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Iron polynitroporphyrins bearing up to eight β-nitro groups as interesting new catalysts for H_2O_2-dependent hydrocarbon oxidation: unusual regioselectivity in hydroxylation of alkoxybenzenes

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A series of iron porphyrins bearing one to eight β-nitro substituents were synthesized and evaluated as catalysts for hydrocarbon oxidation with H_2O_2; iron porphyrins bearing five or six β-nitro groups were the best catalysts for cyclooctene epoxidation and adamantane or anisole hydroxylation without need of a cocatalyst, and led to very different regioselectivities with either H_2O_2 or PhIO as oxidants, as shown by an unusual *ortho*-hydroxylation of alkoxybenzenes highly favored in the H_2O_2-dependent oxidations.

Three successive generations of Fe(III) porphyrins have been developed during the last fifteen years as catalysts mimicking cytochromes P450.[1–3] Recently, iron porphyrins bearing electronegative substituents have been shown to catalyze olefin epoxidation and alkane hydroxylation with H_2O_2 in aprotic solvents without cocatalysts.[4] However, iron porphyrin–H_2O_2 systems efficient for other difficult P450-type monooxygenations, such as aromatic hydroxylation, remain to be found.

Quite recently, we have reported a new general method for selective polynitration of a Zn(II) porphyrin which affords a full series of zinc porphyrins bearing one through to eight β-nitro groups in high yields.[5] This opens the way towards metalloporphyrins with a remarkably wide span of redox potentials.[5] This communication reports a first comparison of the catalytic properties of a full series of new iron(III) β-polynitroporphyrins, that became available by this method,[6] in oxidations of hydrocarbons with H_2O_2. It shows that some of them catalyze not only alkene epoxidation but also alkane and aromatic hydroxylation with H_2O_2, without the need of any cocatalyst, and with chemo- and regio-selectivities very different from those of the corresponding oxidations with PhIO.

Eqn. (1) shows the procedure that was used for preparing the

$$\mathrm{Zn(TDCPP)} \xrightarrow[\mathrm{HNO_3,\ CF_3SO_3H}]{\mathrm{(CF_3SO_2)_2O}} \mathrm{Zn(TDCPN}x\mathrm{P)} \xrightarrow[\substack{\mathrm{ii\ FeBr_2}\\ \mathrm{iii\ O_2,\ HCl}}]{\mathrm{i\ H^+}} \mathrm{Fe(TDCPN}x\mathrm{P)Cl} \qquad (1)$$

eight iron porphyrins, Fe(III)(TDCPNxP)Cl bearing one through to eight β-nitro substituents (x = 1–8), from Zn(TDCPP).[7] The key step is a reaction of Zn(TDCPP) with increasing amounts of a HNO_3–CF_3SO_3H–$(CF_3SO_2)_2O$ mixture which leads to each compound of the Zn(TDCPNxP) series with yields between 50 and 95%.[5] All Zn(II) and Fe(III)Cl complexes of the TDCPNxPH_2 porphyrins were completely characterized by mass spectrometry, UV–VIS, ^{1}H NMR and EPR (for the iron complexes) spectroscopy; their detailed synthesis and characteristics will be published elsewhere. The reduction potential of the Fe(III)Cl complexes vary from −225 (for x = 0) to +660 mV (for x = 8) (*vs.* SCE[7]).

As shown in Table 1, Fe(TDCPP)Cl is a poor catalyst for cyclooctene expoxidation with H_2O_2 in CH_2Cl_2–MeCN, in accord with previous literature data.[3] Increasing the number of β-NO_2 substituents of the porphyrin led to a spectacular increase of the epoxidation yield from 5 to 90%. This optimal yield was obtained with Fe(TDCPN$_5$P)Cl, a further increase of the number of β-NO_2 substituents leading to much lower yields. Fe(TDCPN$_5$P)Cl was also the best catalyst for hydroxylation of adamantane with H_2O_2 with a total yield (1- and 2-adamantanols) of 35% based on starting H_2O_2. For this alkane, very low yields were found for Fe(TDCPP)Cl, with a progressive increase of the yield with catalysts bearing one through to four β-nitro groups and optimum yields for Fe(TDCPN$_5$P)Cl and Fe(TDCPN$_6$P)Cl.

A similar trend was observed for aromatic hydroxylation of anisole with H_2O_2 catalyzed by this iron porphyrin series. Fe(TDCPP)Cl is almost inactive for this reaction, whereas iron porphyrins bearing from three to six β-NO_2 substituents led to the formation of *ortho*- and *para*-hydroxylated products with total yields between 13 and 17% (Table 1). Interestingly, the regioselectivity of these Fe(TDCPNxP)Cl-catalyzed aromatic hydroxylations varies significantly as a function of x (Table 1). The *ortho*:*para* ratio is in favor of *para*-hydroxylation for x = 0, 1 and 2, whereas it progressively increases to values up to 5.5 for Fe(TDCPN$_6$P)Cl. This remarkable change of regioselectivity as a function of x should be due to a change in the nature and/or reactivity of the active species formed in these reactions. Possible involvement of further oxidations of *o*- and *p*-phenols in determining the *ortho*:*para* ratio is unlikely because of the

Table 1 Oxidation of cyclooctene, adamantane and anisole with H_2O_2 in the presence of the Fe(TDCPN$_x$P)Cl catalysts

Catalyst Fe(TDCPNxP)Cl		x = 0	1	2	3	4	5	6	7	8
Reaction		Yield[d] (%)								
Cyclooctene epoxidation[a]		5	20	48	68	80	90	15	6	2
Hydroxylation	ol-1	1.5	3	1.5	2	7	26	25	17	4
of adamantane[b]	ol-2	1	1.5	1	0.5	2.5	9	10	7	2
Hydroxylation	*p*-OH	1	2	3	5	6	3	2	1	2
of anisole[c]	*o*-OH	< 1	< 1	1.5	9.5	11	13.5	11	3	9
	o/*p*			0.5	1.9	1.8	4.5	5.5	3	4.5

[a] *Conditions*: catalyst:H_2O_2:cyclooctene molar ratio = 1:300:100 in CH_2Cl_2–MeCN (1:1) for 2 h at 20 °C, with [catalyst] = 1 mM. [b] *Conditions*: catalyst:H_2O_2:adamantane molar ratio = 1:40:300 in CH_2Cl_2–MeCN (1:1) for 2 h at 20 °C; [catalyst] = 1 mM. Small amounts of adamantan-2-one were also detected (yield < 1%). [c] *Conditions*: catalyst:H_2O_2:anisole molar ratio = 1:20:3000 in H_2O–MeCN (1:9); [catalyst] = 2 mM. *p*-OH and *o*-OH are used for *p*- and *o*-hydroxyanisole. [d] Yields are based on starting H_2O_2 except for cyclooctene epoxidations for which H_2O_2 was used in excess relative to substrate; yields for cyclooctene epoxidation were thus based on cyclooctene.

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Table 2 Comparison of the Fe(TDCPN$_5$P)Cl-catalyzed oxidations of various substrates either with H_2O_2 or with PhIO

Substrate	Oxidant	Products (yield in %)[d]				
Adamantane[a]		ol-1	ol-2	one-2	ol-1/ol-2	
	PhIO	62	30	2	2.1	
	H_2O_2	26	9	< 1	2.9	
Limonene[b]		1,2-Oxide	8,9-Oxide	Oxide ratio	Carveols	Carvone
	PhIO	35	18	1.9	8	4
	H_2O_2	24	9	2.7	2	< 1
Anisole[c]		*o*-OH	*p*-OH	*o*/*p*	Phenol	
	PhIO	< 1	7	< 0.1	2	
	H_2O_2	11	4	2.75	4	
Ethoxybenzene[c]		*o*-OH	*p*-OH	*o*/*p*	Phenol	
	PhIO	< 1	8	< 0.1	2	
	H_2O_2	14	5	2.8	7	

[a] *Conditions*: Fe(TDCPN$_5$P)Cl : oxidant : adamantane molar ratio = 1 : 40 : 300 in CH_2Cl_2–MeCN (1 : 1) for 2 h at 20 °C; [catalyst] = 2 mM; ol-1, ol-2 and one-2 denote adamantan-1-ol, -2-ol and -2-one. [b] *Conditions*: Fe(TDCPN$_5$P)Cl : oxidant : limonene = 1 : 40 : 800 in CH_2Cl_2–MeCN (1 : 1). Carveols and carvone are the products resulting from allylic hydroxylation of limonene (at position 6).[3a] [c] *Conditions*: Fe(TDCPN$_5$P)Cl : oxidant : alkoxybenzene = 1 : 20 : 3000 in CH_2Cl_2–MeCN (1 : 1). *o*-OH and *p*-OH are used for the *ortho*- and *para*-hydroxylation products. [d] Yields are based on starting H_2O_2 or PhIO. All the experiments described in Tables 1 and 2 were usually performed under aerobic conditions. However, it is noteworthy that many experiments were also done under anaerobic conditions (under Ar) and gave almost identical results, showing that the observed regioselectivities were not affected by the presence of O_2.

huge excess of substrate used in these reactions (catalyst : H_2O_2 : substrate = 1 : 20 : 3000). Moreover, identical experiments performed under stoichiometric conditions (iron porphyrin : H_2O_2 : substrate = 1 : 1 : 3000) led to almost identical regioselectivities for anisole hydroxylation. It is noteworthy that the Fe(TDCPN*x*P)Cl catalysts were stable under the conditions described in Table 1. This was shown by their visible spectra that were found to be unchanged at the end of the reactions, and by their catalytic activity that remained almost identical after a further addition of H_2O_2 in the reaction medium.

The aforementioned results show the particular efficiency of iron porphyrins bearing around five β-nitro substituents to catalyze alkene epoxidation and alkane and aromatic hydroxylations with H_2O_2 in the absence of a cocatalyst. In order to have a first idea of the nature of the major active species responsible for these oxidations, we compared the oxidations of several substrates with H_2O_2 and Fe(TDCPN$_5$P)Cl to those performed with PhIO and the same catalyst under identical conditions. Table 2 clearly shows marked differences in the chemo- and regio-selectivities of the H_2O_2- and PhIO-dependent oxidations. This changes from small significant albeit small differences in the regioselectivity of adamantane hydroxylation (ol-1/ol-2 molar ratio of 2.9 with H_2O_2 *cf.* 2.1 with PhIO) and in the regioselectivity of limonene epoxidation (1,2 oxide/8,9 oxide = 2.7 *cf.* 1.9) to more dramatic differences in the regioselectivity of anisole and ethoxybenzene hydroxylations (major formation of *ortho*-hydroxylated products with H_2O_2 instead of almost exclusive *para* hydroxylation with PhIO).

Several years ago, a similar comparison between the chemo- and regio-selectivities of the oxidations of alkenes and alkanes with either PhIO or H_2O_2, in the presence of the Mn(TDCPP)Cl catalyst and imidazole cocatalyst, led to the conclusion that both systems involve the same active oxygen species, presumably a high-valent Mn=O complex.[3a] The results of Table 2 strongly suggest that the Fe(TDCPN$_5$P)Cl–H_2O_2 and Fe(TDCPN$_5$P)Cl–PhIO systems involve different active oxygen species. If one assumes that the active species formed with PhIO is a (por$^{+\bullet}$)Fe(IV)=O intermediate, as has been proposed for many other iron porphyrins,[1] one is led to the conclusion that different active species are involved in the H_2O_2-dependent oxidations. Several authors have already mentioned the possible formation of a ferric–hydroperoxo complex as an intermediate towards the high-valent iron–oxo species, in reactions of H_2O_2 with iron porphyrins[1,8] [eqn. (2)]. *Ortho*-hydroxylation of anisole from transfer of the terminal oxygen atom of such a ferric–hydroperoxo complex should be less sterically restricted than the transfer of the oxygen atom of a high-valent (TDCPN*x*P) iron–oxo intermediate.[9] Preferential involvement of a Fe(III)–OOH intermediate in reaction of H_2O_2 with iron–β-polynitroporphyrins, which should be less prone to stabilize high-valent iron–oxo species, is likely and could explain the surprising regioselectivity observed in the hydroxylation of anisole and ethoxybenzene. However, additional experiments are necessary to determine the nature of the active intermediate(s) involved in reactions using H_2O_2 and iron–β-polynitroporphyrins. Nonetheless, the preliminary results reported here indicate that the Fe(TDCPN*x*P)Cl complexes with *x* ⩾ 4 are interesting catalysts for alkane and aromatic hydrocarbon oxidation with H_2O_2 without need of a cocatalyst, that lead to new regioselectivities, especially in the hydroxylation of aromatic molecules.

$$(\text{por})\text{Fe}^{\text{III}} + \text{H}_2\text{O}_2 \xrightarrow{-\text{H}^+} [(\text{por})\text{Fe}^{\text{III}}\text{–OOH}] \xrightarrow[-\text{H}_2\text{O}]{+\text{H}^+} [(\text{por}^{+\bullet})\text{Fe}^{\text{IV}}\text{=O}] \quad (2)$$

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6 The only Fe(III)(β-polynitroporphyrin)complexes described so far[4a] have been obtained from a nitration method that only led to a mixture of penta- and hexa-nitroporphyrin derivatives.

7 TDCPP and TDCPN*x*P represent tetrameso(2,6-dichlorophenyl)porphyrin dianion and TDCPP bearing *x* β-NO_2 substituents (1 ⩽ *x* ⩽ 8) respectively; SCE = saturated calomel electrode.

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