New manganese β-polynitroporphyrins as particularly efficient catalysts for biomimetic hydroxylation of aromatic compounds with H_2O_2

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A series of Mn porphyrins bearing one to eight β-nitro substituents were synthesized in high yield in three steps by using a new general method for selective nitration of a Zn(*meso*-tetraarylporphyrin); this Mn porphyrin series exhibits a remarkably wide span of Mn(III)/Mn(II) redox potentials from −290 to + 1150 mV (*vs.* SCE), and the Mn porphyrins bearing one to five β-nitro groups are particularly good catalysts for hydroxylation of aromatic compounds with H_2O_2, with yields up to 98, 83, 80 and 12%, respectively for anisole, naphthalene, acetanilide and ethylbenzene.

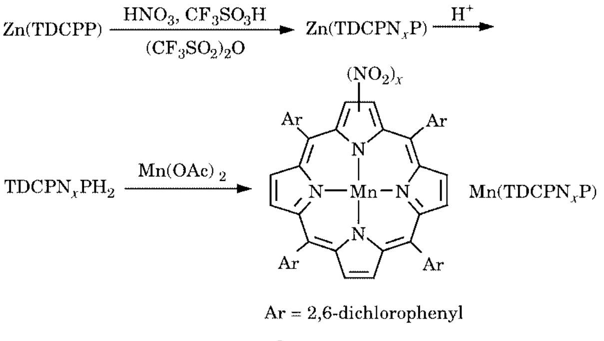
Cytochrome P450-dependent monooxygenases very efficiently catalyze the epoxidation of alkenes, the hydroxylation of alkanes and of aromatic rings, as well as N- or S-oxidations by O_2 or oxygen atom donors.[1] Three successive generations of Fe(III) and Mn(III) porphyrins have been developed during the last fifteen years as catalysts mimicking cytochrome P450 chemistry.[2] Several systems based on such Fe(III) or Mn(III) porphyrins were found to be very efficient for alkene epoxidation with quantitative yields and high turnover numbers, and for alkane hydroxylation with satisfactory yields.[2] Reproducing the P450-dependent selective hydroxylation of aromatic rings appears to be more difficult, presumably because of the very easy further oxidation of the expected phenol products in the medium. In fact, systems using strong oxidants such as PhIO that directly react by themselves with phenols generally led to low hydroxylation yields.[3] The best reported aromatic hydroxylation yields with these systems have been obtained with H_2O_2, a milder oxidizing agent.[3c,d,f] However, even these H_2O_2-dependent systems only led to hydroxylation yields of between 10 and 60% for the most reactive aromatic molecules. Some of the best reported yields were obtained with H_2O_2 in the presence of Mn(III) porphyrins bearing several electron-withdrawing substituents.[3d]

Based on these data, it appeared to us that it would be interesting to compare the abilities of Mn-porphyrins bearing one to eight β-nitro substituents as catalysts for aromatic hydroxylation with H_2O_2. We have recently reported[4] the synthesis of a Mn β-heptanitroporphyrin and showed that the redox potential of this Mn-porphyrin is more than 1 V higher than that of Mn(TDCPP).[5] Much more recently, we have succeeded in finding a new general method for selective nitration of Zn(TDCPP) which affords a full series of Zn porphyrins bearing one through to eight β-nitro groups in high yield. Here we report that some of the corresponding Mn complexes are particularly good catalysts for the hydroxylation of aromatic compounds with H_2O_2.

Scheme 1 shows the procedure used for preparing the eight Mn-porphyrins, Mn(TDCPN$_x$P) with ($1 \leqslant x \leqslant 8$), from Zn(TDCPP). Titration of Zn(TDCPP) with increasing amounts of HNO_3–CF_3SO_3H–$(CF_3SO_2)_2O$ selectively afforded the eight compounds of the Zn(TDCPN$_x$P) series with yields between 50 and 95%. All compounds of the Zn(TDCPN$_x$P) and TDCPN$_x$PH$_2$ series were fully characterized by elemental analysis and UV–VIS, ^{1}H NMR spectroscopy and mass spectrometry. Their detailed synthesis and characteristics will be published elsewhere.

Preparation of the corresponding Mn complexes was performed by reaction of $Mn(OAc)_2$ with the free bases TDCPN$_x$PH$_2$. Insertion of Mn(II) was increasingly easier as the number of NO_2 substituents increased. For instance, insertion of Mn(II) in TDCPPH$_2$ required several hours reaction at 153 °C in DMF, whereas insertion in TDCPN$_5$PH$_2$ was complete within a few minutes at 20 °C in $CHCl_3$–CH_3OH (80:20). After purification by column chromatography and treatment with gaseous HCl in aerobic CH_2Cl_2, the Mn-porphyrin complexes bearing between one and four β-nitro groups exhibited UV-VIS spectra characteristic of Mn(III)Cl porphyrins with a red-shifted Soret peak around 490 nm (482, 487, 493 and 498 nm for x = 1, 2, 3 and 4, respectively) and a smaller peak around 400 nm. Their mass spectra (MALDI) showed molecular peaks appearing as isotopic clusters identical to those simulated for Mn(TDCPN$_x$P)Cl, and major peaks corresponding to Mn(TDCPN$_x$P). Above x = 4, the Mn(TDCPN$_x$P) compounds mainly exist as Mn(II) complexes. For x = 5, even treatment with HCl in aerobic CH_2Cl_2 led to a mixture of Mn(II) (TDCPN$_5$P) and Mn(III) (TDCPN$_5$P)Cl. For x = 6, 7 and 8, it was only possible to isolate the Mn(II) (TDCPN$_x$P) complexes, which showed a single Soret peak at 466, 467 and 468 nm, respectively, and molecular peaks by mass spectrometry (MALDI) corresponding to Mn(TDCPN$_x$P). The existence of these electron-poor Mn porphyrins as Mn(II) complexes is not surprising; similar behavior was previously reported for β-polyhalogenated Mn-porphyrins[6] and for Mn(TDCPN$_7$P) itself.[4] This is also easily explained if one considers the high redox potentials (*vs.* SCE) found for the Mn(III)/Mn(II) couple which vary from +750 mV for x = 5 to + 1150 mV for x = 8. In fact, the Mn(TDCPN$_x$P) series with x = 1–8 exhibits a remarkably wide span of Mn(III)/Mn(II) redox potentials that range from −290 to +1150 mV (*vs.* SCE in 0.1 M NBu_4PF_6–CH_2Cl_2). The oxidation states of the Mn complexes were clearly established on the basis of their UV-VIS and EPR spectra and of their electrochemical properties.

The ability of these Mn-porphyrin complexes to act as catalysts for the hydroxylation of aromatic compounds with H_2O_2 was studied in the presence of a cocatalyst, ammonium



Scheme 1

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Table 1 Hydroxylation of aromatic compounds with H_2O_2 in the presence of Mn β-polynitroporphyrins and ammonium mandelate[a]

Substrate	Anisole			Naphthalene			Ethylbenzene					
Products	*p*-OH	*o*-OH	Total yield (%)	α-OH	β-OH	Total yield (%)	PhCHOH-CH_3	$PhCOCH_3$	*p*-OH	*o*-OH	*p*-OH + *o*-OH	arom./benz. (%)
Mn(TDCPP)Cl	67	6	73	62	5	67	20	22	< 1	< 1	< 2	< 5
Mn(TDCPNP)Cl	90	7	97	72	7	79	23	15	2	1	3	8
Mn(TDCPN$_2$P)Cl	88	8	96	75	8	83	27	15	2	1	3	7
Mn(TDCPN$_3$P)Cl	88	10	98	61	8	69	21	14	6	3	9	26
Mn(TDCPN$_4$P)Cl	71	8	79	43	6	49	26	15	8	4	12	29
Mn(TDCPN$_5$P)	32	5	37	39	5	44	22	5	6	4	10	37
Mn(TDCPN$_6$P)	7	1	8	20	3	23	7	12	< 1	< 1	< 2	
Mn(TDCPN$_7$P)	5	< 1	5	18	3	21	4	24	< 1	< 1	< 2	
Mn(TDCPN$_8$P)	< 1	< 1	< 2	1	< 1	1	1	5	< 1	< 1	< 2	

[a] *Conditions*: Mn-porphyrin : H_2O_2 : cocatalyst ratio = 1 : 50 : 20, [Mn-porphyrin] = 2 mM in CH_2Cl_2–CH_3CN (1 : 1), 2 h at 20 °C in the presence of substrate in excess; substrate/catalyst = 3000, 1600 and 500 for anisole, ethylbenzene and naphthalene, respectively. Yields (%) are based on H_2O_2; *p*-OH and *o*-OH represent *para*- and *ortho*-hydroxylated products; arom./benz. is the ratio (%) between aromatic hydroxylation and benzylic oxidation products derived from ethylbenzene.

acetate, that was previously described to give good results for the Mn porphyrin-catalyzed transfer of an oxygen atom of H_2O_2 to various hydrocarbon substrates.[7] Thus, Mn(TDCPP)Cl catalyzed the hydroxylation of anisole to *para*- and *ortho*-hydroxyanisole with 60 and 4% yields based on starting H_2O_2 when anisole was used in large excess relative to H_2O_2. From various ammonium carboxylates that have been tested as necessary cocatalysts for that reaction, ammonium mandelate gave the best hydroxylation yields. The latter cocatalyst was thus used in our comparison of the various Mn-porphyrins (Table 1). Interestingly, Mn(TDCPN$_1$P)Cl led to markedly higher yields of anisole hydroxylation with an almost quantitative use of H_2O_2 for formation of 90% and 7% *para*- and *ortho*-hydroxyanisole respectively. Mn(TDCPN$_2$P)Cl and Mn(TDCPN$_3$P)Cl also gave very high total yields based on H_2O_2 and were recovered unchanged at the end of the reaction (*ca.* 50 turnovers under the used conditions). With more β-nitro substituents, the hydroxylation yields greatly decreased from 79% with Mn(TDCPN$_4$P)Cl to < 2% with Mn(TDCPN$_8$P). Similar results were observed for hydroxylation of naphthalene, the best total yield of formation of α- and β-naphthols being maximum (83%) for Mn(TDCPN$_2$P)Cl (Table 1). Interestingly, the regioselectivity slightly changed upon increasing the number of β-nitro substituents [α : β ratio from 12 with Mn(TDCPP)Cl to *ca.* 6 for Mn(TDCPN$_7$P)]. The most spectacular results were observed in the case of ethylbenzene. Its Mn(TDCPP)Cl catalyzed oxidation with H_2O_2 exclusively led to products arising from hydroxylation of its very reactive benzylic position, 1-phenylethanol and acetophenone. Upon introduction of an increasing number of β-NO_2 substituents on the catalyst, *para*- and *ortho*-hydroxyethylbenzene were formed in significant amounts and the aromatic hydroxylation yield increased up to 12% for $x = 4$; then it markedly decreased for $x > 5$. Thus, the aromatic hydroxylation/benzylic hydroxylation ratio reaches maximum values *ca.* 30% for $x = 3$–5.

The above results illustrate the particular efficiency of Mn-porphyrins bearing between one and four β-nitro substituents for hydroxylation of aromatic molecules with H_2O_2 in the presence of an NH_4CO_2R cocatalyst. By a proper choice of the Mn catalyst it is possible to hydroxylate anisole and naphthalene, used in excess relative to H_2O_2, with yields (based on H_2O_2) up to 98 and 83%, respectively. Even ethylbenzene, that has a very reactive benzylic position, was hydroxylated at its aromatic ring with yields up to 12%. Another aromatic compound bearing an electron-donating substituent, acetanilide, was hydroxylated with the Mn(TDCPN$_2$P)Cl–H_2O_2–ammonium mandelate system, affording *p*-hydroxyacetanilide in 80% yield. Benzene itself or aromatic compounds bearing electron-withdrawing substituents were much poorer substrates, and lead to phenol yields < 5%.

The origin of the particular efficiency of Mn(TDCPN$_x$P)Cl catalysts, with $x = 1$–4, for hydroxylation of electron-rich aromatic compounds with H_2O_2, and of the changes observed in the regioselectivity of these hydroxylations as a function of x (Table 1) is currently under investigation. It is likely that the lower activities of Mn catalysts with $x = 5$–8 are due to their pronounced tendency to exist in the Mn(II) state.

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