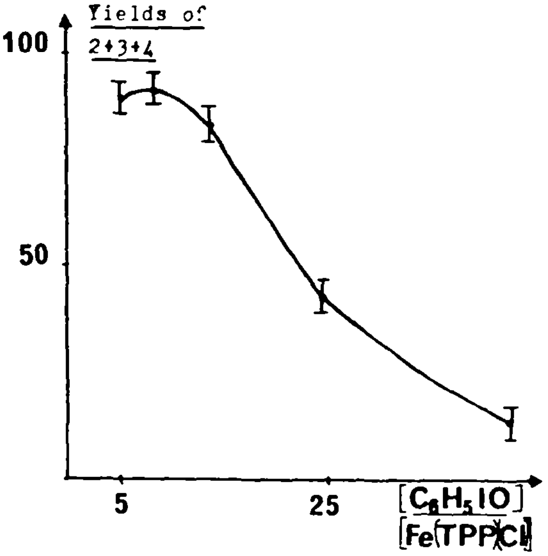


Figure 1. Variations of the yields of (2 + 3 + 4) as a function of the oxidant : catalyst ratio.
Conditions : 1 M 1, 10 mM Fe(TPP)(Cl) in aerobic C_6H_6 at 20°C.

As shown in Fig. 1, the optimal yield is obtained with a ratio of C_6H_5IO to Fe(TPP)(Cl) between 5 and 10. With higher concentrations of the oxidant, one observed a marked decrease of the yield based on starting C_6H_5IO as well as significant destruction of the catalyst (followed by visible spectroscopy) presumably by an irreversible oxidation of the porphyrin ring[9c]. None of products 2, 3 and 4 was formed if any component of the system (Fe(TPP)(Cl) or C_6H_5IO) is omitted. The aldehyde 4 is not derived from isomerization of the epoxide 2 in the medium, since treatment of 2 by the complete system, omitting the olefin 1, under identical conditions, fails to give 4. It is noteworthy that the Fe(TPP)(Cl)-C_6H_5IO system does not either lead to any hydroxylation of the aromatic ring of compound 1 nor to any formation of phenol and hex-5-ene-1-al which could have been derived from the hydroxylation of a C-H bond in the α-position relative to the -OC_6H_5 group. Moreover, the formation of the primary allylic alcohols, Z- and E-6-phenoxyhex-2-enols, which are isomers of compound 3, could not be detected(by mass spectrometry : authentic samples were available for comparison).

The oxidation of hex-1-ene under identical conditions leads to a similar yield of the corresponding epoxide but to a considerably lower yield of the secondary allylic alcohol hex-1-en-3-ol (Table 1). Styrene is oxidized in very good yield to the corresponding epoxide and to minor amounts of phenylacetaldehyde (Table 1), as previously reported[9h].

Oxidation of 1, hex-1-ene and styrene by C_6H_5IO in the presence of Fe-, Mn- and Cr-porphyrins

Table 1 compares the results from the oxidation of these three olefins by C_6H_5IO in the presence of metalloporphyrin catalysts which differ only by the nature of the metal. Fe(TPP)(Cl) and Mn(TPP)(Cl) give very similar results, the main difference between the two corresponding systems being the formation of significant amounts of the allylic ketones hex-1-en-3-one and its

6-phenoxy derivative, 5, with Mn(TPP)(Cl), these ketones being undetected with Fe(TPP)(Cl). One observes the formation of aldehydes from oxidation of the three olefins by the Mn(TPP)(Cl)-dependent system whereas the aldehyde derived from hex-1-ene was not detected from oxidation by the Fe(TPP)(Cl)-dependent system.

The Cr(TPP)(Cl)-C_6H_5IO system gives very different results, since it leads only to allylic oxidation products in the case of olefin 1 and fails to oxidize the olefins investigated to the corresponding aldehydes.

Table 2 lists results from the oxidation of styrene and olefin 1 by C_6H_5IO in the presence of Fe(or Mn in one case)-tetraaryl-porphyrins, which differ only by the nature of the substituents of the phenyl groups in the meso position of the porphyrin ring. The presence of a single electronwithdrawing or electron-donating substituent (Cl or CH_3 respectively) in the para position of the phenyl groups, as in Fe(TpClPP(data not shown) or TTP)(Cl) has no significant influence on the ratio of oxidation products derived from 1 or styrene. On the contrary, the iron tetrakis-(pentafluorophenyl)-porphyrin, where all the phenyl substituents are fluorine atoms, leads to an important modification of the chemi- and regioselectivity of olefin 1 oxidation. In particular, it leads to a consirable increase of the epoxide : allylic alcohol ratio (3. instead of 0.86 with Fe(TPP)(Cl)) as well as a significant increase of the aldehyde proportion in the oxidation product mixture (4 % instead of 1.5 % with Fe(TPP)(Cl)). Very similar conclusions can be drawn from the comparison of 1 oxidation catalyzed either by Mn(tetrakis-pentafluorophenylporphyrin)(Cl) or by Mn(TPP)(Cl). The total yield of the oxidation products amounts to above 90 % in both cases, but the epoxide:allylic oxidation products (alcohol + ketone) ratio increases from 1.1 in the case of Mn(TPP)(Cl) to about 2.1 in the case of the fluoroporphyrin catalyst. As for their iron analogues, the aldehyde proportion increases from 2.2 % to about 5.1 % upon substitution of the phenyl rings of the Mn-porphyrin by fluorine atoms. A similar increase of the aldehyde proportion is also observed upon styrene oxidation by Fe- or Mn-porphyrins upon substitution of their phenyl hydrogens by fluorine atoms.

Two iron-"basket-handle" porphyrins which are derived from TPP by the presence of two alkyl chains on both sides of the porphyrin plane[20] (Fig. 2) have been used as catalysts. In the two complexes Fe(BH_1)(Cl) and Fe(BH_2)(Cl) (see Fig. 2 for the nomenclature), the iron environment

Table 2. Oxidation of olefin 1 and styrene by iodosobenzene catalyzed by various Fe- or Mn-tetra-aryl-porphyrins $^{(a)}$

PRODUCTS	Yields$^{(b)}$						
	Fe(TPP)(Cl)	Fe(TTP)(Cl)	Fe(TFPP)(Cl)	Mn(TFPP)(Cl)	Fe(BH_1)(Cl)	Fe(BH_2)(Cl)	Fe(TMP)(Cl)
2	40 ± 3	42 ± 3	26 ± 2	58 ± 4	40 ± 3	41 ± 3	44 ± 3
3	48 ± 4	44 ± 3	9 ± 0.8	25 ± 2	11 ± 1	10 ± 1	2.3 ± 0.3
4	1.4 ± 0.1	1.5 ± 0.1	1.5 ± 0.1	4.8 ± 0.5	8.5 ± 0.7	8 ± 0.7	nd$^{(c)}$
5	nd$^{(c)}$	nd$^{(c)}$	nd$^{(c)}$	5 ± 0.3	nd$^{(c)}$	nd$^{-c)}$	nd$^{(c)}$
Styrene oxide	75 ± 7	72 ± 7	50 ± 5	77 ± 6	44 ± 4		70 ± 7
Phenylacetaldehyde	3 ± 0.3	3 ± 0.3	3 ± 0.3	6.5 ± 0.5	15 ± 1.5		nd$^{-c)}$

For notes(a), (b), (c) see Table 1. Abbreviations used for mesotetraarylporphyrins:aryl = C_6H_5 (TPP), 4-methylphenyl (TTP), C_6F_5 (TFPP), 2,4,6-trimethylphenyl (TMP). BH_1 and BH_2 as indicated in Figure 2.

is considerably modified, when compared to Fe(TPP)(Cl), as also should the approach of the substrate. A similar situation may occur in the active site of cytochrome P-450, the protein residues which are in close proximity of the heme being able to control at least in part the substrate approach.

Fe(BH_1)(Cl) and Fe(BH_2)(Cl) are also able to catalyze the oxidation of olefins by C_6H_5IO, although more slowly than Fe(TPP)(Cl). In conditions identical to those described previously, C_6H_5IO is completely transformed into C_6H_5I within 3 h only. The yields of oxidation products derived from olefin 1 or styrene are indicated in Table 2. The oxidation products profiles given by the two iron-"basket-handle" porphyrins are nearly identical. However, this profile is very different from that observed with Fe(TPP)(Cl), the allylic alcohol : epoxide ratio having decreased from 1.2 to about 0.25, and the aldehyde proportion in the oxidation products mixture having increased from 1.5 % to about 14 % in the case of 1, and from to 3.8 % to 25.4 % in the case of styrene.

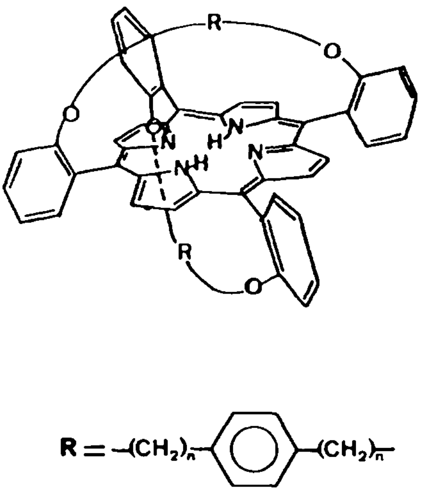
Finally, Fe(tetramesitylporphyrin = TMP)(Cl) was used as a catalyst particularly hindered around the iron. This catalyst leads almost exclusively to the epoxides of styrene and olefin 1 since it fails to give aldehydes and gives only very low amounts of the allylic alcohols 3 (Table 2).

DISCUSSION

In the presence of the different metalloporphyrin catalysts investigated in this study, iodosobenzene oxidizes the polyfunctional olefin 1 only at the level of its double bond, leading to the corresponding epoxide and aldehyde, and at the level of its allylic C-H bonds, leading to allylic alcohols and ketones. With all tested catalysts, no hydroxylation of the phenyl ring of 1 and no hydroxylation of the non-allylic CH_2 positions could be detected. The strong preference of the C_6H_5IO-metalloporphyrin systems for the oxidation of a double bond or allylic C-H bonds over that of an aromatic ring or less activated C-H bonds has also been observed for cytochrome P-450-C_6H_5IO systems[19]. Actually, compounds 2, 3 and 4 are the only products that could be detected upon incubation of 1 with C_6H_5IO and hepatic microsomal cytochromes P-450 from phenobarbital-treated rats[19]. Minor amounts of the phenol derived from para-hydroxylation of the phenyl ring of 1 have been detected only when the enzymatic oxidation was performed in the presence of NADPH and O_2, the usual cofactors of cytochrome P-450 dependent monooxygenases[19].

The present study confirms that the iron- and manganese-catalysts lead to epoxides as major products and also shows that, at least in the case of monosubstituted olefins like 1 or hex-1-ene, allylic alcohols are formed as important secondary products. It also establishes the occurence of a new oxidative transformation of monosubstituted olefins by metalloporphyrin-C_6H_5IO systems leading finally to the corresponding aldehydes. The formation of arylacetaldehydes upon oxidation of styrenes by C_6H_5IO and iron-porphyrins was very recently mentioned[9h] ; our results show that this aldehyde formation is a general reaction occuring on simple monosubstituted alkenes not only with iron- but also with manganese-porphyrins. Recent results showed that such aldehydes formation also occurs upon cytochrome P-450-dependent oxidation of olefin 1 and styrene by C_6H_5IO[17]. In these enzymatic oxidations as well as in the chemical oxidations described in this paper, the aldehydes do not derive from an isomerization of the corresponding epoxide which is the major reaction product.

The formation of three observed classes of products, the epoxides, allylic alcohols and aldehydes can be easily interpreted by considering the mechanism generally admitted for olefins epoxidation and alkanes hydroxylation by C_6H_5IO in the presence of Fe- or Mn-porphyrins[9,10]. The active species formed upon reaction of C_6H_5IO with these catalysts, which is described as a high-alent Fe(V)=O (or Mn(V)=O) complex, exhibits a free radical-like reactivity[9,10]. Thus, it can react with olefins such as 1 or hex-1-ene either by abstraction of an allylic hydrogen leading to the



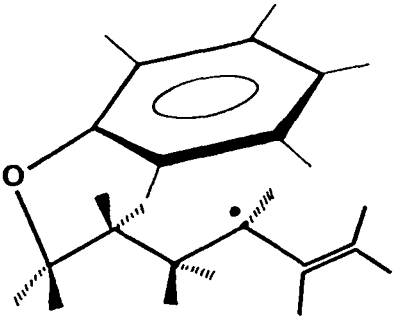


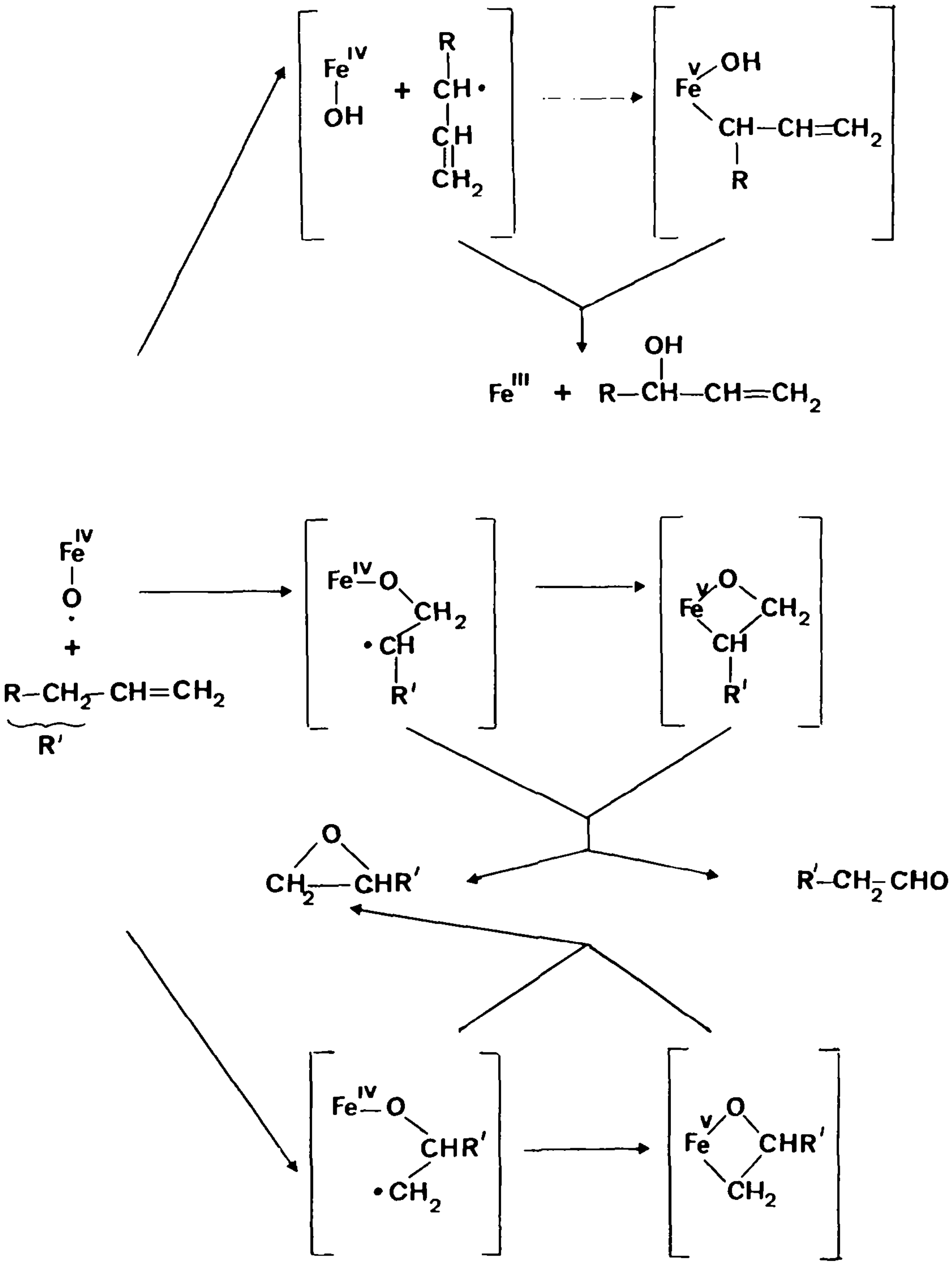
Figure 2 : "Basket-handle" porphyrins (BH). BH$_1$ corresponds to n = 3. BH$_2$ corresponds to n = 4.

Figure 3 : Possible conformation of the allylic radical of 1.

corresponding allylic free radical, or by addition to the double bond leading to an Fe(IV)-O-CH$_2$-$\dot{C}$HR or Fe(IV)-OCHR-$\dot{C}$H$_2$ radical (Scheme 2). An oxidative transfer of the OH ligand of the intermediate Fe(IV)-OH complex gives the allylic alcohols, 3 and hex-1-en-3-ol. An analogous intramolecular oxidation of the Fe(IV)-OCH$_2\dot{C}$HR or of the Fe(IV)-CHR-$\dot{C}$H$_2$ radical gives the observed epoxides. The epoxides could be derived from a combination of the carbon free radical with iron leading to a four-membered metallocycle followed by a reductive elimination of the two cis-ligands of the iron (Scheme 2). The formation of such metallocycles has been proposed in the epoxidation of olefins by Cr=O complexes[21], and such σ-alkyl Fe(V)-R' complexes have been proposed as intermediates in alkanes hydroxylation by cytochrome P-450[22]. The Fe(IV)-OCH$_2$-$\dot{C}$HR radicals, or the corresponding metallocycles, are the common precursors of the observed epoxides and of the aldehydes. The latter can be derived either by oxidation of the radical by Fe(IV) with elimination of a hydrogen in the β-position or from a concerted decomposition of the metallocycle involving a 1,2-hydrogen migration (Scheme 2). In that regard, it is noteworthy that such a 1,2-hydrogen migration has been recently demonstrated during oxidation of 1,1-dichloroethylene into dichloroacetaldehyde by cytochrome P-450[23]. Actually, as we mentioned it earlier,two radicals can be formed upon addition of Fe(IV)O• to the double bond of the olefins RCH=CH$_2$ depending upon the sense of the addition.

Aldehydes should derive from the Fe(IV)-OCH$_2$-$\dot{C}$HR radicals whereas one could expect that ketones RCOCH$_3$ would derive from the less stable Fe(IV)-OCHR$\dot{C}$H$_2$ radicals by analogous mechanisms. However, such methylketones have never been observed upon oxidation of olefin 1, styrene and hex-1-ene by all the systems used in this study[24].

If one compares the regioselectivity of the oxidations of hex-1-ene and olefin 1 by C$_6$H$_5$IO catalyzed by Mn(TPP)(Cl) or Fe(TPP)(Cl), one notes a strikingly larger importance of the allylic oxidation in the case of olefin 1. The allylic alcohol : epoxide ratio increases from 0.075 for hex-1-ene to 1.2 for olefin 1 in the case of oxidations catalyzed by Fe(TPP)(Cl) (Table 1). Since the only difference between the two olefins is the presence of a phenoxy substituent in the ω-position of hex-1-ene, we propose that the increased importance of the allylic oxidation for olefin 1 could be due to a stabilization of the corresponding intermediate allylic radical by intramolecular complexation with the phenyl ring in good position (Fig. 3).



Scheme 2. Possible mechanism for monosubstituted olefin oxidation by C_6H_5IO and iron-porphyrins

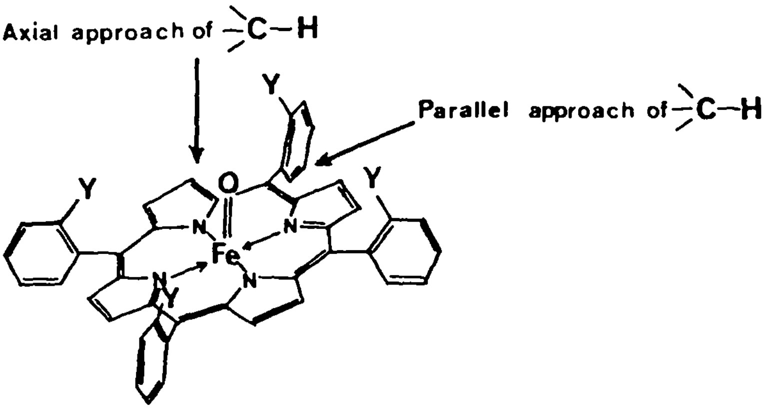
Tables 1 and 2 clearly show that the chemi- and regioselectivity of olefin 1 oxidation are very much dependent upon the nature of the metal catalyst and porphyrin substituents. Table 3 compares the (epoxide + aldehyde) : allylic alcohol (+ ketone when present) ratio R, which reflects the regioselectivity of the oxidation, and the epoxide : aldehyde ratio R' which reflects the competition between the two routes of evolution of the intermediate $Fe(IV)-OCH_2-\dot{C}HR$ radical (or of the corresponding metallocycle). The Cr(V)=O species which has been proposed as a reactive intermediate in the $C_6H_5IO-Cr(TPP)(Cl)$ system[13] is able to epoxidize with good yields styrene (Table 1) as well as olefins having no reactive allylic C-H bonds[13] but reacts exclusively with olefin 1 by allylic hydrogen abstraction. The Fe(V)=O and Mn(V)=O species give both allylic hydrogen abstraction and addition, the relative importance of these reactions being greatly dependent upon the metal environment. Although the substitution of the para-H of the porphyrin phenyls by Cl or CH_3 groups does not significantly modify R, a substitution of the ortho-H increases R to a great extent : R increases from 0.86 to about 3 in the case of F ortho-substituents on the four meso phenyl groups, to about 4.5 in the case of OR ortho substituents on two opposite phenyl groups (Fe(BH)(Cl)) and to about 19, in the case of CH_3 ortho substituents on the four phenyl groups. The steric effects of these ortho substituents which could control the approach of the olefin to the Fe=O species seems to be the major factor determining the regioselectivity, since (i) substituents having opposite electronic effects on the electron-density of the porphyrin (F and OR or CH_3) all lead to an increase of R, (ii) the greater the steric hindrance caused by the ortho-substituents of the phenyl rings, the greater the R value obtained. Actually, space-filling models reveal that, on each side of the porphyrin plane, the 4 ortho-substituents of the phenyl groups surround the Fe=O species controlling its interaction with substrates (Scheme 3). The steric hindrance caused by them is in the order : 4H(TPP)<4F(fluoroporphyrin)<2OR + 2H (basket-handle porphyrins)< $4CH_3$(Fe(TMP)(Cl)), as the corresponding R values 0.86<3<4.5<19. Actually, the yields of products deriving from the addition of Fe(IV)-O• to the double bond (2 + 4) (Table 2) are not greatly affected by the steric hindrance caused by the phenyl substituents. On the contrary, the yield of formation of the allylic alcohol 3 drastically decreases when passing from Fe(TPP)(Cl) to Fe(TMP)(Cl), indicating that the variation of R (Table 3) observed upon increasing the steric hindrance around the Fe=O moiety is mainly due to a decrease of the allylic oxidation rate. These results are not consistent with an axial approach of the C-H allylic bond in the hydroxylation reaction, as in scheme 3, which should have not been so drastically disfavored by CH_3 ortho-substituents (Scheme 4). On the other hand, they are in complete agreement with a parallel approach of C-H allylic bonds which requires an important non-bonded interaction between the olefin and ortho-substituents (Scheme 4). A very similar conclusion concerning the substrate approach has been recently drawn by Groves and Nemo[9i] from studies of alkanes hydroxylations by different iron-tetraarylporphyrins and C_6H_5IO. Our results give a further clear illustration of the control of the regioselectivity of substrates oxidations by metallo-porphyrin-C_6H_5IO systems as a function of the catalyst struc-

Table 3. Variation of the (epoxide + aldehyde)/allylic alcohol (R) and epoxide/aldehyde (R') ratios observed for 1 and styrene oxidation catalyzed by various iron-porphyrins

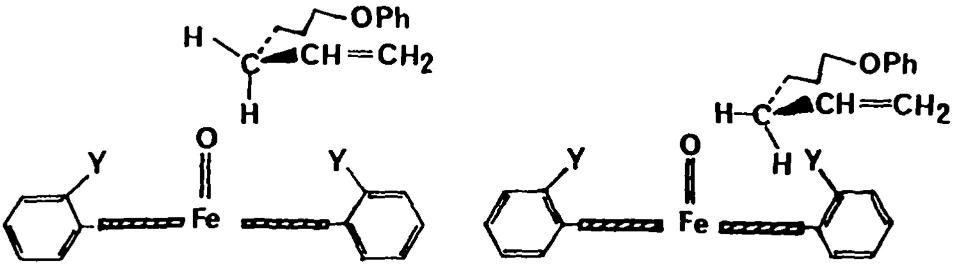
Olefin		Fe(TPP)(Cl)	Fe(TTP)(Cl)	Fe(TFPP)(Cl)	$Fe(BH_1)(Cl)$	$Fe(BH_2)(Cl)$	Fe(TMP)(Cl)	P-450(a)
Styrene	R'	25 ± 5	24 ± 4	16.7 ± 3	2.9 ± 5		>150(b)	26.5 ± 4
1	R	0.86 ± 0.1	1 ± 0.1	3 ± 0.4	4.4 ± 0.7	4.9 ± 0.8	19 ± 4	3 ± 0.5
	R'	28.5 ± 4	28 ± 4	17.3 ± 2	4.7 ± 0.7	5.1 ± 0.8	>90(b)	9.7 ± 1

(a) values obtained upon 1 and styrene oxidation by C_6H_5IO catalyzed by liver microsomal cytochromes P-450 from phenobarbital treated rats[25]. (b) estimated from the detection limit of the aldehyde in our conditions.

Scheme 3.



Scheme 4.



ture, since by using Fe(TMP)(Cl) instead of Fe(TPP)(Cl), one can almost completely orientate the oxidation of 1 toward epoxidation. Interestingly, microsomal cytochromes P-450 catalyze the oxidation of 1 by C_6H_5IO with formation of 2, 3 and 4, with R-values around 3 (Table 3)[17,19]. These values are intermediate between those obtained with Fe(TPP)(Cl) for which the steric constraints for the olefin approach are minimum and with the sterically hindered Fe(TMP)(Cl), suggesting that steric constraints presumably due to interactions between the olefin and the protein chains that are in close proximity of the heme do exist during cytochrome P-450 dependent oxidation. Preliminary results concerning oxidation of 1 catalyzed by highly purified cytochrome P-450 LM_2 from rabbit liver [25] gave R=11.5, indicating even more important constraints for olefin 1 approach in that case.

Ortho-substituents of the TPP phenyl rings also greatly affect the competition between epoxide and aldehyde formation. The variation of R' which is similar for olefin 1 and styrene, is more complex than the variation of R (Table 3). For instance in the case of 1, R' decreases from 28.5 for Fe(TPP)(Cl) to 17.3 for the fluoroporphyrin and 5 for the iron-basket-handle porphyrins but dramatically increases with Fe(TMP)(Cl) since no aldehyde formation could be detected with this catalyst. One thus cannot interpret the R' variation as the R variation by taking into account only one major factor. Electronic effects of the phenyl substituents on the Fe=O moiety play an important role for controlling the fate of the $Fe(IV)-OCH_2-\dot{C}HR$ intermediate. However, it is presently difficult to interpret these results in the absence of a definite mechanism for aldehydes formation.

Acknowledgment. We are grateful to Dr. M. Momenteau for a gift of iron- "basket-handle" porphyrins Fe^{III}(BH)(Cl)[20].

EXPERIMENTAL SECTION

Physical measurements. The metalloporphyrin catalysts were studied by visible spectroscopy of the organic phase, using an Aminco DW 2 spectrophotometer. ^{1}H NMR spectra of authentic samples were run on a Varian EM 390 spectrometer operating at 90 MHz or on a Cameca 250 spectrometer operating at 250 MHz.

The formation of oxidation products was followed by g.l.c with an Intersmat IG 120 FL equipped with a hydrogen flame ionization detector. The glass columns used for this study were packed with the following materials : 5% w/w FFAP on chromosorb WAW for hex-1-ene, 5% w/w Carbowax on Anachrom SD for styrene. For 6-phenoxyhex-1-ene a fused silica capillary column coated with CPsil 5 was used ; the carrier gas was He. For combined gas chromatography-mass spectrometry, a Riber R 1010 mass spectrometer and PDP8 computer were coupled with a Girdel 30 chromatograph. The temperature of the CPsil 5 silica column increased from 80 to 250°C at a rate of 5°C per min., the carrier gas was helium at a pressure of 1 Bar. The retention times and the mass spectra of the oxidation products were compared with those of authentic samples.

TLC was performed on Silica gel 60 F254 (Merck) using the solvent system given in parentheses.

Materials. Styrene was purchased from Prolabo. Hex-1-ene , Phenylacetaldehyde and styrene oxide were obtained from Fluka, hex-1-en-3-one from Aldrich, hex-1-en-3-ol from Janssen. Hex-1-ene oxide was synthetized from hex-1-ene with m-chloroperbenzoic acid by a standard procedure[26] : bp 117°C (Lit[27] 116-119°C). Iodosobenzene[28], Fe-, Mn- or Cr-tetraphenylporphyrin[29], iron-"basket-handle" porphyrin Fe^{III}(BH)(Cl)[20] and Fe or Mn tetra-(pentafluorophenyl) porphyrin (TFPP)[30] were prepared as previously described.

6-phenoxyhex-1-ene (1). To 4.2 g of oil free NaH, 70 ml of DMSO were added, then a solution of 20.6 g of phenol in 80 ml of DMSO dropwise ; when hydrogen production had ceased, 14.4 g of 6-bromohex-1-ene (from Fluka) was slowly added. The mixture was heated 4 h at 80°C under argon. The reaction mixture was extracted with hexane, the hexane phase washed with 0.1 N NaOH and water and dried over Na_2SO_4. After evaporation of the solvent, 6-phenoxyhex-1-ene (1) was distilled under reduced pressure (11.7 g : 75%).
bp (0.2 mmHg) 69°C. ^{1}H NMR : ($CDCl_3$ ppm/hexamethyldisiloxane (HMDS) : 1.53 (m, 2H, $-CH_2-$) ; 1.75 (m, 2H, CH_2-) ; 2.06 (m, 2H, $CH_2-CH=$) ; 3.83 (t, 2H, $O-CH_2$, J=6.5 Hz) ; 4.86 (m, 2H, $CH_2=$) ; 5.6 (m, 1H, $-CH=CH_2$) ; 6.73 (m, 3H, meta and para phenyl H) ; 7.06 (m, 2H, ortho-phenyl H). MS : m/z (abundance %) 176($M^{+\cdot}$)(39),133($C_6H_5-OCH=CH-CH_2$)(2.3), 120($C_6H_5OCH=CH_2$) (3.4), 107($C_6H_5OCH_2$)(7.5), 94(C_6H_5OH)(100) (Calc. for $C_{12}H_{16}O$: C,81.9 ; H,9.15. Found : C,82.0; H,9.2 %).

6-phenoxyhex-1-ene oxide (2). To 4 ml of CH_2Cl_2 at 0°C, 2.12 g of 6-phenoxyhex-1-ene and 2.6 g of meta-chloroperbenzoic acid (MCPBA from Aldrich, 85%) were added and then stirred for 3 h under argon. The reaction was followed on TLC (Silica gel 60F254 Merck, 3 : 1 n-hexane-ethyl-acetate as eluant, Rf : 0.47). After 3 h, the excess of MCPBA was destroyed with sodium bisulfite, then the solution was washed with water dried over $MgSO_4$. After evaporation of the solvent, compound 2 was distilled under reduced pressure (1.95 g ; 85%), bp (10 mmHg) 125°C. ^{1}H NMR ($CDCL_3$, ppm/HMDS): 1.2 (m, 2H, $-CH_2$) ; 1.58 (m, 2H, CH_2), 1.8 (m, 2H, $CH_2-CH=$) ; 2.44, 2.71, 2.89 (m, 3 x 1H, protons of the epoxide ring) ; 3.93 (t, 2H, $-OCH_2$, J=6.5 Hz) ; 6.87 (m, 3H, para and meta-phenyl H) 7.26 (m, 2H, ortho-phenyl H). MS : m/z (abundance %) 192 ($M^{+\cdot}$) (22.5), 107($C_6H_5OCH_2$)(7.5), 94(C_6H_5OH)(100)(Calc. for $C_{12}H_{16}O_2$: C, 75.1 ; H,8.4. Found : C,75.3 ; H, 8.35 %).

6-phenoxyhex-en-3-ol (3). To a solution of 6.4 ml t-butylhydroperoxide 90% (Merck) and 35.5 mg of SeO_2 (Prolabo) in 6 ml 1,2-dichloroethane was added 2.82 g of 6-phenoxyhex-1-ene. The mixture was stirred at 25°C. After 48 h, the reaction mixture was diluted with 10 ml of 1,2-dichloroethane, then the organic phase was washed with 10 % KOH and water and dried over Na_2SO_4. After evaporation of the solvent, the residue was treated by 264 mg of $NaBH_4$ in 10 ml of ethanol containing 5% H_2O (1 h). The crude product 3 was purified by TLC (Silica gel 60F254 Merck, 2 : 1 n-hexane-ethylacetate, Rf=0.85)(1.25 g ; 40%). ^{1}H NMR : ($CDCl_3$, ppm/HMDS) : 1.74 (m, 4H, $(CH_2)_2-$) ; 3.96 (t, 2H, OCH_2-, J=6.5 Hz) ; 4.14 (m, 1H, CHOH) ; 5.18 (m, 2H, $CH_2=$) ; 5.87 (m, 1H, $CH=$) ; 6.9 (m, 3H, meta and para-phenyl H) ; 7.26 (m, 2H, ortho-phenyl H). MS : m/z (abundance %) 192 ($M^{+\cdot}$)(22.5) ; 133($C_6H_5OCH=CH-CH_2$)(7.5) ; 120($C_6H_5OCH=CH_2$)(9.8) ; 107($C_6H_5OCH_2$)(12.8) ; 99($CH_2)_3-CHOH-CH=CH_2$)(37); 94(C_6H_5OH)(68.5) ; 57($CH_2=CH-CHOH$)(100).

6-phenoxyhex-1-en-3-one (5). The allylic ketone was synthetized by treatment of the mixture obtained in the preparation of 3 with 1.4 g MnO_2. The crude product 5 was purified by T.L.C. (Silica gel 60F254 Merck, 2 : 1 n-hexane-ethyl-acetate, Rf=0.66)(1.06 g ; 35 %). ^{1}H NMR : ($CDCl_3$, ppm/HMDS) : 1.96 (m, 2H, CH_2) ; 2.66 (t, 2H, CH_2-CO, J=6.5Hz) ; 3.88 (t, 2H,OCH_2-, J=6.5 Hz) ; 5.66 (m, 1H, $CH=CH_2$) ; 6.1 (m, 2H, $CH_2=CH-$) ; 6.73 (m, 3H, para and meta-phenyl H) ; 7.1 (m, 2H, ortho-phenyl H). MS : m/z (abundance %) 190 ($M^{+\cdot}$)(15) ; 97 ($(CH_2)_3-COCH=CH_2$) (37.6) ; 94 (C_6H_5OH)(7.5) ; 77(C_6H_5)(14.3) ; 55($CH_2=CH-CO$)(100)(Calc. for $C_{12}H_{14}O_2$: C,75.9 ; H,7.4. Fond : C,76.0 ; H,7.4%).

6-phenoxyhexanal (4). A solution of 0.5 g of 2 in 5 ml ether was treated (15 min stirring) by 425 mg of $BF_3(Et_2O)$ at 0°C. After washing with water and evaporation of the solvent, compound 4 was purified by TLC (Silica gel 60F254 Merck, 10 : 1 n-hexane-ethyl-acetate, Rf=0.2)(399 mg ; 80%). bp(0.06 mmHg) 110°C (lit[31] : bp(0.06 mmHg) 105°C. ^{1}H NMR : ($CDCl_3$ ppm/HMDS) : 0.9 (m, 2H, CH_2) ; 1.3(m, 2H, CH_2) ; 1.64 (m, 2H, CH_2) ; 2.36 (m, 2H, CH_2-CHO) ; 4 (t, 2H, OCH_2, J=6.5 Hz) ; 7 (m, 3H, meta and para-phenyl H) ; 7.38 (m, 1H, ortho-phenyl H) ; 9.5 (s, 1H, CHO). MS : m/z (abundance %) 192($M^{+\cdot}$)(10) ; 163($C_6H_5O-(CH_2)_2-$)(0.4) ; 107($C_6H_5OCH_2$)(6.7) ; 99($-CH_2)_5-CHO$)(25.5) ; 94(C_6H_5OH)(100).

Typical procedure for the oxidation of substrates by various metallo-tetraaryl-porphyrins with C_6H_5IO 5 µmol of C_6H_5IO were added to 1 µmol of metallo-tetra-aryl-porphyrins and 0.1 mmol of olefin in 0.1 ml C_6H_6. The solution vas stirred at room temperature under anaerobic conditions. After all C_6H_5IO was consumed (1 h reaction), the mixture was analyzed by g.l.c. and mass spectrometry after addition of heptan-4-ol, phenylethylketone and nonadecane as internal standards respectively for hex-1-ene, styrene and 6-phenoxyhex-1-ene. No oxidation took place when either C_6H_5IO or the metalloporphyrin was omitted. When reactions were performed under aerobic conditions, the yields vere unchanged.

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