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ALKANE HYDROXYLATION CATALYZED BY METALLOPORPHYRINS : EVIDENCE FOR DIFFERENT ACTIVE OXYGEN SPECIES WITH ALKYLHYDROPEROXIDES AND IODOSOBENZENE AS OXIDANTS.

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Abstract A comparative study of cyclohexane and n-heptane hydroxylations by cumylhydroperoxide and iodosobenzene, catalyzed by various metalloporphyrins, indicates that different active oxygen species, presumably the cumyloxy radical and a metal-oxo intermediate, are involved in these reactions.

Cytochrome P450 catalyzes the hydroxylation of several substrates not only by dioxygen and NADPH but also by single-oxygen atom donors such as alkylhydroperoxides and iodosoarenes[1]. The latter oxidants have also been shown to hydroxylate alkanes at room temperature in the presence of catalytic amounts of certain metalloporphyrins[2]. Since hemoproteins such as peroxidases lead, upon reaction with different single-oxygen donors, to "Fe O" active oxygen complexes, the structure of which are independent of the nature of the oxidant[3], it was interesting to know whether metalloporphyrin-catalyzed hydroxylations of alkanes by alkylhydroperoxides and iodosoarenes also involve a common active oxygen species. This paper reports a comparative study of metalloporphyrin-catalyzed hydroxylation of alkanes by cumylhydroperoxide (CumOOH) and iodosobenzene (PhIO), and shows that these reactions involve mechanisms and active oxygen species which greatly differ as a function of the oxidant nature.

In table I are compared the results of cyclohexane oxidation either by CumOOH or PhIO, in the presence of catalytic amounts of various metallo-tetraphenylporphyrins, (M(TPP)(Cl)) under an argon atmosphere (conditions[2f]: 20°C, M(TPP)(Cl) 2.5 mM, oxidant 50 mM in anaerobic cyclohexane-benzene 1:1). Although with different rates (very high for the Fe-, Co- and Rh-catalysts but very low for Mn (TPP)(Cl)), all the metalloporphyrins mentioned in table I are effective as catalysts for cyclohexane oxidation by CumOOH[2f], with similar final yields and an almost identical cyclohexanol to cyclohexanone ratio of about 2. The iodosobenzene-dependent oxidations display very different characteristics, the yields and cyclohexanol-cyclohexanone ratio being on the contrary very dependent on the nature of the metal. For instance, Mn(TPP)(Cl) and Fe (TPP)(Cl) give almost only cyclohexanol whereas Rh(TPP)(Cl) fails to catalyse cyclohexane oxidation, and Cr(TPP)(Cl) leads to low but similar yields of cyclohexanone

Table 1 Cyclohexane hydroxylation by $C_6H_5C(CH_3)_2OOH$ or C_6H_5IO catalyzed by various metalloporphyrins. [a]

CATALYST	$C_6H_5C(CH_3)_2OOH$			C_6H_5IO		
	$C_6H_{11}OH$	$C_6H_{10}O$	alcool/cétone	$C_6H_{11}OH$	$C_6H_{10}O$	alcool/cétone
	yields (%)[b]					
Fe(TPP)(Cl)	40	20	2	24	2.5	10
Mn(TPP)(Cl)	25	12	2	30	3	10
Co(TPP)(Cl)	40	20	2	5	1 5	3 3
Rh(TPP)(I)	30	14	2 1	< 1	< 1	-
Cr(TPP)(Cl)	33	13	2.5	4	4	1

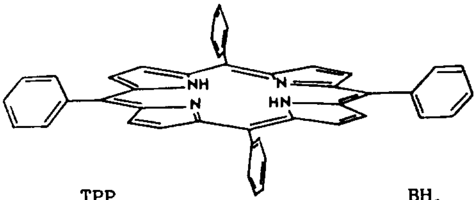
a) conditions indicated in the text b) yields ($\pm$2)in mole per mole of starting oxidant, after complete comsumption of the oxidant 4-15h for PhIO-dependent reactions, about 30mn for the Cum OOH-dependent reactions except for Cr(TPP)(Cl)(24h) and Mn(TPP)(Cl) (7 days)

n-Heptane is hydroxylated on carbons 2,3 and 4, but only to a negligible extent on carbon 1, by CumOOH and PhIO in the presence of catalytic amounts of Fe(TPP)(Cl) (table 2 conditions identical to those of table 1). The results of n-heptane hydroxylation either by CumOOH or by PhIO with different Fe(tetraarylporphyrin)(Cl) catalysts are compared in Table 2 The three Fe-porphyrins used in this study involve different environments of the iron the two "basket-handle" porphyrins [4] BH_1 and BH_2 are tetraarylporphyrins with an alkyl chain on both sides of the porphyrin ring (Figure) The regioselectivity of the CumOOH-dependent hydroxylation of heptane is completely independent on the nature of the iron-porphyrin used and thus of the iron environment. The reverse is true for the PhIO-dependent hydroxylation, and it is noteworthy that the relative importance of ω-1 hydroxylation increases when the iron accessibility of the catalyst decreases Actually hydroxylation at the most accessible ω-1 position is the most important with $Fe(BH_1)(Cl)$ which has the lowest iron accessibility

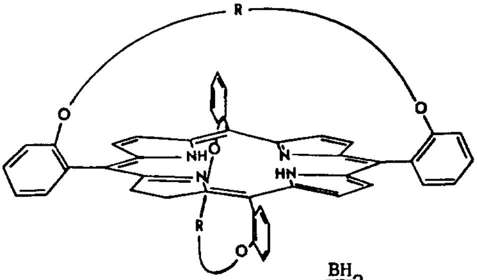
Table 2 Hydroxylation of n-heptane by $C_6H_5(CH_3)_2OOH$ or C_6H_5IO catalyzed by various Fe(III)(porhyrin)(Cl) complexes [a]

	PRODUCTS RATIO (%) [b]					
	$C_6H_5C(CH_3)_2OOH$			C_6H_5IO		
	Porphyrin					
	TPP	BH_2	BH_1	TPP	BH_2	BH_1
heptanol-2	20	20	20	33	45	48
-3	13	13	13	38	35	33
-4	9	10	10	19	16	15
heptanone-2	31	30	30	3	2	2
-3	19	19	20	4	1	1
-4	8	8	7	2	1	1

a) conditions as in table 1 b) the total yields of oxidized products in mole per mole of starting oxidant are ∼20%, except for the PhIO-dependent reactions catalyzed by Fe(BH_1)(Cl) and Fe(BH_2)(Cl)(5%) , The "basket-handle" porphyrin – dependent reactions are slower: complete consumption of the oxidant within 30mn for Fe(TPP)(Cl) + CumOOH, 4h for Fe(TPP)(Cl) + PhIO, 2h for Fe(BH)(Cl) + CumOOH and 16h for Fe(BH)(Cl) + PhIO



TPP



BH_1 $R=(CH_2)_4-C_6H_4-(CH_2)_4$

BH_2 $R=(CH_2)_{11}$

The results of tables 1 and 2 show that the PhIO-dependent hydroxylation of alkanes is dramatically dependent on the nature of the metal and on its environment. This is consistent with the previously proposed [2a-e] metal-oxo nature of the active oxygen species and mechanism of the PhIO-dependent oxidations catalyzed by Fe-, Mn- and Cr-porphyrins

$$M^n(P) + PhIO \xrightarrow{-PhI} (P)M^{n+2}{=}O \xrightarrow{+RH} (P)M^{n+1}{-}OH + R^{\bullet} \longrightarrow ROH + M^n(P)$$

On the contrary, several characteristics of the CumOOH-dependent hydroxylation of alkanes are almost independent on the nature of the metal (at least of those indicated in table 1) and of its environment. This suggests a different active species that does not include the metal The alkoxy radical Cum $O^\bullet$, formed by a "Fenton Type" reaction, is a good candidate within the possible following mechanism

$$M^n(P) + CumOOH \longrightarrow (P)M^{n+1}\!-\!OH + CumO^\bullet \xrightarrow[-CumOH]{+RH} R^\bullet + (P)\, M^{n+1}\!-\!OH \longrightarrow ROH + M^n(P)$$

Similarly, it has been shown recently that some cytochrome P450-catalyzed oxidations of substrates by alkylhydroperoxides or peracids could involve a similar mechanism with alkoxy or acyloxy radicals as active species for C-H bond activation [5]

Taking into account the known characteristics of the $RO^\bullet$ active species possibly involved in the metalloporphyrin-CumOOH system, one should expect that this system would be unable to epoxidize olefins. Accordingly, we found that this is true at least for cyclohexene[2a] and 1-hexene On the contrary, the Fe-, Mn-, and Cr-porphyrin-PhIO systems were found to epoxidize olefins efficiently, their corresponding metal-oxo species being able to add to double bonds [2a-e]

1 V. Ullrich, Topics in Current Chemistry, (1979), 83, 68

2 a) J T Groves, T E Nemo and R S Myers, J. Amer. Chem. Soc., (1979), 101, 1032
b) J T. Groves and W J Kruper Jr , ibid, (1979), 101, 7613 , c) C K Chang and E Ebina Chem. Comm., (1981), 103, 778 , d) C L. Hill and B.C Schardt, J. Amer. Chem. Soc.(1980),102,6374 , e) J T Groves, W J Kruper and R C Haushalter, ibid, (1980),102 6375 , f) D. Mansuy, J F Bartoli, J C Chottard and M Lange, Angew. Chem. Int. Edit Engl. (1980), 19, 909 , D Mansuy, P Dansette, F Pecquet and J C Chottard, Biochem. Biophys Res. Comm., (1980), 96, 433

3 H B Dunford and J S Stillman, Coor. Chem. Rev., (1976),19, 187

4 M Momenteau, B Loock, J Mispelter, E Bisagni, Nouv. J. Chimie, (1979), 3, 77

5 a) R E. White, S G Sligar and M J Coon, J Biol Chem., (1980) 225, 11108 ,
b) R C Blake II and M J Coon, ibid., (1981), 256, 12127

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