A Free-Radical Mechanism in a Novel Metalloporphyrin-Catalyzed Oxidation of Phenols by *t*-BuOOH

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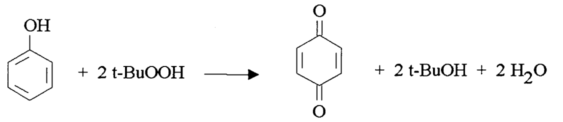
Metalloporphyrins, a chemical model of cytochrome P450, catalyze the oxidation of phenols with the para-position free to the corresponding p-quinones. Evidences of a free-radical mechanism are reported, including the results obtained with p-cresol.

Recently, we[1] have reported evidences concerning the involvement of t-BuO• and t-BuOO• radicals in the oxidation and halogenation of alkanes, alkenes and alkylbenzenes by t-BuOOH, catalyzed by Fe(III) and Mn(III) porphyrins. Since alkoxy and peroxy radicals react very quickly with phenols (eqs. 1 and 2),[2] we have considered the possibility of oxidizing phenols by t-butylhydroperoxide by metalloporphyrin catalysis

$$\text{Ar-OH} + \text{t-BuOO}^{\cdot} \xrightarrow{k_1} \text{Ar-OH} + \text{t-BuOO}^{\cdot} \qquad (1)$$
$$k \sim 10^4 - 10^6\ \text{M}^{-1}\text{s}^{-1} \text{ at r.t.}$$

$$\text{Ar-OH} + \text{t-BuO}^{\cdot} \xrightarrow{k_2} \text{Ar-O}^{\cdot} + \text{t-BuOH} \qquad (2)$$
$$k \sim 10^9\ \text{M}^{-1}\text{s}^{-1} \text{ at r.t.}$$

The reaction of phenol with t-BuOOH and catalytic amount of pyridine and metalloporphyrin, Fe-tetraphenylporphyrin chloride (FeTPPCl) or Mn-tetra(dichlorophenyl)-porphyrin chloride (MnTDClPPCl) in CH_2Cl_2 or benzene at 0°C or 20°C gave p-benzoquinone (**1**) (eq.3) and 2-t-butoxy-p-benzoquinone (**2**) as a byproduct.



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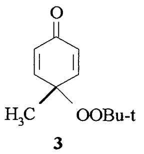
The results are summarized in the Table. In the absence of pyridine only traces of phenol reacted. The selectivity was affected by temperatures and the presence of oxygen. This latter observation suggests that a free-radical mechanism must be involved. This is supported by the results obtained with p-cresol: compounds **3** and **4** have been obtained in a 1.2 : 1 ratio.



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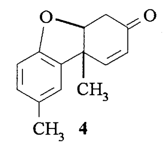

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The following free-radical mechanism is highly consistent with these results: t-BuOOH reacts with metalloporphyrins according to our previous results[1b] (eq.4, P = porphyrin)

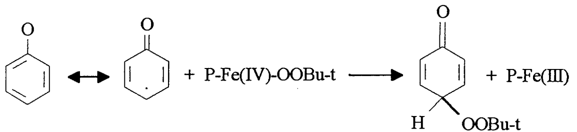
$$\text{P-Fe(III)Cl} + \text{t-BuOOH} \longrightarrow \text{P-Fe(IV)=O} + \text{t-BuO}^{\cdot} + \text{HCl} \qquad (4)$$

It is well known[2] that hydrogen abstraction from phenol (eq.2) is quite a fast process and it gives the phenoxy radical, which is oxidized (eq.5) to the peroxide **5**, regenerating the catalyst. We have recently reported[1b, 3] evidences indicating that hydroperoxides can be considered as pseudohalides and that they can be transferred to carbon-centered radicals by a ligand-transfer process from coordinated metal salts.

Table. Oxidation of phenol by metalloporphyrins[a]

Metallo porphyrin	Solvent	Time (h)	T (°C)	Conv.[b] (%)	Selectivity[c] (%)
MnTDClPPCl[d]	CH_2Cl_2	4	20	--	--
FeTPPCl[d]	CH_2Cl_2	24	20	4	(**1**) 91
FeTPPCl	CH_2Cl_2	23	20	60	(**1**) 33; (**2**) 6
FeTPPCl	CH_2Cl_2	24	0	66	(**1**) 47; (**2**) 7
FeTPPCl	benzene	4	0	58	(**1**) 65; (**2**) 30
MnTDClPPCl	benzene	19	20	38	(**1**) 49; (**2**) 6
FeTPPCl[e]	benzene	4	20	28	(**1**) 41; (**2**) 56
FeTPPCl[f]	benzene	4	20	34	(**1**) 50; (**2**) 6

[a] 5 mmol of phenol, 10 mmol t-BuOOH, 10^{-3} mmol metalloporphyrin, 0.3 mmol pyridine; 10 mL solvent, air atmosphere. [b] Based on phenol; [c] Based on the reacted phenol. [d] Without pyridine; [e] Under nitrogen atmosphere with 5 mmol t-BuOOH. [f] Under oxygen atmosphere with 5 mmol t-BuOOH



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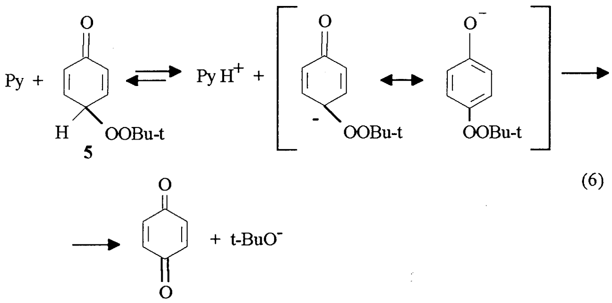
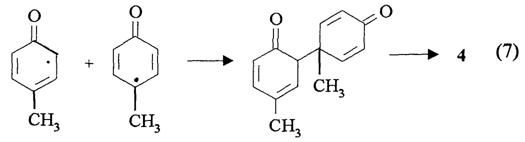
The decomposition of **5**, catalyzed by pyridine, leads to p-benzoquinone.



(6)

Pyridine has a double function: it coordinates the metalloporphyrin, making the redox process of eq. 4 easier, as we[1b] have recently emphasized, and at the same time it catalyzes the decomposition of **5** according to eq.6. It is known[4] that mixed peroxides between t-butyl and secondary alkyl groups are decomposed to carbonyl compounds and t-BuOH by pyridine. With m-cresol, 2-methyl-p-benzoquinone (**6**) was formed with 80% selectivity and 82% conversion of the phenol. Preliminary results indicate that 2,3,6-trimethylphenol and 2-methylnaphthol give the corresponding p-quinones (**7**) and (**8**) in 45% and 38% yields respectively, while β-naphthol gives the o-quinone **19** (24%).

With p-cresol, the ligand-transfer process of eq.5 is less selective for steric reason and the asymmetrical coupling of the phenoxy radical competes, leading to compound **4** (eq.7)



Moreover, the peroxide **3** is stable towards the pyridine-catalyzed decomposition of eq.6, because of the absence of a C-H bond in the α -position to the peroxy group.

The quinones **1** and **6-9** and the ketone **4** are known and they were identified by GC-MS analysis and comparison with authentic samples. Compound **2** has been isolated by flash chromatography and analyzed by ^{1}H-NMR ($CDCl_3$); δ 1.65 (s, 9H), 6.08 (d, 1H), 6.68 (m, 2H); MS 180 (M^+), 165, 125, 96, 69, 57. The peroxide **3** has been isolated by flash chromatography and analyzed by iodometric titration and ^{1}H-NMR ($CDCl_3$); δ 1.16 (s, 9H), 1.39 (s, 3H), 6.18 (d, 2H), 6.86 (d, 2H).

References.

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