Metalloporphyrin-Catalyzed Oxidation of 2-Methylnaphthalene to Vitamin K_3 and 6-Methyl-1,4-naphthoquinone by Potassium Monopersulfate in Aqueous Solution

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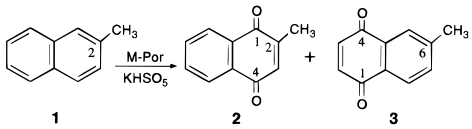
The metalloporphyrin-catalyzed oxidation of 2-methynaphthalene (**1**) by potassium monopersulfate produced mainly two naphthoquinones: 2-methyl-1,4-naphthoquinone (**2**) (menadione or vitamin K_3) and 6-methyl-1,4-naphthoquinone (**3**). In aqueous solution and at room temperature in the presence of 5 mol % of the water-soluble metalloporphyrins MnTPPS or FeTMPS, 2-methylnaphthalene was quantitatively oxidized to quinones **2** and **3**. Based on experiments performed in ^{18}O-labeled water and according to the "redox tautomerism" mechanism previously described for such catalysts, the oxidation to quinones is proposed to be mainly due to a cytochrome P-450-type oxygenation reaction (oxygen atom transfer), rather than a peroxidase-type oxidation (electron transfer).

Introduction

Vitamin K, the blood-clotting vitamin, serves as an essential cofactor of the carboxylase involved in the activation of the blood-clotting cascade proteins.[1] Vitamin K_3 (menadione), a synthetic naphthoquinone derivative having the antihemorrhagic activity of vitamin K, is prepared in 38 to 60% yield from 2-methylnaphthalene by the well-known chromium oxidation carried out with stoichiometric quantities of chromium trioxide in sulfuric acid.[2] However, the weak point of this process is the necessary treatment of chromium-containing wastewater. Alternative procedures using manganese(III) sulfate, a powerful one-electron oxidant, have been proposed.[3] As the stoichiometric use of transition metal oxidants is undesirable from economic and environmental viewpoints, the electrochemical recycling of oxidants has been investigated with some benefits using ceric methanesulfonate.[4] As another alternative, the oxygen transfer may involve the reaction of an inexpensive and environmentally acceptable oxygen atom donor with 2-methylnaphthalene in the presence of a transition metal catalyst. Some procedures, carried out in acetic acid and employing hydrogen peroxide and either methyltrioxorhenium (conversion of **1** was 81%, affording 47% of **2** and 7% of **3**)[5] or Pd^{II}−polystyrene sulfonic acid resin[6] as catalysts, have been reported (see Scheme 1 for structures of **1**−**3**). In the rhenium-catalyzed oxidations, highly concentrated hydrogen peroxide solution (83%) gave the best conversion but makes this reaction rather hazardous.[7] In a different way, the two-phase oxidation of **1** was accomplished by using ammonium persulfate in the catalytic presence of cerium ammonium sulfate, silver nitrate, and sodium dodecyl sulfate as micellar catalyst. In this latter case, the best yield was 73% in both naphthoquinones **2** and **3**.[8] Metalloporphyrin complexes have been widely used as catalysts to mimic monooxygenases and peroxidases when associated to various oxygen atom donors (PhIO, NaOCl, $KHSO_5$, H_2O_2, ...).[9] Quinone derivatives have been recently prepared by metalloporphyrin-catalyzed oxidations of various unactivated or substituted arenes.[10−14] Following our recent experiments on the ability of water-soluble manganese porphyrins to catalyze cytochrome P-450-type monooxygenations in monophasic aqueous solutions,[15,16] we report here the results that we obtained on the oxidation of 2-methylnaphthalene performed with potassium monopersulfate as primary oxidant[14] in the presence of various water-soluble metalloporphyrins as catalysts.

Scheme 1. Catalytic Oxidation of 2-Methylnaphthalene (1) by Metalloporphyrins and $KHSO_5$



Results and Discussion

Two categories of iron and manganese porphyrins (Scheme 2) were used as catalysts: (i) polyanionic water-

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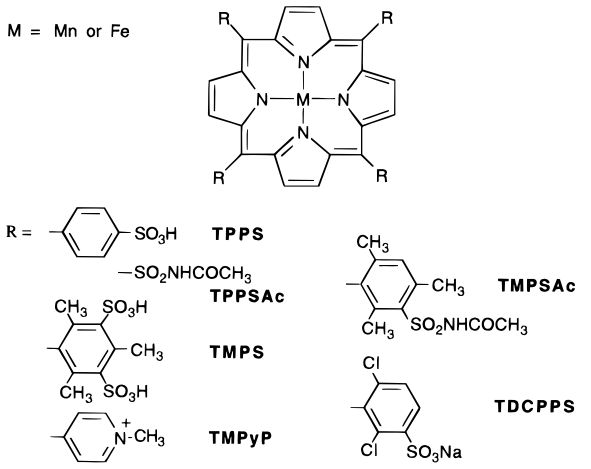
Table 1. Metalloporphyrin-Catalyzed Oxidation of 2-Methylnaphthalene (1) by Potassium Monopersulfate[a]

catalyst	reaction time (h)	pH	% conversion of **1**	% yield **2**	% yield **3**	**2** + **3** quinones selectivity[b]	vit K_3 (**2**) selectivity[b]
MnTPPS	2	5	86[c]	46	40	100	53
FeTPPS	1	3	58	30	21	88	52
MnTMPS	3	5	53	10	12	42	19
FeTMPS	1	3	100	40	57	97	40
MnTMPyP	3	5	90	16	18	38	18
MnTDCPPS	1	5	100	2	4	6	2
FeTDCPPS	0.2	6	100[d]	25	58	83	25
MnTPPSAc	5	5	93[e]	23	27	54	25
FeTPPSAc	1	3	52	20	10	58	38
MnTMPSAc	5	5	37	16	17	89	43
FeTMPSAc	1	3	95	42	47	94	44

[a] Reactions were performed at room temperature: catalyst/**1** molar ratio = 1/20, solvent: CH_3CN/acetate buffer pH 5 = 30/70 (v/v) for manganese catalysts and CH_3CN/distilled water = 30/70 for iron catalysts (the final pH value being 3 due to the acidity of monopersulfate) except for particular cases (see c−e). [b] Selectivity in quinone was defined as the ratio % yield of **2** (or **2** + **3**) divided by % conversion of **1**. [c] Solvent: CH_3CN/acetate buffer pH 5 = 35/65. [d] Catalyst/**1** molar ratio = 1/100, solvent: CH_3CN/phosphate buffer pH 6 = 30/70. [e] Solvent: CH_3CN/phosphate buffer pH 5 = 50/50.

Scheme 2. Structure of the Porphyrin Ligands and Their Metalated Derivatives



soluble derivatives such as tetrasodium *meso*-tetrakis(*p*-sulfonatophenyl)porphyrin (TPPS), octasodium *meso*-tetrakis(3,5-disulfonatomesityl)porphyrin (TMPS), tetrasodium *meso*-tetrakis(2,6-dichloro-3-sulfonatophenyl)porphyrin (TDCPPS), and *meso*-tetrakis(4-(*N*-methylpyridiniumyl))porphyrin (TMPyP), (ii) weakly acidic porphyrins like *meso*-tetrakis(4-(acetamidosulfonyl)phenyl)-porphyrin (TPPSAc), and *meso*-tetrakis(3-(acetamidosulfonyl)mesityl)porphyrin (TMPSAc). All the data were obtained with 5 mol % of catalyst with respect to **1** (except for some studies on the influence of the metalloporphyrin/2-methylnaphthalene ratio on the catalytic reaction) at pH 3, 5, or 6 in a homogeneous aqueous phase consisting of acetonitrile and either water or acetate (or phosphate) buffer, respectively. In such conditions, 2-methylnaphthalene (**1**) was oxidized to 2-methyl-1,4-naphthoquinone (**2**) (vitamin K_3) and 6-methyl-1,4-naphthoquinone (**3**). Substrate conversions, yields of quinones **2** and **3**, overall selectivities in quinones **2** + **3**, and selectivity in quinone **2** are summarized in Table 1.

Among the different catalysts, three of them, MnTPPS, FeTMPS, and FeTMPSAc, were able within 1 or 2 h to transform **1** into quinones **2** and **3** with 86, 100, and 95% of conversion and a very high overall selectivity in quinones, 100, 97, and 94%, respectively. Turnover rates based on conversions measured after 2 min of reaction were ranging from 4 to 8 cycles/min (data not shown). Yields of **2** (vitamin K_3) were 46, 40, and 42% for these three catalysts, respectively. These data can favorably be compared to the results obtained with the methyltrioxorhenium/hydrogen peroxide system[5] which gave 47% yield for **2** (in this latter case the overall selectivity in quinones was only 67%). However, the only drawback of these metalloporphyrin-catalyzed oxidations is the rather low regioselectivity of the quinone formation: **2** and **3** were produced in similar yields (the **2**/**3** ratio varied from 0.4 to 2.0).

We checked different oxidants, including hydrogen peroxide, but potassium monopersulfate gave the best conversions and quinone yields. MnTDCPPS and FeTDCPPS, two metalloporphyrin catalysts of the second-generation[9a] and MnTMPyP, a cationic complex commonly used as chemical nuclease,[9a] were highly efficient in converting **1** (conversions = 90−100%), but the selectivity in quinone **2** was low (2−25%). Among the acetylsulfonamide metalloporphyrin catalysts, FeTMPSAc gave the best results, quite similar to that obtained with FeTMPS, the related parent complex.

Influence of acetonitrile/buffer ratio or pH was studied for MnTPPS and FeTMPS (Figure 1). Bell-shape curves were observed in studies on the influence of acetonitrile on the catalytic reactivity, with 35 and 30% as optimal percentages of acetonitrile when using MnTPPS and FeTMPS, respectively (Figures 1A and 1C). We have no convincing explanation for such a behavior, but a similar bell-shape curve was previously observed in the metalloporphyrin-catalyzed oxidations of lignin models by potassium monopersulfate.[11a]

The catalytic activity of MnTPPS as well as the yields in quinones **2** and **3** were very weak at low pH values (<3), reached an optimum at pH 5, and then decreased (Figure 1B). In the case of FeTMPS, the situation was quite different: the highest activities were observed at pH values below 4 where conversion was 100%, the maximal yield in vitamin K_3 being observed at pH 4. Above pH 5, the reactivity of FeTMPS dramatically decreased (Figure 4D). The **2** + **3** quinone selectivity was also maximal at pH 4 (100%) and then sharply decreased when increasing the pH value (54 and 26% at pH 5 and 7, respectively). The optimal pH values for FeTDCPPS and MnTMPyP were 6 and 5, respectively (data not shown).

It should also be noted that **2** + **3** quinones selectivity dropped when the catalyst/substrate ratio was lowered. Typically, in the case of FeTMPS, when this ratio decreased from 5 to 1%, selectivity in both quinones decayed from 97 to 62%, and conversion from 100 to 69%.

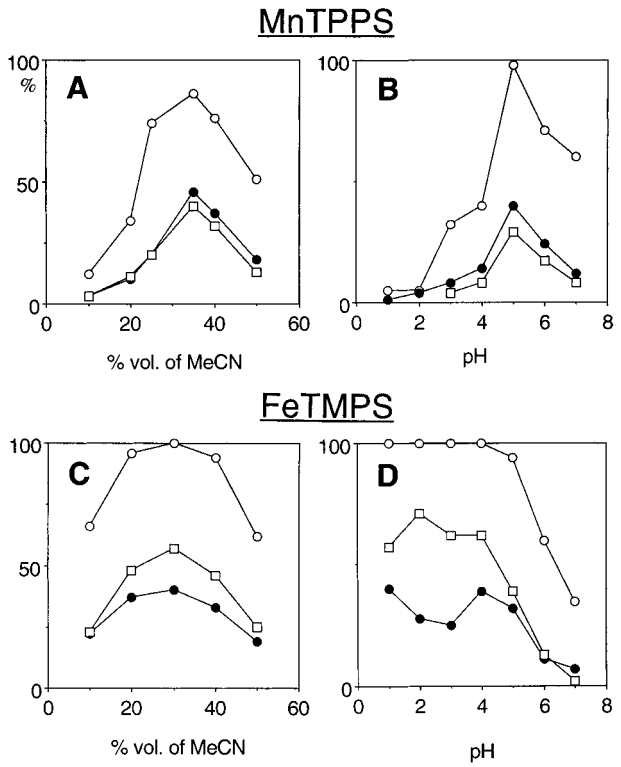


Figure 1. Influence of the acetonitrile/buffer ratio and pH on the catalytic activities of MnTPPS and FeTMPS. (○) % conversion of 2-methylnaphthalene; (●) % yield of vitamine K_3 **2**; (□) % yield of **3**.

In the case of FeTDCPPS, when the catalyst/substrate ratio decreased from 5 to 0.2%, the **2** + **3** quinones selectivity decayed from 63 to 37%, although the conversion remained unchanged (100%).

Except in the case of metalated TPPS, quinones **2** and **3** (Table 1) were formed in better yield with iron porphyrin catalysts, compared to the corresponding manganese complexes. However, manganese derivatives still behave as rather efficient catalysts in this homogeneous aqueous medium, whereas they were unable to catalyze the oxidation of unactivated arenes to *p*-quinones in a biphasic system under phase-transfer conditions.[17]

In control experiments, we checked that the reaction did not occur in the absence of catalyst and that the two quinones **2** and **3** were stable, at least for 5 h, in the catalytic oxidation conditions. Also, we neither observed 2,3-epoxy-2-methyl-1,4-naphthoquinone and phthiocol (overoxidation products) that might be derived from further oxidation of **2**, nor hydroxylated products or side alkyl substituent oxidation products observed by Baciocchi *et al.*[17] when using a hydrophobic iron porphyrin associated to magnesium monoperphthalate in a biphasic system (dichloromethane/water).

^{18}O-Labeling experiments. In order to investigate the mechanism of this metalloporphyrin-catalyzed oxidation of 2-methylnaphthalene and to distinguish between either a cytochrome P-450-type oxygenation reaction with incorporation of oxygen atoms from the oxidant or a peroxidase-type oxidation (electron abstraction from the substrate) with incorporation of oxygen atoms from water,[18] we decided to analyze the oxygen atom-content

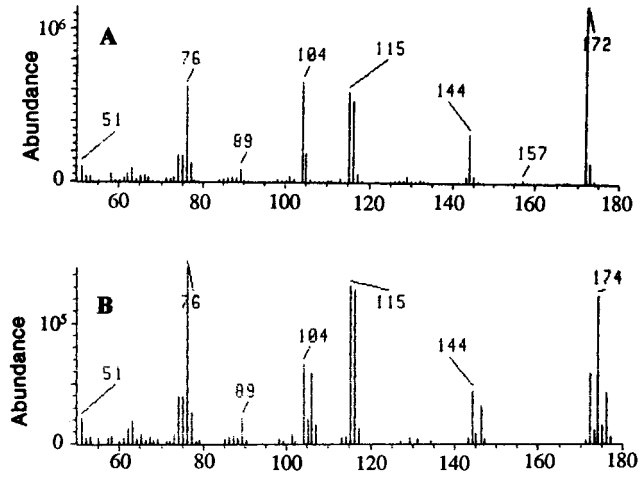
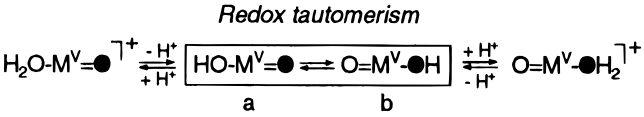


Figure 2. MS spectra of naphthoquinone **2** produced during the $KHSO_5$ oxidation of **1** catalyzed by FeTDCPPS at pH 4 using $H_2{}^{16}O$ (A) and $H_2{}^{18}O$ (B) as solvent.

Scheme 3. Redox Tautomerism (○ = ^{16}O; ● = ^{18}O)



of quinone **2** in reaction mixtures containing 98% ^{18}O-labeled water.

In control experiments, we checked that light oxygen atoms of naphthoquinone **2** did not exchange with heavy oxygen atoms of labeled water or, at least in the range of pH used (4−5), that this exchange was limited below 2%. We checked also that *$KHSO_5$ itself did not exchange oxygen atoms with water*: in addition to our previous work on $KHSO_5$ epoxidation of olefins catalyzed by hydrophobic metalloporphyrins,[19] we showed that even after 1 h of preincubation of unlabeled $KHSO_5$ in ^{18}O-labeled water at room temperature, either at pH 5 or 7, the catalytic reaction provided only a ^{16}O-labeled epoxide (>99% ^{16}O-label).

We recently reported, in olefin epoxidation[15] or hydroxylation of C−H bonds of DNA sugars[16] performed in aqueous medium with water-soluble metalloporphyrin catalysts, that half of the oxygen atom incorporated in the epoxide or in the hydroxylated sugar derivative came from the solvent and half from $KHSO_5$, the primary oxidant. A redox tautomerism mechanism involving the metal-oxo and the *trans* axial hydroxo ligand has been proposed to explain these results (Scheme 3).[15] The ^{18}O incorporation in quinone **2** during oxidation of **1** catalyzed by MnTMPyP (this catalyst was used in the early studies on the redox tautomerism[15,16]) and by FeTDCPPS (one of the most efficient catalysts used in the present work) was followed by determination of the molecular ion percentages at 172 (M), 174 (M + 2), and 176 (M + 4) corresponding to the incorporation of none, one, or two heavy oxygens in quinone **2** (Figure 2). The ^{18}O incorporation was deduced to be 30% and 49% for MnTMPyP and FeTDCPPS, respectively (Table 2). Analyses performed on quinone **3** gave similar results (23 and 55% of ^{18}O incorporation with MnTMPyP and FeTDCPPS catalysts, respectively) and suggest that the ^{18}O-incorporation in the quinones is not modulated by the presence of a methyl group. These results indicated that more than

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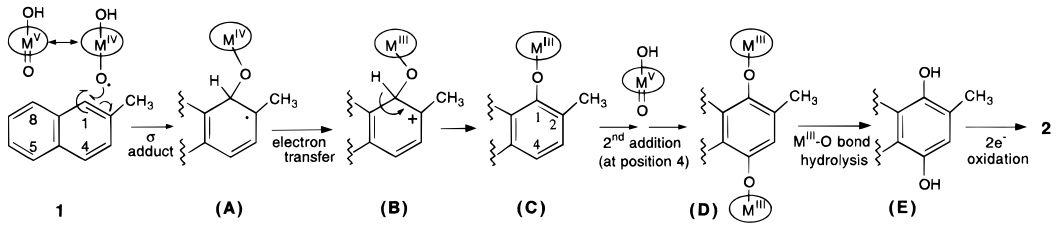
Table 2. Incorporation of ^{18}O from $H_2{}^{18}O$ in Vitamin K_3 (2) during the Oxidation of 2-Methylnaphthalene (1) or 2-Methyl-1-naphthol Catalyzed by MnTMPyP or FeTDCPPS

				yield (%)		incorp of ^{18}O into **2** (or **3**) molecular ion %			
catalyst (%/subst)[a]	pH	substrate	conv (%)	**2**	**3**	M	M + 2	M + 4	% incorp
MnTMPyP (5%)	5	2-methylnaphthalene	90	16	18	50 (54)	41 (46)	9 (*b*)	30 (23)
	5	2-methyl-1-naphthol	100	17		60	40		40
FeTDCPPS (2%)	4	2-methylnaphthalene	100	18	45	23 (18)	56 (53)	21 (29)	49 (55)
	4	2-methyl-1-naphthol	100	30		20	80		80
Theoretical isotopic distribution of molecular peak for two consecutive oxygen transfers according to a 70/30 redox tautomerism (70% ^{16}O and 30% ^{18}O incorp):						49	42	9	
to a 50/50 redox tautomerism (50% ^{16}O and 50% ^{18}O incorp):						25	50	25	

[a] Reactions were performed in a mixture of acetonitrile/acetate buffer pH 4 or 5 (3/7, v /v). [b] Peak of too low intensity to be accurately quantified.

Scheme 4. Proposed Mechanism of $KHSO_5$ Oxidation of 2-Methylnaphthalene Catalyzed by Metalloporphyrins in Aqueous Solution



45% of the oxygen atoms incorporated into the quinone came from $KHSO_5$, the unlabeled primary oxidant. These data strongly suggest that the quinone generation results from of a catalytic oxygenation of **1** via a P-450-type mechanism involving an oxygen transfer from a high-valent metal-oxo species. They allow exclusion of the formation of a radical cation (electron abstraction) followed by addition of a water molecule which should lead to 100% ^{18}O incorporation into the quinone (see ref 18 for an example of full water label incorporation in a quinone-imine formation catalyzed by a peroxidase).

In the case of FeTDCPPS, the experimental isotopic distribution was coherent with two consecutive oxygen transfers from the active metal-oxo species, involving a redox tautomerism mechanism with a theoretical isotopic distribution of 50/50. The experimental molecular peak percentages (50/41/9) found for quinone **2** in the MnTMPyP-catalyzed oxidation of **1** were compatible with the theoretical isotopic distribution 49/42/9 in a 70/30 redox tautomerism (see Table 2). These data suggest that the redox tautomerism equilibrium **a** ⇔ **b** (Scheme 3) is probably tuned by small variations of kinetic parameters, including the solvent effects and/or differences in the kinetic parameters of the oxygen transfer from the metal-oxo to the substrate and the different steps necessary to reach the tautomeric equilibrium oxygen transfer steps.

A controversal matter in the literature concerns the possible role of 1-naphthol as menaquinone precursor in bacteria (see ref 20 and references therein) or as reaction intermediate during the metalloporphyrin-catalyzed formation of 1,4-naphthoquinone from naphthalene.[17] In our case, 2-methyl-1-naphthol was never detected in the course of the catalytic oxidation of 2-methylnaphthalene. In addition, when a reference sample of this phenol was oxidized with either MnTMPyP/ or FeTDCPPS/$KHSO_5$ systems, vitamin K_3 was produced in 17 and 30% yield, respectively (conversion being 100% in both cases). When the reaction was performed in $H_2{}^{18}O$ with MnTMPyP as catalyst, the ^{18}O incorporation was 40% (Table 2), as for epoxidation of carbamazepine under the same conditions (data not shown), suggesting that oxidation of 2-methyl-1-naphthol to naphthoquinone **2** more likely resulted from one oxygen transfer via a P-450 type oxygenation reaction[15] and not from an electron transfer in a peroxidase-type reaction[18] (which should lead to a higher level of heavy oxygen incorporation). In fact, such a high ^{18}O incorporation was observed with FeTDCPPS as catalyst (80% of ^{18}O incorporation, Table 2), indicating that, in this case, the naphthol derivative was not involved as reaction intermediate during the oxidation of 2-methylnaphthalene, as already suggested for the metalloporphyrin-catalyzed oxidation of naphthalene to 1,4-naphthoquinone in biphasic medium.[17] At the present time, in the case of this particular naphthol, we have no explanation for the better oxygenation (*versus* oxidation) properties of Mn(TMPyP)-oxo compared to Fe(TDCPPS)-oxo.

Taking into consideration the main features of these metalloporphyrin-catalyzed oxidations of 2-methylnaphthalene to quinone **2**, i.e. the catalytic transfer of two oxygens in a monooxygenase mode and the absence of 2-methyl-1-naphthol as reaction intermediate, we can propose that these oxidations are mediated by a high-valent metal-oxo species with the coordinated oxygen atom having a strong electrophilic radical character (see Scheme 4). In Scheme 4, the active species, depicted as $(Por)M^{IV}-O^{\bullet}$ (a limit form of $(Por)M^{V}=O$; the other limit form $(Por^{+\bullet})M^{IV}=O$ being considered as responsible for a peroxidase activity) is attacking the aromatic ring of **1** at position 1 (Hückel calculations indicated that the coefficients of the HOMO orbital are decreasing in the following order: C1 (−0.46), C8 (0.42), C4 (0.40), and C5 (−0.39), explaining why the two quinones **2** and **3** are equally produced) to create a new carbon−oxygen bond forming the σ adduct **A**; the following electron transfer leads to the carbocation **B** and then to **C**, after a fast elimination of the proton from position 1. In order to

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explain why 2-methyl-1-naphthol was not an intermediate in the catalytic oxidation of **1**, hydrolysis of the metal(III)−O-aromatic bond should be slower than the addition of a second metal-oxo species at position 4, then giving in several steps the intermediate **D**. The fact that yield of quinones **2** + **3** decayed when the catalyst amount decreased supports this hypothesis. The hydrolysis of both metal−O-aromatic bonds present in **D** gives rise to 2-methylnaphthohydroquinone **E**, which is quickly oxidized to quinone **2**. We checked that a reference sample of **E** was very quickly oxidized to the naphthoquinone **2** by $KHSO_5$, even in the absence of catalyst. Such a stepwise mechanism is in agreement with that one proposed by Burka *et al.* for the hydroxylation of halobenzenes mediated by microsomal cytochrome P-450.[21] Recent semiempirical molecular orbital calculations confirmed these mechanistic proposals.[22]

Although Jerina et al. observed the formation of stable intermediate epoxides in the cytochrome P-450-catalyzed hydroxylation of naphthalene,[23] recent studies on P-450-mediated oxidation of benzene derivatives indicated that the formation of arene oxides is not a general phenomenon in monooxygenase-catalyzed oxidation.[24,25] At this stage of the study, we can exclude the possibility of long-life kinetic arene oxides as intermediates in the formation of quinones **2** and **3** during the metalloporphyrin-catalyzed oxidation of 2-methylnaphthalene.

Conclusion

The metalloporphyrin-catalyzed oxidation of 2-methylnaphthalene by potassium monopersulfate produced mainly two naphthoquinones, 2-methyl-1,4-naphthoquinone (**2**) (menadione or vitamin K_3) and 6-methyl-1,4-naphthoquinone (**3**). In aqueous solution and at room temperature in the presence of 5 mol % percent of the water-soluble metalloporphyrins MnTPPS or FeTMPS, 2-methylnaphthalene was quantitatively oxidized to quinones **2** and **3**.

^{18}O-labeling experiments suggest that, in an aqueous solution, the metalloporphyrin-catalyzed oxidation of 2-methyl-naphthalene (**1**) to *p*-quinones involves two consecutive oxygen transfers from an intermediate metal-oxo entity in a cytochrome P-450-type oxygenation reaction. The data show that the redox tautomerism mechanism previously described for metalloporphyrin-catalyzed oxygenation reactions in aqueous medium[15] is probably involved and responsible for 30 to 55% indirect incorporation of ^{18}O from water into the generated quinones.

Experimental Section

Chemicals. 2-Methylnaphthalene (**1**), 2-methyl-1,4-naphthoquinone (**2**), styrene, benzyldimethyltetradecylammonium and 4-*tert*-butylpyridine were obtained from Aldrich. 2-Methyl-1-naphthol from Aldrich was purified (precipitation by addition of HCl from a 0.1 M NaOH aqueous solution) before use in order to eliminate any trace of vitamin K_3. 2-Methyl-1,4-naphthohydroquinone, 2,3-epoxy-2-methyl-1,4-naphthoquinone and phthiocol were prepared according to ref 2. Potassium monopersulfate was the triple salt $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$ (Curox) was a gift from Interox. The iron and manganese derivatives of tetrasodium *meso*-tetra(*p*-sulfonatophenyl)porphyrin (TPPS),[11] octasodium *meso*-tetrakis(3,5-disulfonatomesityl)porphyrin (TMPS),[26] tetrasodium *meso*-tetrakis(2,6-dichloro-3-sulfonatophenyl)porphyrin (TDCPPS),[27] *meso*-(4-(*N*-methylpyridiniumyl))porphyrin (TMPyP),[28] *meso*-tetrakis(4-(acetamidosulfonyl)phenyl)porphyrin (TPPSAc),[29] and *meso*-tetrakis(3-(acetamidosulfonyl)mesityl)porphyrin (TMPSAc)[29] were prepared in our laboratory according to published syntheses (see Scheme 2 for structures). *meso*-Tetraphenylporphyrin manganese complex was from Strem Chemicals. $H_2{}^{18}O$ (98 atom %) was supplied by Eurisotop (Gif-sur-Yvette, France).

General Procedure for the Catalytic Oxidation of 2-Methylnaphthalene. Metalloporphyrin-catalyzed oxidations of 2-methylnaphthalene were performed in a one-phase solution constituted of acetonitrile and either distilled water or a buffer solution, at room temperature (23 °C) and under aerobic conditions, according to the same general procedure: the reaction mixture (2 mL) contained 10 μmol of substrate introduced as a 80 mM acetonitrile solution of **1** (or 2-methyl-1-naphthol) with also trichlorobenzene as internal standart, 0.5 μmol (or lower concentration when mentioned) of catalyst introduced as 20 mM solution in water, required amounts of acetonitrile and 0.1 M buffer to obtain the desired ratio organic phase/water, and at last 50 μmol of $KHSO_5$ introduced as 0.67 M solution in water. Reactions at pH 4.0 and pH 5.0 were performed in a 0.1 M acetate buffer, at pH 2.0 and 3.0 in a 0.1 M citrate−phosphate buffer[30] and at pH 6.0 and 7.0 in a 0.1 M phosphate buffer. Catalytic oxidations were started by addition of the monopersulfate solution (50 μmol correspond to 15.4 mg of Curox).

$H_2{}^{18}O$ Experiments. Reactions were carried out in $H_2{}^{18}O$ (98 atom %) according to the following procedure. A mixture of 12.5 μL of substrate (80 mM in CH_3CN), 2.5 μL of metalloporphyrin (20 mM in water), and 350 μL of 0.1 M acetate buffer (pH 4 and 5) was taken to dryness using a Speed-Vac. A 300 μL volume of $H_2{}^{18}O$ and 150 μL of CH_3CN were added to the residue. Reaction was started by addition of 3.9 mg of $KHSO_5$ in 50 μL of $H_2{}^{18}O$. Control experiments in order to check the exchange of oxygen between $H_2{}^{18}O$ and naphthoquinone were carried out under the same conditions by using **2** instead of **1** as initial substrate. Control experiments in order to check the exchange of oxygen between $H_2{}^{18}O$ and $KHSO_5$ were carried out as follows: 350 μL of 0.1 M acetate buffer (pH 5.0) or 0.25 M phosphate buffer (pH 7.0) were taken to dryness, and 3.9 mg of $KHSO_5$ (12.7 μmol) and 350 μL of $H_2{}^{16}O$ − $H_2{}^{18}O$, 50/50, were added. A resulting solution was stirred for 1 h at 20 °C. Then 1 mL of a CH_2Cl_2 solution containing the manganese complex of *meso*-tetraphenylporphyrin (76 nmol), 4-*t*-BuPy (1.59 μmol), styrene (6.35 μmol), and benzyldimethyltetradecylammonium chloride (318 nmol) was added. Ratios between reagents were the same as those published in ref 19. After 30 min of additional stirring, conversions of styrene and yields of epoxide were upper than 50%. The organic layer was separated, concentrated, and then analyzed by GC-MS. More than 99% of the styrene oxide contained light oxygen, indicating that no oxygen exchange between $KHSO_5$ and $H_2{}^{18}O$ occurred either at pH 5 or at pH 7 during the 1 h preincubation time or in the course of the reaction.

Substrate conversion and yields of **2** and **3** were determined by GC on a Intersmat IGC 120 FID gas chromatograph, using

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(30) Using Sorensen's citrate buffer which contains HCl led to variable amounts of chlorinated products on the aromatic ring. So we recommend use of Mellvaine's citric acid−phosphate buffer, deprived of chloride anions, to avoid the formation of these side products.

a 6 ft × 1.125 in. column packed with 10% SE-30 on chromosorb WHP 80−100 mesh. Nitrogen was the carrier gas, and trichlorobenzene was used as internal standard. The reaction mixture was directly injected. Retention times were 3.1, 4.9, 11.8, 12.7, and 14.6 min for trichlorobenzene, **1**, **2**, **3,** and 2-methylnaphthol, respectively. Reaction products were extracted with diethyl ether and purified on Merck TLC plate RP-18F 254S (eluent: dichloromethane/hexane = 50/50, v/v) before identification. The mixture of both naphthoquinones **2** and **3** was directly analyzed by ^{1}H NMR (Brucker 250 MHz spectrometer) and GC-MS (Hewlett-Packard 5890 instrument equipped with a nonpolar column, cross-linked methylsilicone gum 12 m × 0.2 mm HL-1, using electron-impact ionization at 70 eV). NMR ($CDCl_3$): **2**, δ 2.18 (d, 3H, J = 1.4 Hz, CH_3), 6.83 (q, 1H, J = 1.4 Hz, H_3), 7.68−7.75 (m, 2H, H_6 and H_7), 8.01−8.12 (m, 2H, H_5 and H_8); **3**, δ 2.48 (s, 3H, CH_3), 6.93 (s, 2H, H_2 and H_3), 7.53 (dd, 1H, J = 9.8 and 1.8 Hz, H_7), 7.86 (s, 1H, J = 1.8 Hz, H_5), 7.96 (d, 1H, J = 9.8 Hz, H_8). MS data (EI): **2**, m/z = 172 (M^+), 144 $(M - CO)^+$, 116 $(M - 2CO)^+$, 115 $(M - 2CO - H)^+$, 104 $(M - COCHCHCH_3)^+$, 76 $(C_6H_4)^+$; **3**, m/z = 172 (M^+), 144 $(M - CO)^+$, 118 $(M - C_2H_2)^+$, 116 $(M - 2CO)^+$, 115 $(M - 2CO - H)^+$, 90 $(CH_3C_6H_3)^+$, 89 $(C_7H_5)^+$, 63 $(C_5H_3)^+$.

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