A Mechanistic Study of the Oxidation of Phenols in Aqueous Solution by Oxoiron(IV) Tetra(*N*-methylpyridyl)porphyrins. A Model for Horseradish Peroxidase Compound II?

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The reaction of oxoiron(IV) tetra(2-*N*-methylpyridyl)porphyrin ($OFe^{IV}T2MPyP$), generated from iron(III) tetra(2-*N*-methylpyridyl)porphyrin and *tert*-butyl hydroperoxide, with 3-cyanophenol in aqueous solution (pH 7.7) shows first-order dependence on the concentration of the phenol and the oxidant. The pH dependence of the measured second-order rate constant (pH 7.7–8.6) indicates that the phenol, and not the phenolate ion, is the substrate oxidised by $OFe^{IV}T2MPyP$.

Substituent effects on the second-order rate constant were obtained from the oxidation of phenol and six monosubstituted derivatives and these data were analysed by Hammett and modified Hammett equations. The ρ values obtained, in conjunction with the results from an EPR study of the oxidation of the water soluble hindered phenol, Trolox C, and the oxidation of [O-$^2H_1$]-4-fluorophenol, suggest that the rate-determining step in these reactions involves hydrogen atom abstraction from the phenol by the oxoiron(IV) species.

The Hammett analyses of rate data from the oxidation of phenols by horseradish peroxidase compound **II** have been reexamined and compared with those from the present study. This leads to the conclusion that the enzymatic process involves a rate determining electron transfer from the phenol to the oxo-haem.

In the reaction sequence of horseradish peroxidase, an initial two-electron oxidation of the haem group by hydrogen peroxide (or alkyl hydroperoxide) generates compound **I** (HRP I)† which subsequently reverts *via* compound **II** (HRP II) to the resting enzyme by two one-electron reductions [reactions (1)–(4)].[1]

$$\text{HRP} + RO_2H \longrightarrow \text{HRP I} + ROH \quad (1)$$

$$\text{HRP I} + \text{Sub-H} \longrightarrow \text{HRP II} + \text{Sub}^{\bullet} \quad (2)$$

$$\text{HRP II} + \text{Sub-H} \longrightarrow \text{HRP} + \text{Sub}^{\bullet} + H_2O \quad (3)$$

$$\text{Sub}^{\bullet} \longrightarrow \text{Products} \quad (4)$$

Phenols, which are typical substrates for the enzyme, are oxidised to phenoxyl radicals.[2] Mechanistic studies by Dunford[2c,d] and Sakurada[2c] and their coworkers suggest that phenols rather than their phenolate anions are the substrates and that oxidation occurs *via* simultaneous removal of a proton and an electron. However, since the haem prosthetic group in HRP is almost entirely surrounded by a protein matrix,[3] oxidations are restricted to electron transfer at the edge of the porphyrin ring and do not involve the $O{=}Fe^{IV}$ group directly. For this reason oxygen transfer from HRP to substrates are rarely, if ever, observed.

Despite the widespread interest in metalloporphyrin-catalysed oxidations, there is relatively little information on the mechanism of phenol oxidations by non-enzymic oxoiron(IV) porphyrins. This is mainly as a result of the low stability of the high valent oxoiron(IV) intermediates which have prevented direct kinetic measurements on their reactions at ambient temperature. Thus Traylor *et al.*[4] studied the oxidation of phenols using the HRP I analogue derived from 3-chloroperoxybenzoic acid and a chelated protohaemin in methanol and in dichloromethane. However, because of the instability of the oxoiron species the relative reactivities of the phenols had to be determined from competitive reactions. The only model system for which rate constants for phenol oxidation have been reported involved the generation of an active oxidant from H_2O_2 and iron(III) deuterioporphyrin.[5] The precise structure of this active oxidant is uncertain although it is most likely to be at the same oxidation level as HRP II.

In recent studies we[6] and others[7] have shown that oxoiron(IV) species derived from ionic iron(III) porphyrins are surprisingly stable in aqueous alkaline solution. This provides the opportunity to carry out detailed kinetic studies of oxidations by these HRP II analogues. In this paper we report the results from our investigations of the mechanism of phenol oxidation by oxoiron(IV) tetra(*N*-methylpyridyl)porphyrins in aqueous solution.[8]

Results

The Generation of Oxoiron(IV) *Species from Bu^tO_2H and Iron*(III) *Tetra*(N-*methylpyridyl*)*porphyrins*.—UV–VIS Spectroscopy shows that the addition of a half-molar equivalent of Bu^tO_2H to 1.2×10^{-5} mol dm^{-3} $Fe^{III}T2MPyP$ in 0.05 mol dm^{-3} aqueous phosphate buffer (pH 7.7) and ionic strength ($NaNO_3$) 0.20 mol dm^{-3} generates $OFe^{IV}T2MPyP$ in less than 3 min (Fig. 1). For $Fe^{III}T2MPyP$: Bu^tO_2H molar ratios of 2 or less the oxoiron(IV) species decays slowly back to the parent iron(III) porphyrin (first $t_{\frac{1}{2}}$ 10.7 h for 2:1 ratio porphyrin:peroxide) with no apparent bleaching. Spectral simulation reveals that the stoichiometry of the $Fe^{III}T2MPyP$ oxidation by Bu^tO_2H is less than the maximum value of 2 (Table 1). An analogous study with $Fe^{III}T4MPyP$ generated $OFe^{III}T4MPyP$ (λ_{max} Soret band 426 nm),[6] however, the latter species is significantly less stable than its isomer $OFe^{IV}T2MPyP$ having a first $t_{\frac{1}{2}}$ for decay of *ca.* 6 min.

Kinetic Studies of the Oxidation of Substituted Phenols by $OFe^{IV}T2MPyP$.—Characteristics of the kinetic equation. The

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† The following abbreviations are used, HRP I and HRP II for horseradish peroxidase compounds **I** and **II**; T2MPyP and T4MPyP for the tetra(2-*N*-methylpyridyl)porphyrin and tetra(4-*N*-methylpyridyl)porphyrin ligands, respectively.

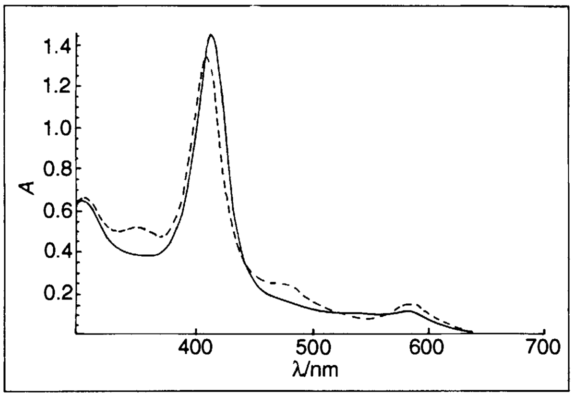

Fig. 1 UV–VIS spectrum of the reaction of Fe^{III}T2MPyP (1.2×10^{-5} mol dm^{-3}) with a half-molar equivalent of Bu^tO_2H at pH = 7.7, μ = 0.20 mol dm^{-3} at 30 °C after 0 min (– – –) and 3 min (——)

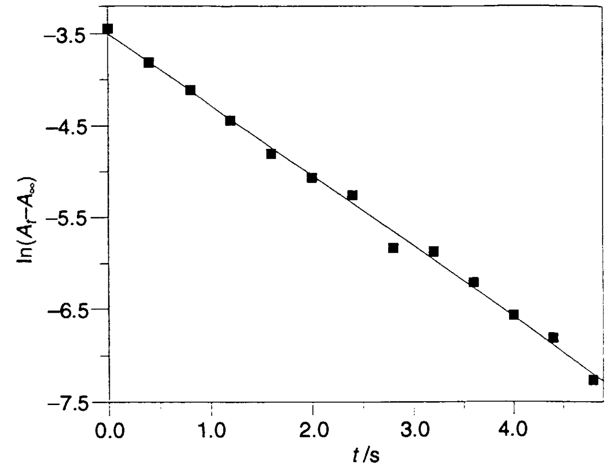

Fig. 2 Plot of the integrated first-order rate equation for reduction of OFe^{IV}T2MPyP (from Fe^{III}T2MPyP 3.30×10^{-6} mol dm^{-3}) by 3-cyanophenol (9.8×10^{-5} mol dm^{-3}), pH = 7.7, μ = 0.20 mol dm^{-3} at 30 °C

Table 1 The yield of OFe^{IV}T2MPyP from the reaction of Fe^{III}T2MPyP with varying amounts of Bu^tO_2H in aqueous solution: Fe^{III}T2MPyP, 1.5×10^{-5} mol dm^{-3}; phosphate buffer, 0.05 mol dm^{-3}, pH = 7.7, μ = 0.20 mol dm^{-3} with $NaNO_3$; 30 °C

Molar ratio Fe^{III}T2MPyP : Bu^tO_2H	Conv. of Fe^{III}T2MPyP to OFe^{IV}T2MPyP (%)[a]
1.00 : 1	100.0
1.06 : 1	99.1
1.14 : 1	97.4
1.23 : 1	93.8
1.33 : 1	87.7
1.59 : 1	82.7
2.00 : 1	72.3

[a] Values obtained by spectral simulation (see Experimental).

standard conditions employed for the oxidations were 0.05 mol dm^{-3} aqueous phosphate buffer, ionic strength 0.20 mol dm^{-3} (maintained with $NaNO_3$) and 30 °C. The oxoiron(IV) porphyrin was prepared from a half molar equivalent of Bu^tO_2H and reacted with the phenol in a stopped-flow apparatus attached to a UV–VIS spectrometer. The oxidation of the phenol was monitored by following the decay of OFe^{IV}T2MPyP (λ_{max} Soret band 416 nm) at 0.1 s time intervals.

The kinetic equation for phenol oxidation, under the above conditions, was defined using 3-cyanophenol as the substrate. Typically OFe^{IV}T2MPyP, generated from 3.30×10^{-6} mol dm^{-3} Fe^{III}T2MPyP and 1.65×10^{-6} mol dm^{-3} Bu^tO_2H, was reacted with an excess of 3-cyanophenol (4.89–44.00 $\times 10^{-5}$ mol dm^{-3} *). The decay of the oxoiron(IV) porphyrin followed first-order kinetics for more than three halflives (Fig. 2). For each 3-cyanophenol concentration the pseudo first-order rate constant (k_{obs}) was determined from the average of more than 12 reactions. The observed spread of the k_{obs} values was small, *e.g.* for 2.93×10^{-4} mol dm^{-3} 3-cyanophenol k_{obs} was 1.64 ± 0.04 s^{-1} where the error represents the 95% confidence limits. A plot of the k_{obs} values against the unionised 3-cyanophenol concentration revealed a linear dependence of the rate constant on the concentration of the phenol (Fig. 3).

At constant 3-cyanophenol concentration the k_{obs} values were shown to be independent of the initial concentration of the oxoiron(IV) species (Table 2).

The above results show that the rate of reduction of OFe^{IV}T2MPyP by 3-cyanophenol follows the kinetic eqn. (A).

$$-d[OFe^{IV}P]/dt = k_2[OFe^{IV}P][ArOH] \qquad (A)$$

The second-order rate constant, k_2, was determined from the slope of the plot in Fig. 3 (Table 3).

The effect of substituents on the second-order rate constants for phenol oxidation by OFe^{IV}T2MPyP. Linear k_{obs} *vs.* substrate concentration plots, equivalent to Fig. 3, and hence k_2 values were also obtained for six other phenols (Table 3). The concentration range employed for each phenol was dependent on its reactivity, however, the minimum value was always ≥nine times greater than that of the oxoiron(IV) species (assuming a 72.3% conversion of Fe^{III}T2MPyP by Bu^tO_2H, see Table 1) to ensure pseudo first-order reaction conditions.

For five of the phenols, the reaction was also investigated with oxoiron(IV) porphyrin generated from Fe^{III}T2MPyP with a molar equivalent of Bu^tO_2H. Under pseudo first-order conditions all the phenols gave linear k_{obs} *vs.* [ArOH] plots from which the second-order rate constants were obtained (Table 4). Comparison of the data in Tables 3 and 4 shows that the excess of Bu^tO_2H present in the second study has no detectable effect on the measured rate constants.

pH Dependence of the second-order rate constants of the oxidation of 3-*cyanophenol and* 4-*chlorophenol.* The rate of oxidation of 3-cyanophenol was also investigated at pH 8.2 and 8.6 in 0.1 mol dm^{-3} aqueous borate buffer (μ = 0.20 mol dm^{-3} maintained with $NaNO_3$) at 30 °C. The oxoiron(IV) porphyrin was generated from 1.65×10^{-6} mol dm^{-3} Bu^tO_2H with 3.30×10^{-6} mol dm^{-3} Fe^{III}T2MPyP and reacted with an excess of the phenol. As described above the reactions followed first-order kinetics. The second-order rate constants (k_{app}) were obtained from the slopes of the linear plots of k_{obs} *vs.* total [3-cyanophenol] (Table 5). These values represent second-order rate constants uncorrected for the extent of phenol ionisation. The corresponding corrected values based on the calculated concentrations of the phenol and phenolate anion are also given in Table 5.

The oxidation of 4-chlorophenol was studied in pH 11.3, 0.025 mol dm^{-3} aqueous phosphate buffer, μ = 0.20 mol dm^{-3} at 30 °C. Under these conditions, in the absence of an oxidisable substrate, OFe^{IV}T2MPyP, which is reported to be hexacoordinated with an axial hydroxy ligand,[7c] has a Soret band with λ_{max} 428 nm. The oxoiron(IV) species has a first $t_{\frac{1}{2}}$ of approximately 4 h and, as observed under the more acidic conditions, it decays back to Fe^{III}T2MPyP without measurable bleaching. The reaction of OFe^{IV}T2MPyP, generated from 3.3×10^{-6} mol dm^{-3} and a half-molar equivalent of Bu^tO_2H,

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* 3-Cyanophenol concentrations refer to unionised phenol only (see Discussion).

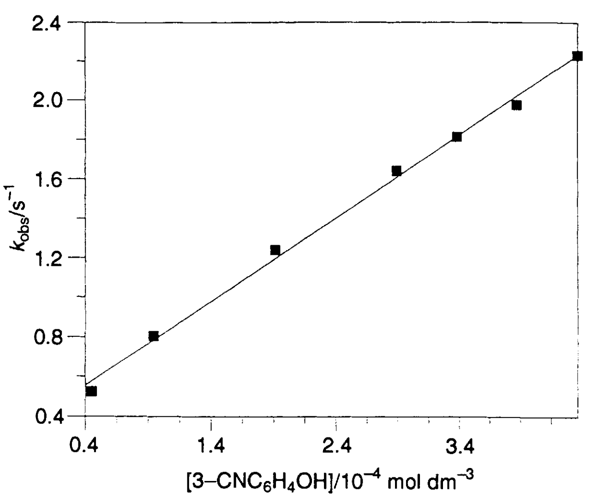


Fig. 3 Dependence of the pseudo first-order rate constant, k_{obs} for the reduction of OFe^{IV}T2MPyP by 3-cyanophenol on [3-cyanophenol], pH = 7.7, μ = 0.20 mol dm^{-3} at 30 °C

Table 2 The dependence of k_{obs} on [OFe^{IV}T2MPyP] for reaction of 3-cyanophenol with OFe^{IV}T2MPyP in aqueous solution: unionised 3-cyanophenol, 1.95 × 10^{-4} mol dm^{-3}; phosphate buffer 0.05 mol dm^{-3}; pH = 7.7; μ = 0.20 mol dm^{-3}; 30 °C

Conc. of Fe^{III}T2MPyP used to prepare OFe^{IV}T2MPyP[a] 10^5/mol dm^{-3}	k_{obs}/s^{-1}
1.40	1.338
1.15	1.371
0.90	1.357
0.64	1.382
0.39	1.368
0.19	1.402
0.14	1.337

[a] OFe^{IV}T2MPyP prepared by addition of $\mathrm{Bu^tO_2H}$ to two molar equivalents of Fe^{III}T2MPyP.

Table 3 Second-order rate constants for the reaction of OFe^{IV}T2MPyP (generated from Fe^{III}T2MPyP with half an equivalent of $\mathrm{Bu^tO_2H}$) with phenols in aqueous solution: OFe^{IV}T2MPyP prepared from 3.30 × 10^{-6} mol dm^{-3} Fe^{III}T2MPyP; phosphate buffer, 0.05 mol dm^{-3}; pH = 7.7; μ = 0.20 mol dm^{-3}; 30 °C

$XC_6H_4OH(pK_a)$[a] X =	Phenol conc. range[b]/ 10^{-5} mol dm^{-3}	k_2[c]/10^4 mol^{-1} dm^3 s^{-1}
3-CN (8.6)	4.89–44.00	0.424 ± 0.028
3-F (9.2)	3.20–11.70	1.57 ± 0.15
H (10.0)	2.19–10.90	1.78 ± 0.13
4-F[d] (9.9)	4.37–12.00	1.92 ± 0.02
4-Cl (9.4)	2.15–9.70	2.44 ± 0.27
4-Me (10.3)	2.19–6.59	4.05 ± 0.28
4-OMe[e] (10.1)	0.488–0.910	19.6 ± 1.7

[a] pK_a values from ref. 9. [b] Unionised phenol concentrations. [c] Errors in k_2 calculated to give 95% confidence limits for linear fits of k_{obs} *vs.* [ArOH] plots. [d] OFe^{IV}T2MPyP prepared from 4.4 × 10^{-6} mol dm^{-3} Fe^{III}T2MPyP. [e] OFe^{IV}T2MPyP prepared from 8.0 × 10^{-7} mol dm^{-3} Fe^{III}T2MPyP.

Table 4 Second-order rate constants for the reaction of OFe^{IV}T2MPyP (generated from equimolar quantities of Fe^{III}T2MPyP and $\mathrm{Bu^tO_2H}$) with phenols in aqueous solution: OFe^{IV}T2MPyP prepared from 2.20 × 10^{-6} mol dm^{-3} Fe^{III}T2MPyP; phosphate buffer, 0.05 mol dm^{-3}; pH = 7.7; μ = 0.20 mol dm^{-3}; 30 °C

XC_6H_4OH X =	Phenol conc. range[a]/ 10^{-5} mol dm^{-3}	k_2[b]/10^4 mol^{-1} dm^3 s^{-1}
H	2.19–9.85	1.71 ± 0.30
4-F	2.19–13.10	1.98 ± 0.08
4-Cl	2.16–10.80	2.40 ± 0.16
4-Me	2.20–6.59	4.04 ± 0.47
4-OMe[c]	0.498–0.919	21.6 ± 3.6

[a] Unionised phenol concentrations. [b] Errors in k_2 quoted to 95% confidence limits (see Table 3). [c] OFe^{IV}T2MPyP prepared from 5.0 × 10^{-7} mol dm^{-3} Fe^{III}T2MPyP.

Table 5 pH Dependence of the second-order rate constants for the oxidation of 3-cyanophenol and 4-chlorophenol by OFe^{IV}T2MPyP in aqueous solution; OFe^{IV}T2MPyP prepared from 3.30 × 10^{-6} mol dm^{-3} Fe^{III}T2MPyP; μ = 0.20 mol dm^{-3}; 30 °C

Substrate (pK_a)	pH	k_{app}/ 10^3 mol^{-1} dm^3 s^{-1}	k_2 for ArOH/ 10^3 mol^{-1} dm^3 s^{-1}	k_2 for ArO$^-$/ 10^3 mol^{-1} dm^3 s^{-1}
3-Cyanophenol	7.7[a]	3.77 ± 0.28	4.24 ± 0.32	33.7 ± 2.2
(8.6)[a]	8.2[b]	3.20 ± 1.60	4.47 ± 2.34	11.3 ± 5.6
	8.6[b]	2.56 ± 0.48	5.12 ± 0.96	5.12 ± 0.96
4-Chlorophenol	7.7[a]	24.0 ± 2.7	24.4 ± 2.7	1230 ± 140
(9.4)	11.3[c]	1.19 ± 0.07	95.8 ± 6.0	1.20 ± 0.08

[a] Phosphate buffer, 0.05 mol dm^{-3}. [b] Borate buffer, 0.1 mol dm^{-3}. [c] Phosphate buffer, 0.025 mol dm^{-3}.

with 6.0–21.0 × 10^{-4} mol dm^{-3} 4-chlorophenol (monitored at 428 nm) gave good pseudo first-order kinetics. The second-order rate constants (k_{app}) based on the total chlorophenol concentration and corrected for ionised and unionised 4-chlorophenol were obtained as described above (Table 5).

Oxidation of 4-*fluorophenol in deuteriated phosphate buffer.* The oxidation of 4-fluorophenol was investigated in deuteriated 0.05 mol dm^{-3} phosphate buffer at μ = 0.20 mol dm^{-3} at 30 °C. The buffer, which was prepared in D_2O, gave a value of 7.8 on the pH meter. Applying the necessary correction factor of 0.4 when using a glass pH electrode in D_2O,[10] this corresponds to a pD value of 8.2. When the trace amounts of H_2O, arising from the buffer salts, and other proton sources had been taken into account, the 4-fluorophenol was calculated to be > 99% in the deuteriated form, ArOD. The measured pseudo first-order rate constants for oxidations with a 14–45-fold excess of the unionised phenol (pK_a 10.4 in D_2O)[11] over OFe^{IV}T2MPyP gave the second-order rate constant 14 500 ± 810 mol^{-1} dm^3 s^{-1}.

Temperature dependence of the second-order rate constant for oxidation of 3-*cyanophenol.* The temperature dependence of the phenol oxidations was studied by measuring the second-order rate constant for 3-cyanophenol at seven temperatures between 15.7 and 45.0 °C. At each temperature the oxoiron(IV) species was generated from 3.3 × 10^{-6} mol dm^{-3} Fe^{III}T2MPyP and 1.65 × 10^{-6} mol dm^{-3} $\mathrm{Bu^tO_2H}$ and reacted with an excess of the phenol. The data gave an excellent Arrhenius plot (Fig. 4) from which an activation energy, E_a, of 57.3 ± 1.0 kJ mol^{-1} and an entropy of activation, $\Delta S^{\ddagger}$, at 30 °C of 5.21 ± 3.33 J K^{-1} mol^{-1} were obtained.

EPR Studies on the Oxidation of Trolox C by OFe^{IV}T2MPyP.—An EPR study of the reaction of OFe^{IV}T2MPyP with a 14-fold excess of the water soluble hindered phenol, Trolox C, in pH 7.7 aqueous phosphate buffer gave the spectrum of the Trolox C radical (Fig. 5). This is essentially identical to that reported by Davies *et al.*[12] from the photolysis of a saturated aqueous dioxygenated solution of $CBrCl_3$, pH 7.4, in the presence of Trolox C. Using stopped-flow and tuning the spectrometer to the field of the central peak of the spectrum of the radical revealed the rapid growth and decay of the signal intensity (Fig. 6). Given the time required to record

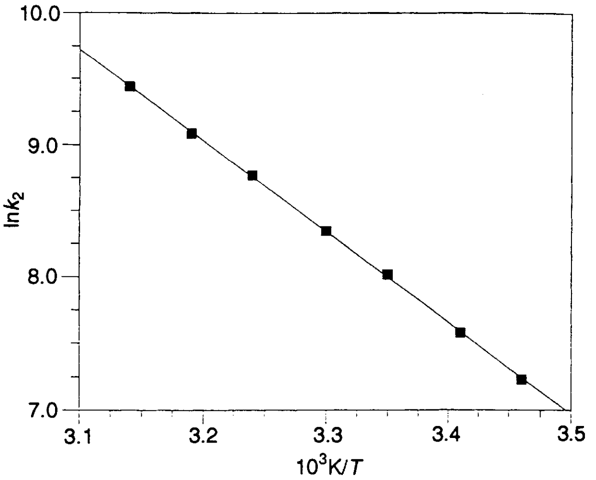
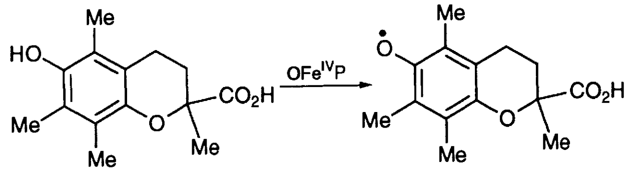


Fig. 4 Arrhenius plot of the second-order rate constants for the reaction of 3-cyanophenol with $OFe^{IV}T2MPyP$ at pH = 7.7 and μ = 0.20 mol dm^{-3}, 15.7–45.0 °C



TROLOX C

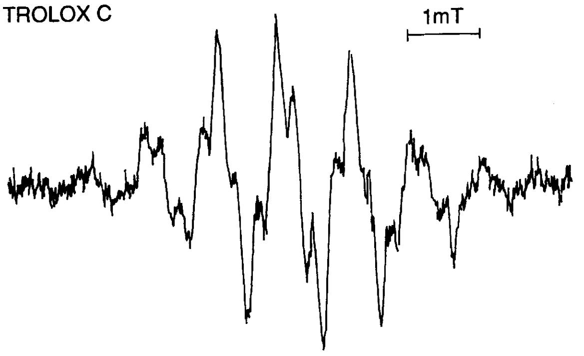


Fig. 5 EPR spectrum of the Trolox C phenoxyl radical from the reaction of $OFe^{IV}T2MPyP$ (from $Fe^{III}T2MPyP$, 1 × 10^{-4} mol dm^{-3}) with Trolox C (1 × 10^{-3} mol dm^{-3}), pH = 7.7, μ = 0.20 mol dm^{-3}, gain 8 × 10^5, modulation amplitude 0.08 mT, time constant 0.08 s, scan time 80 s, field 347.5 mT, scan width 5 mT, power 10 mW, frequency 9.768 GHz, room temp.

the complete EPR spectrum of the radical (*ca.* 80 s), Fig. 5 represents the residual concentration of the radical remaining after the rapid growth and decay.

Although the kinetics of the Trolox C oxidation by $OFe^{IV}T2MPyP$ were not examined, stopped flow UV–VIS spectroscopy showed that the phenol brings about the rapid reduction of the oxoiron(IV) species without bleaching of the porphyrin.

Kinetic Studies of the Oxidation of Phenols by $OFe^{IV}T4MPyP$.—The shorter lifetime of $OFe^{IV}T4MPyP$ than $OFe^{IV}T2MPyP$ made kinetic studies with the former more difficult and for this reason oxidations by this species were restricted to two substrates, 3-cyanophenol and phenol.

The oxoiron(IV) oxidant was generated from 3.6 × 10^{-6} mol dm^{-3} $Fe^{III}T4MPyP$ and 1.80 × 10^{-6} mol dm^{-3} Bu^tO_2H and reacted as described above for $OFe^{IV}T2MPyP$ with an excess of 3-cyanophenol. The kinetics, followed by monitoring the decay of $OFe^{IV}T4MPyP$ (λ_{max} 426 nm), were first-order for > three halflives. The k_{obs} values which were obtained from an average of 12 decay curves showed more scatter than the corresponding reaction of $OFe^{IV}T2MPyP$. However, a plot of the k_{obs} values against concentration of the unionised 3-cyanophenol gave a good linear relationship (Fig. 7) from which a second-order rate constant of 2.26 ± 0.39 × 10^4 mol^{-1} dm^3 s^{-1} was obtained. The analogous study with phenol gave even more scattered k_{obs} values and a second-order rate constant with a large error 1.35 ± 0.62 × 10^5 mol^{-1} dm^3 s^{-1}.

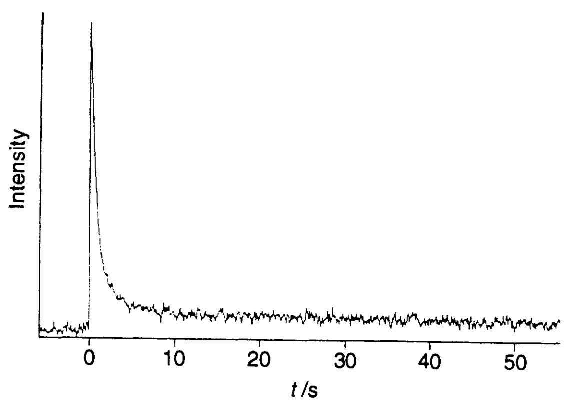


Fig. 6 Time dependence of the signal from the Trolox C radical from the reaction of $OFe^{IV}T2MPyP$ with Trolox C followed by stopped-flow EPR spectroscopy; conditions as given for Fig. 5

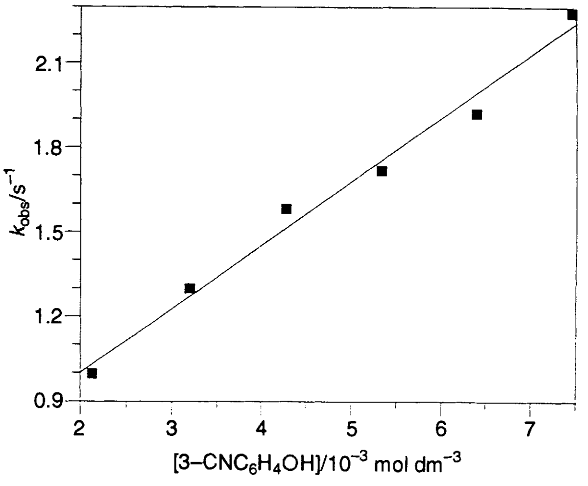


Fig. 7 Dependence of the pseudo first-order rate constant, k_{obs}, for the reduction of $OFe^{IV}T4MPyP$ by 3-cyanophenol on [3-cyanophenol]; conditions as given for Fig. 3

Discussion

Recent research has shown that oxoiron(IV) derivatives of ionic iron porphyrins are relatively stable in aqueous alkaline solution at ambient temperatures.[6,7] Of these, $OFe^{IV}T2MPyP$ and to a lesser extent its isomer $OFe^{IV}T4MPyP$, are particularly long-lived and have been well characterised in the literature.[6,7] For these reasons, these two oxoiron(IV) porphyrins were selected for the present study.

Spiro and Su and their coworkers[7] report that in strongly alkaline aqueous solution the iron atom in both the oxoiron(IV) (*N*-methylpyridyl)porphyrins is hexacoordinated with a hydroxide ligand in the sixth position. However, in less alkaline solution this species is in equilibrium with a pentacoordinated species [reaction (5)].

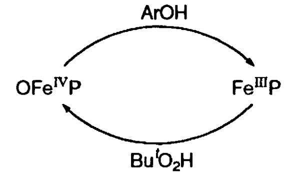
$$OFe^{IV}P + 2H_2O \rightleftharpoons OFe^{IV}P(OH) + H_3O^+ \quad (5)$$

$$pK_a \text{ for } OFe^{IV}T2MPyP = 10.0 \text{ and for } OFe^{IV}T4MPyP = 10.5$$

The kinetics were carried out at pH 7.7 to allow easier comparison with previous work on the oxidation of phenols by

HRP II[2d,e] and by the iron(III) deuterioporphyrin–H_2O_2 system[5] and to ensure that the oxidant was present almost entirely as a single species, the pentacoordinated oxoiron(IV) porphyrin. The phenols were all predominantly unionised under the reaction conditions (pK_a values in Table 3).

For the large majority of the kinetic studies the oxoiron(IV) species were generated from the reaction of the Fe(III)P with a half-molar equivalent of Bu^tO_2H. These relative proportions of reactants were used initially to ensure that no excess of Bu^tO_2H, from the oxoiron(IV) porphyrin preparation, remained during the kinetic measurements since it had the potential to complicate the kinetics by recycling the iron porphyrin (Scheme 1).



Scheme 1 Oxoiron(IV) porphyrin recycling in the presence of an excess of Bu^tO_2H

However, this precaution proved to be unnecessary since the rate constants for the phenol oxidations are all significantly greater than the likely rate constant for the reaction of Bu^tO_2H with Fe^{III}T2MPyP at pH 7.7. For, although the latter value has not been reported, it would be expected to be approximately the same as the rate constant for the reaction of the isomer Fe^{III}T4MPyP (59 $mol^{-1}\ dm^3\ s^{-1}$).[13] The large difference in the concentration of Bu^tO_2H and the phenol substrate would also disfavour the recycling of the iron porphyrin. In confirmation of this conclusion, the rate constants were unaffected by generating the oxoiron(IV) species from equimolar quantities of Bu^tO_2H and Fe^{III}T2MPyP; conditions where an excess of the hydroperoxide would have been present.

Mechanistic Analysis of the Oxidation of Phenols by Oxoiron(IV) Tetra(N-methylpyridyl)porphyrins.—The oxidation of phenols by the oxoiron(IV) porphyrins used in this study could take place by oxygen transfer, electron transfer or hydrogen atom abstraction. The first of these is considered unlikely for, although oxoiron(IV) porphyrin π-radical cations are known to oxidise organic compounds by oxygen transfer,[14] there are few reports of equivalent reactions with oxoiron(IV) porphyrins. Ellis and Lyons[15] have suggested that oxoiron(IV) derivatives of porphyrins with electron-withdrawing substituents can hydroxylate alkanes by an oxygen rebound mechanism (an overall oxygenation although the initial step is hydrogen atom abstraction) [reaction (6)]. Weber and his co-workers[16] have similarly proposed that ferryl porphyrin, generated from the photolysis of μ-oxo dimers, can hydroxylate aliphatic C–H bonds.

$$\mathrm{R{-}H + OFe^{IV}P \longrightarrow \underset{\text{solvent cage}}{[R^{\bullet}\ HOFe^{III}P]} \longrightarrow ROH + Fe^{II}P} \qquad (6)$$

Evidence against oxygen transfer from oxoiron(IV) tetra(*N*-methylpyridyl)porphyrins comes from a recent study in our laboratory where OFe^{IV}T4MPyP was mixed with a range of potential substrates in aqueous borate buffer (pH 9.2).[17] This revealed that only substrates which are readily oxidised by electron transfer or hydrogen atom abstraction reduce the ferryl species, whilst those that should be susceptible to oxygen transfer (*e.g.* pyridine, triethylamine, dimethyl sulfoxide and triethylphosphite) are unreactive.

The elimination of oxygen transfer leaves the three alternative oxidation mechanisms in reactions (7)–(9); electron transfer from the phenol or from its phenolate ion and hydrogen atom abstraction from the phenol, respectively. In agreement with each of these mechanisms EPR spectroscopy shows that the oxidation of Trolox C by OFe^{IV}T2MPyP gives the corresponding phenoxyl radical. This sterically hindered water soluble phenol was chosen for the EPR studies as its phenoxyl radical is known to be relatively stable in aqueous solution.[18] However, in the presence of OFe^{IV}T2MPyP it is surprisingly short-lived, suggesting that not only the phenols but also phenoxyl radicals are readily oxidised by the oxoiron(IV) porphyrin. If this interpretation of the results is correct, by applying a steady state treatment, it has the effect of reducing the absolute values of the second-order rate constants reported in this study by a factor of 2.

$$\mathrm{OFe^{IV}P + ArOH \xrightarrow[+H^+]{-e^-} ArOH^{\bullet+} + HOFe^{III}P \xrightarrow{-H^+} ArO^{\bullet}} \qquad (7)$$

$$\mathrm{OFe^{IV}P + ArO^- \xrightarrow[+H^+]{-e^-} ArO^{\bullet} + HOFe^{III}P} \qquad (8)$$

$$\mathrm{OFe^{IV}P + ArOH \xrightarrow[\text{or } -H^+,\ -e^-]{-[H^{\bullet}]} ArO^{\bullet} + HOFe^{III}P} \qquad (9)$$

To establish whether OFe^{IV}T2MPyP reacts with phenols or their anions [*e.g.* reactions (7) and (9) as opposed to (8)] the pH dependence of the reaction of 3-cyanophenol was examined. This substrate was chosen, since of all the phenols studied, its pK_a (8.6)[9] was furthest away from that of the oxoiron(IV) species (pK_a 10.0).[7c] Thus measuring the second-order rate constant for oxidation of 3-cyanophenol at pH 7.7, 8.2 and 8.6 covered a significant change in the relative proportions of the phenol and its anion, whilst the oxidant was maintained almost entirely in its penta-coordinated form [reaction (5)].

Comparing the second-order rate constants (k_{app}), uncorrected for the 3-cyanophenol ionisation, at the three pHs shows that k_{app} decreases as the solution becomes more alkaline. This is only consistent with the undissociated phenol being the reactive form of the substrate [eqn. (B)]. In agreement with this conclusion when k_{app} is corrected for the undissociated phenol the k_2 values generated are almost constant (Table 5). The slight increase in k_2 with pH might be accounted for by the small increase in the hexacoordinated form of Fe^{IV}T2MPyP, if this is more reactive than the pentacoordinated species (see below). The calculated percentages of the hexacoordinated oxidant at the three reaction pHs are 0.50, 1.56 and 3.83% for pH 7.7, 8.2 and 8.6, respectively.

$$k_{app} = k_2[\mathrm{ArOH}]/([\mathrm{ArOH}] + [\mathrm{ArO^-}]) = k_2/(1 + K_a/[\mathrm{H^+}]) \qquad (B)$$

where K_a for 3-cyanophenol = $10^{-8.6}\ mol\ dm^{-3}$

Had the phenolate ion been the reactive form of the substrate the k_{app} values would have shown a 4.5-fold increase in changing the pH from 7.7 (ArO^-, 11.2%) to 8.6 (ArO^-, 50%) in accordance with eqn. (C). This was clearly not the case.

$$k_{app} = k_2[\mathrm{ArO^-}]/([\mathrm{ArOH}] + [\mathrm{ArO^-}]) = k_2/(1 + [\mathrm{H^+}]/K_a) \qquad (C)$$

A brief kinetic study of the oxidation of 4-chlorophenol at pH 11.3, where the predominant species will be the phenolate ion, with the hexacoordinated oxoiron(IV) species, shows that the reaction obeys the same rate law as at pH 7.7. Interestingly k_{app} (1190 $mol^{-1}\ dm^3\ s^{-1}$) under these conditions is significantly less than that at pH 7.7 (24 000 $mol^{-1}\ dm^3\ s^{-1}$). If the phenolate ion

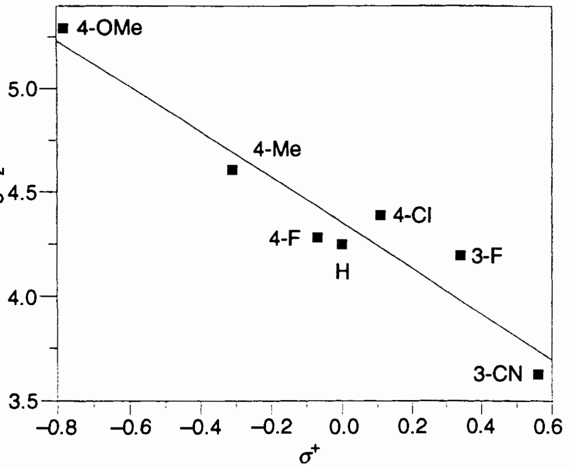


Fig. 8 Correlation of log k_2 *vs.* σ^+ for phenol oxidations by $\mathrm{OFe^{IV}T2MPyP}$; conditions as given for Fig. 3

Table 6 Log k_2 values for the oxidation of phenols by $\mathrm{OFe^{IV}T2MPyP}$ and substituent constants[a]

XC_6H_4OH X =	log k_2	σ	σ^+	$\sigma^\bullet$
3-CN	3.63	0.56	0.56	−0.039
3-F	4.20	0.34	0.34	−0.018
H	4.25	0	0	0
4-F	4.28	0.06	−0.07	−0.011
4-Cl	4.39	0.23	0.11	0.017
4-Me	4.61	−0.17	−0.31	0.015
4-OMe	5.29	−0.27	−0.78	0.034

[a] σ Values from ref. 20, σ^+ from ref. 21 and $\sigma^\bullet$ from ref. 22.

is the assumed substrate, oxidation must occur by electron transfer and the k_2 values corrected for the anion concentration are 1200 and 1.23×10^6 mol^{-1} dm^3 s^{-1}, respectively. However, it is noteworthy that the one-electron reduction potentials of $\mathrm{OFe^{IV}T2MPyP}$[7b] and the 4-chlorophenoxyl radical[19] at pH 11 predict that an outer sphere electron-transfer oxidation of the 4-chlorophenolate ion by $\mathrm{OFe^{IV}T2MPyP}$ is not possible. If the unionised phenol is assumed to be the reactant the corrected second-order rate constants are 2.44×10^4 and 9.58×10^4 mol^{-1} dm^3 s^{-1} at pH 7.7 and 11.3, respectively.

The k_2 values would be expected to be pH dependent even assuming the mechanism is the same at both pHs, since the oxidant at pH 7.7 would be pentacoordinated in contrast to the hexacoordinated species at pH 11.3. Based on the previously reported pH dependence of the self-reaction of $\mathrm{OFe^{IV}T2MPyP}$[7c] and of $\mathrm{OFe^{IV}T4MPyP}$[6] in aqueous solution and of the reduction potential of $\mathrm{OFe^{IV}T2MPyP}$,[7b] the k_2 values from the present study would be expected to decrease rather than increase with increasing pH. That is, an axial hydroxide ligand stabilises the ferryl species. However, the mechanisms of the two processes will be different and they may not show a similar dependence on pH. Furthermore, in this study the lifetime of $\mathrm{OFe^{IV}T2MPyP}$ was unexpectedly greater at pH 7.7 than at 11.3. Clearly further work is needed to compare the reactivity of the penta- and hexa-coordinated species.

The results above suggest that phenols and not their anions are the substrates for oxidation by $\mathrm{OFe^{IV}T2MPyP}$. In order to determine whether they react by electron transfer [reaction (7)] or hydrogen atom abstraction [reaction (9)], a Hammett analysis of the rate data from the substituted phenols was undertaken. Plots of log k_2 *vs.* σ and σ^+ values (Table 6) gave ρ values of -1.52 and -1.10, respectively with the latter showing the better linear correlation (Fig. 8) (correlation coeff. 0.881 and 0.956, respectively). These relatively small negative ρ values suggest that there is a small development of positive charge on the substrate in the transition state. Comparison with literature ρ values for related electron transfers (Table 7) and hydrogen atom abstractions (Table 8) suggests that the phenolic oxidations in the present study occur by the latter mechanism. Hydrogen atom abstractions by electrophilic radicals typically show small positive ρ values and correlate better with σ^+ than σ.

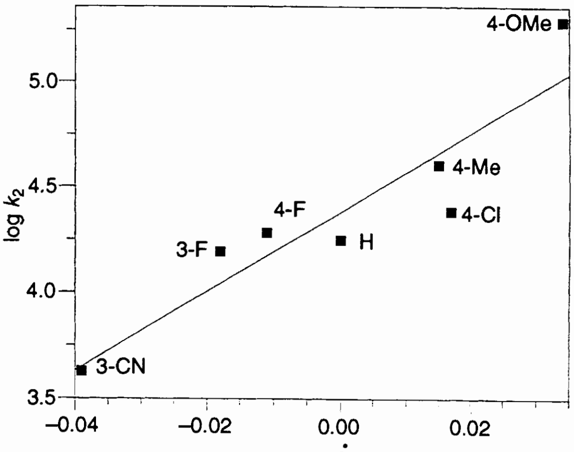


Fig. 9 Correlation of log k_2 *vs.* $\sigma^\bullet$ for phenol oxidations by $\mathrm{OFe^{IV}T2MPyP}$; conditions as given in Fig. 3

The log k_2 values were also plotted against the $\sigma^\bullet$ constants of Arnold and his coworkers.[22] This scale of σ values was derived from substituent effects on the hyperfine coupling constants in the EPR spectra of benzyl radicals. Bearing in mind the similar structures of benzyl and phenoxyl radicals, rates of reactions that involve the formation of phenoxyl radicals might be expected to correlate with $\sigma^\bullet$. It should, however, be noted that since radical stabilising effects of substituents are small compared with their charge stabilising effects on ions, $\sigma^\bullet$ correlations are commonly only observed in reactions where charge development is small or unimportant. The data from this study gave $\rho^\bullet = 18.8$ with a correlation coeff. of 0.92 (Fig. 9), suggesting a significant amount of radical character in the oxidation transition state in agreement with a hydrogen atom-abstraction mechanism. By comparison, an electron-transfer transition state would be expected to be more polar and the polar substituent effects would dominate any radical stabilisation.

In an attempt to quantify both the polar and radical stabilising effects on the phenol oxidation, the dual parameter eqn. (D) of Dust and Arnold[22] has been applied to the rate data. This gives a good linear correlation (correlation coeff. 0.972) with ρ and $\rho^\bullet$ values of -0.735 and 7.36, respectively (Fig. 10). The ratio of $\rho^\bullet/\rho$ is a measure of the relative importance of the radical and polar effects in the transition state. Compared with some other known hydrogen atom abstractions this reveals a significant radical character in the transition state (Table 9).

$$\log (k_X/k_H) = \rho\sigma^+ + \rho^\bullet\sigma^\bullet \qquad \text{(D)}$$

Su and his co-workers[7b] have measured the $\mathrm{Fe^{IV/III}T2MPyP}$ reduction potential in aqueous solution. The electron transfer is coupled to a proton transfer [reaction (10)] and in the pH range 8.2–10.0 the E values show a linear relationship with pH. Extrapolation of these data to pH 7.7, the value used in this study, gives $E = 0.67$ V (*vs.* Ag/AgCl). It is noteworthy that Spiro and his coworkers[7c] have carried out a less extensive study and obtained significantly higher E values. The origin of this difference is unclear.

Table 7 Hammett analyses (using σ^+) of some electron-transfer oxidations

Oxidant	Substrate	Solvent (T/°C)	Reaction constant, ρ	Ref.
$Pb(OAc)_4$	$ArNMe_2$	Ac_2O–$CHCl_3$ (38.5)	-2.4^a	23
$C_4F_9O_2^{\bullet}$	ArOH	MeOH (22)	-2.3	24
$CCl_3O_2^{\bullet}$	ArOH	MeOH (22)	-3.3	24
$Fe(CN)_6^{3-}$	Dihydronicotinamides	MeCN–H_2O (30)	-1.8	25

[a] σ rather than σ^+ values employed.

Table 8 Hammett analyses (using σ^+) of some hydrogen atom-abstraction oxidations

Oxidant	Substrate	Solvent (T/°C)	Reaction constant, ρ	Ref.
$Bu^tO^{\bullet}$	ArOH	CCl_4 (122)	-1.19	26
$Bu^tO^{\bullet}$	ArOH	C_6H_5Cl (122)	-0.74	26
$Bu^tO^{\bullet}$	ArOH	C_6H_6 (22)	-0.90	27
$Bu^tO^{\bullet}$	ArMe	CCl_4 (40)	-0.68	28
$RO_2^{\bullet}$	ArOH	$C_6H_5C_2H_3$ (65)	-1.5	29
$RO_2^{\bullet}$	ArMe	ArCl (30)	-0.6	30
$RO_2^{\bullet}$	$ArCHMe_2$	—(30)	-0.3	30

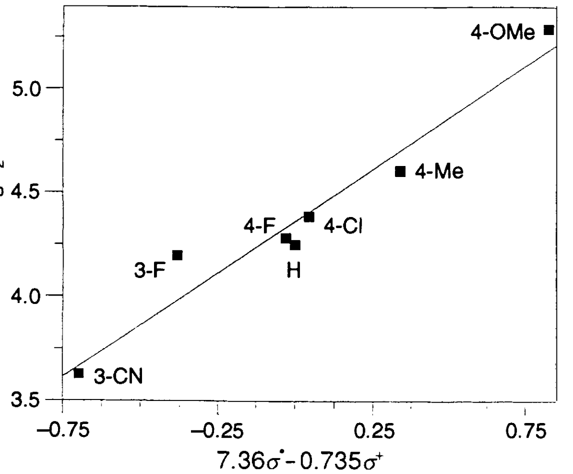


Fig. 10 Correlation of log k_2 *vs.* dual parameter ($\sigma^+ + \sigma^{\bullet}$) for phenol oxidations by $OFe^{IV}T2MPyP$; conditions as given in Fig. 3

$$HOFe^{III}T2MPyP \rightleftharpoons OFe^{IV}T2MPyP + H^+ + e^- \quad (10)$$

Comparing the E potentials of the oxoiron(IV) porphyrin with the one-electron reduction potentials of the phenoxyl radicals (Table 10) reveals that $OFe^{IV}T2MPyP$ is only strong enough to oxidise 4-methyl- and 4-methoxy-phenol by an outer-sphere electron-transfer process. Since the linear free energy correlations suggest all the phenols are oxidised by the same mechanism, it is unlikely that this is an outer-sphere electron-transfer process. This provides additional support for a hydrogen atom-abstraction.

Further evidence for this mechanism comes from the excellent correlation (correlation coeff. 0.989) of the log k_2 values against the energy of the phenolic O–H bond $\Delta\Delta_fH(ArO^{\bullet})$ calculated by Brewster *et al.*[35] [eqn. (E)]

$$\Delta\Delta_fH(ArO^{\bullet}) = \Delta_fH(ArO^{\bullet}) - \Delta_fH(ArOH) \quad (E)$$

The kinetic isotope studies provide further information about the mechanism and the nature of the oxidation transition state. Before the kinetic isotope effect for oxidising 4-fluorophenol by $OFe^{IV}T2MPyP$ can be calculated three factors need to be considered, namely, a correction for measuring the pD value with a pH meter,[10] and the increase in the pK_a value of the phosphate buffering salts[36] and of the phenolic substrate in D_2O.[11] The first two factors result in the pD value of the reaction in the deuteriated buffer being 8.2 as opposed to 7.7 in protiated solution. This difference between the two reaction systems is, however, compensated for by the shift in the pK_a of 4-fluorophenol from 9.9 in H_2O to 10.4 in D_2O with the result that the extent of ionisation of the phenol in the two systems is essentially identical (0.6%). This ensures that the ratio of the second-order rate constants in water (pH 7.7) and in D_2O (pD 8.2), $k_H/k_D = 1.32$, is the correct measure of the kinetic isotope effect for oxidation of 4-fluorophenol by $OFe^{IV}T2MPyP$. Comparable small primary kinetic isotope effects have been observed in other hydrogen atom abstractions (Table 11) and have been interpreted as evidence for transition states with unsymmetrical transfer of the hydrogen atom between substrate and reactant. Interestingly, the chlorination of toluene with $Cl^{\bullet}$ in CCl_4, which is considered to have an early transition state, has an identical kinetic isotope effect to the phenol oxidation above[37] and a similar small negative ρ value (-0.66 against σ^+).[39]

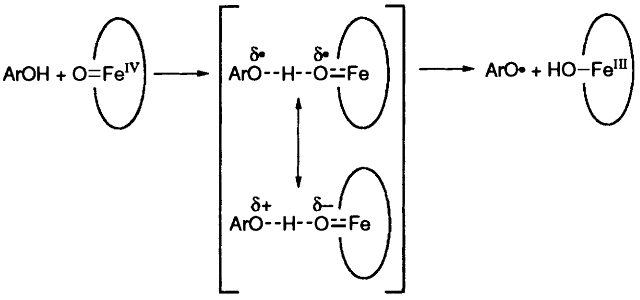


Fig. 11 Proposed mechanism for oxidation of phenols by $OFe^{IV}T2MPyP$ in aqueous solution (pH 7.7)

On the basis of the data discussed above, we propose that the oxidation of phenols by $OFe^{IV}T2MPyP$ in aqueous solution at pH 7.7 is best described by a homolytic hydrogen atom abstraction [reaction 11]. As has been proposed for such reactions by electrophilic radicals, the transition state shows a small degree of charge separation (Fig. 11).

$$ArOH + OFe^{IV}P \longrightarrow ArO^{\bullet} + HOFe^{III}P \quad (11)$$

The kinetic study of phenolic oxidation by $OFe^{IV}T4MPyP$ was restricted by the lower stability of this oxoiron(IV) species. However, from the limited data available, the mechanism of reaction corresponds closely to that of the isomeric $OFe^{IV}T2MPyP$ although the latter ferryl species is less reactive (k_2 for oxidation of 3-cyanophenol by the latter is a factor of five times smaller). The almost identical reduction potentials of the two oxoiron(IV) species (0.68 and 0.67 V, respectively)[40] suggests that the lower reactivity of $OFe^{IV}T2MPyP$ may arise from steric hindrance from the *N*-methyls on the 2-pyridyl groups restricting access of the phenols to the ferryl oxygen.

Comparison of Mechanisms of Oxidation of Phenols by HRP

Table 9 Dual parameter (σ^+, $\sigma^\bullet$) Hammett analyses of some hydrogen atom abstractions

Reaction	ρ	$\rho^\bullet$	$\rho^\bullet/\rho$	Correlation coeff.	Ref.
ArMe with NBS[a]	−1.43	0.672	0.47	0.997	22, 31
ArMe with $Bu^{t\bullet}$	0.462	1.30	2.81	0.978	22, 32
ArMe with Fe^{III}TPP/PhIO	−1.03	18.7	18.2	0.983	33
$ArCHMe_2$ with Fe^{III}TPP/PhIO	−0.62	9.6	15.5	0.969	33
ArOH with OFe^{IV}T2MPyP	−0.735	7.36	10.0	0.972	This study

[a] NBS = *N*-bromosuccinimide.

Table 10 One-electron reduction potentials of substituted phenoxyl radicals *vs.* Ag/AgCl

$XC_6H_4O^\bullet$ X =	*E* at pH 7.7/ V[a]
4-OMe	0.47
4-Me	0.61
4-F	0.67
4-Cl	0.68
4-H	0.71
3-F	0.80[b]
3-CN	0.86[b]

[a] *E* values calculated from reported data at pH 0 using $E_{7.7} = E_0 + 0.059 \log (K_a + 10^{-7.7})$, where $E_{7.7}$ and E_0 are reduction potentials at pH 7.7 and 0, respectively (ref. 34). [b] *E* value determined using the equation above and $E_7 = 0.31\,\sigma^+ + 0.95$ (ref. 34).

Table 11 Some small primary kinetic isotope effects for hydrogen atom abstractions

Reaction	Solvent (T/°C)	k_H/k_D	Ref.
PhMe + $Cl^\bullet$	CCl_4 (77)	1.3	37
PhOH + PhCOPh (triplet)	Wet MeCN (22)	1.2	27
PhOH + Diphenylpicryl hydrazide	CCl_4 (20)	1.38	38
4-F-C_6H_4OH + OFe^{IV}T2MPyP	D_2O, pD 8.2 (30)	1.32	This study

II, Iron(III) *Deuterioporphyrin-H_2O_2 and OFe^{IV}T2MPyP*.—Dunford and his coworkers[2d] have measured the second-order rate constants for the oxidation of a range of substituted phenols by HRP II and have shown, by a pH dependence study, that the phenol and not its anion is the substrate. In Hammett correlations of their data from oxidations at pH 7.0 and 7.6 we have noted that the σ values were taken from several different sources and this selective choice of σ values effectively improves the observed correlations. Further, the σ value used for 3,4-dimethyl substitution is quoted as 0.083, which clearly must be in error. Consequently, we have analysed their data using σ values of McDaniels and Brown[20] for all the substituents except for CHO (this was not included in compilation of σ values). In this case Jaffé's value was used.[41] The σ^+ values were from Okamoto and Brown[21] and $\sigma^\bullet$ constants from Dust and Arnold[22] (Table 12).

Dunford and his coworkers[2d] data correlate with both σ and σ^+ values but, contrary to their analyses, the better fit is with σ^+. However, unlike the results from the OFe^{IV}T2MPyP study above, the data show a very poor correlation with $\sigma^\bullet$. Two other differences between the chemical and enzymic system are the latter's significantly larger ρ values and poor correlation with Brewster's $\Delta\Delta_f H(ArO^\bullet)$ data ($R = 0.841$). These observations point to the HRP II oxidations of phenols occurring by electron transfer followed by proton loss [reaction (7)] rather than the simultaneous loss of H^+ and e^- (proposed by Dunford and his coworkers) or hydrogen atom abstraction. Certainly the reduction potential of HRP II (0.90 V at pH 7.6)[42] is sufficient for it to oxidise most phenols by an outer-sphere electron-transfer mechanism. Interestingly, 4-nitrophenol [*E*, +0.99 V at pH 7.7] was the only phenol in Dunford's study that was unreactive towards HRP II. A similar analysis of Job and Dunford's data for HRP I phenol oxidations[2c] suggests that electron transfer and proton loss may not be simultaneous but rather the former occurs in advance of the latter.

The oxoiron(IV) porphyrin in HRP II is almost completely surrounded by the protein matrix and as a result the ferryl oxygen is inaccessible to the substrate.[3,43] Such a structure would be consistent with electron transfer from the phenol to the exposed edge of the haem group. Subsequent proton transfer occurs to a basic amino acid residue of the protein which is hydrogen bonded to the phenol[2d] (Fig. 12).

A pH dependent study by Jones *et al.*[5] of the oxidation of phenols in aqueous solution by a porphyrin intermediate generated from iron(III) deuterioporphyrin and H_2O_2 showed the oxidation to involve electron transfer from the phenolate anion to the oxidant. In agreement with this conclusion log second-order rate constants for reactions at pH 7.3 correlate best with σ^- ($\rho = -6.85$, $R = 0.925$). The nature of the active oxidant in this sytem was not well defined, however, it was proposed to be an iron(III) porphyrin π-radical cation. This suggests the oxidation is an electron transfer from the phenolate to the porphyrin and does not directly involve the iron atom (Fig. 13).

It is instructive to compare the rate constants of the phenol oxidations by HRP II and the two chemical model systems (Table 13). The OFe^{IV}T2MPyP oxidations which are thought to be hydrogen atom abstractions are the slowest. Of the other two electron transfer processes, the reaction of the phenolate anion with the porphyrin π-radical cation occurs, not unexpectedly, the faster.

Temperature Dependence of 3-*Cyanophenol Oxidation by OFe^{IV}T2MPyP*.—The activation parameters for oxidation of 3-cyanophenol by OFe^{IV}T2MPyP at 30 °C were calculated to be E_a 57.3 ± 1.0 kJ mol^{-1} and $\Delta S^\ddagger$ 5.21 ± 3.33 J K^{-1} mol^{-1}. If, as suggested by the EPR studies, the OFe^{IV}T2MPyP oxidises the phenols and their phenoxyl radicals, the second-order rate constants are half those quoted in this paper. Whilst this will not affect E_a it will result in $\Delta S^\ddagger$ being lowered by 5.82 J K^{-1} mol^{-1}.

Table 14 records reported activation parameters for the oxidation of 4-methylphenol by HRP I and for hydrogen atom abstractions from a selection of phenols and one from the reaction of $Bu^tO^\bullet$ with toluene. From these data it is evident that the oxidation of 3-cyanophenol by OFe^{IV}T2MPyP has the largest E_a and the most positive $\Delta S^\ddagger$. This activation energy may, in part, reflect the strong O–H bond of this phenol but probably, more importantly, it arises from H-bonding and the solvation of the phenol and the oxoiron(IV) porphyrin. The

Table 12 ρ Values from correlations of log second-order rate constants with σ, σ^+ and $\sigma^\bullet$ for oxidations of phenols by $OFe^{IV}T2MPyP$ and HRP II[a] in aqueous solution

		Substituent constant					
		σ		σ^+		$\sigma^\bullet$	
Oxidant	pH	ρ Value	Correlation coeff.	ρ Value	Correlation coeff.	ρ Value	Correlation coeff.
$OFe^{IV}T2MPyP$	7.7	−1.52	0.881	−1.10	0.956	18.8	0.921
HRP II	7.6 and 7.0	−4.70	0.930	−2.70	0.950	—	0.489

[a] Rate constants from Dunford and Adeniran ref. 2(*d*).

Table 13 Second-order rate constants for oxidation of phenols by $OFe^{IV}T2MPyP$, HRP II, HRP I and the iron(III) deuterioporphyrin–H_2O_2 system

	$k_2/10^4$ mol^{-1} dm^3 s^{-1}			
XC_6H_4OH	$OFe^{IV}T2MPyP$ pH 7.7, 30 °C	HRP II pH 7.6, 25 °C[a]	Fe^{III}Deuterioporphyrin pH 7.3, 25 °C[b]	HRP I pH 7.0, 27 °C[c]
3-CN	0.424	0.0147[d]	—	—
3-F	1.57	—	—	—
H	1.78	30.0	71.0	276.0
4-F	1.92	—	—	—
4-Cl	2.44	2.4	27.0	1 130
4-Me	4.05	101.0	4 100	4 200
4-OMe	19.6	560.0	87 000	13 000

[a] Ref. 2(*d*). [b] Ref. 5. [c] Ref. 2(*c*). [d] Ref. 2(*e*).

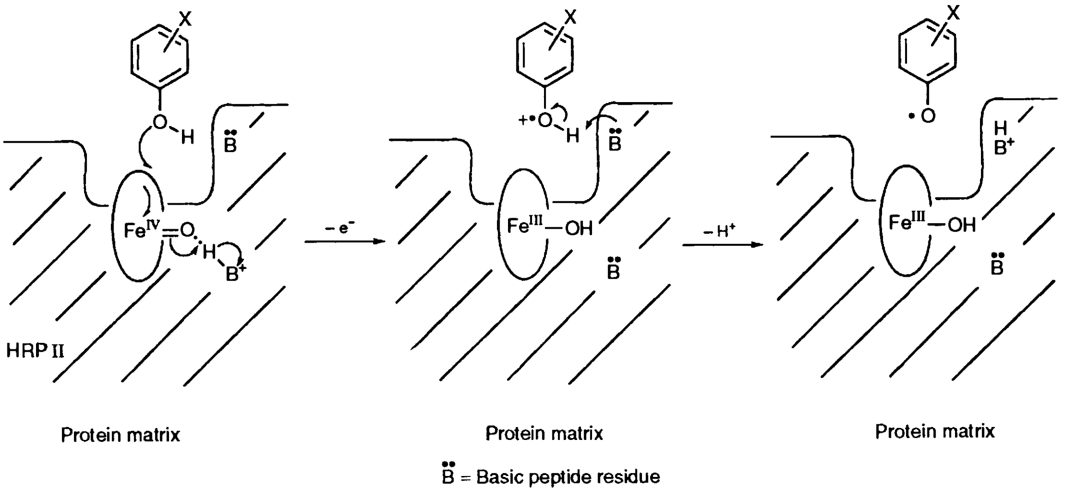


Fig. 12 Schematic diagram of proposed mechanism of oxidation of phenols by HRP II

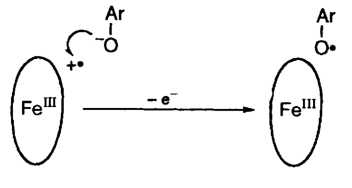


Fig. 13 Proposed mechanism for oxidation of phenols by the iron(III) deuterioporphyrin–H_2O_2 system

comparative reactions of $Bu^tO^\bullet$ and triplet benzophenone were carried out in toluene. The rate reducing effect of H-bonding by the solvent in hydrogen atom abstractions in phenol oxidations by peroxyl radicals has been noted before by Howard and Ingold.[48]

The influence of the solvent is also seen in the surprisingly small $\Delta S^\ddagger$ value. The expected large negative $\Delta S^\ddagger$ from an ordered transition state is probably masked by a disordering of the solvent. Thus, the phenol and oxidant would be highly solvated and their solvent cages would be disrupted in forming the transition state.

Experimental

Materials.—All materials were commercially available (Aldrich Chemical, Fisons Scientific Apparatus and Sigma Chemicals) unless otherwise stated. The phenols were all purified before use in the kinetic studies either by distillation (3-fluoro-

Table 14 Arrhenius parameters for some hydrogen atom-abstraction oxidations

Oxidant (Solvent)	Substrate $X\text{-}C_6H_4OH$	E_a/ kJ mol^{-1}	ln A[a] (ΔS)‡/ J K^{-1} mol^{-1}[b]	BDE(O–H)[c]/ kJ mol^{-1}	Ref.
OFe^{IV}T2MPyP (H_2O)	3-CN	57.4	31.1 (5.21)	393	This study
HRP I (H_2O)	4-Me	20.9	(−25.1)	371	43
$Bu^tO^{\bullet}$ (PhMe)	4-OMe	16.7	27.9 (−21.6)	354	27
	H	11.7	24.6 (−49.2)	376	27
	4-Br	13.4	25.1 (−44.7)	379	27
PhCOPh triplet (PhMe)	4-OMe	15.5	28.8 (−13.8)	354	44
	H	8.8	24.4 (−50.7)	376	44
	4-Br	12.97	26.5 (−33.4)	379	44
$Bu^tO^{\bullet}$	PhMe[d]	23.43	—	343 (C-H)[e]	45

[a] A in mol^{-1} dm^3 s^{-1}. [b] $\Delta S^{\ddagger}$ values calculated at 303 K using reported ln A values. [c] Bond dissociation energies (BDE) from ref. 46. [d] Substrate PhMe. [e] BDE from ref. 47.

and 4-methyl-phenol and phenol) or by recrystallisation from benzene–40-60 petroleum ether (3-cyano-, 4-fluoro-, 4-methoxy- and 4-chloro-phenol). The aqueous *tert*-butyl hydroperoxide was 70% w/w and was regularly checked during the course of this study by iodometric titration. Deionised water was used throughout this study.

Iron(III) tetra(4-*N*-methylpyridyl)porphyrin tetratosylate was purchased from Nentech and iron(III) tetra(2-*N*-methylpyridyl)-porphyrin tetrachloride was prepared as described previously.[49]

Methods.—UV–VIS spectra and kinetic data were recorded on a Hewlett Packard 8452A diode array spectrometer. The data were stored and analysed on a Hewlett Packard HP9500 UV–VIS Chemstation with a kinetics software package 89512A. Spectral simulations to evaluate the conversion of Fe^{III}T2MPyP to OFe^{IV}T2MPyP by Bu^tO_2H were carried out by spectral fitting using the QUANT II software package. For the study of rapid reactions a Photophysics RX 1000 stopped-flow apparatus equipped with 2.5 cm^3 drive syringes and a dual pathlength (10/2 mm) cuvette was attached to the spectrometer. The syringes and reaction chamber were thermostatted at 30 °C.

EPR spectra were measured with a Bruker ESP 300 spectrometer equipped with X-band klystron and 100 kHz modulation. The generation of the Trolox C radical was carried out with a stopped flow apparatus attached to the EPR spectrometer.

pH Measurements were made with a Corning Delta 220 pH meter equipped with a Russells CE7L combined pH/reference electrode.

Kinetic Procedures.—One drive syringe of the stopped-flow apparatus was fitted with freshly prepared oxoiron(IV) porphyrin, formed by the addition of a buffered aqueous solution of Bu^tO_2H to a buffered solution of iron(III) porphyrin and $NaNO_3$ (the final ionic strength of the mixture was 0.20 mol dm^{-3}). The other drive syringe was fitted with a buffered solution of the phenolic substrate. Rapid mixing of equal volumes of the solutions from the drive syringes in the quartz cuvette triggered the recording by the spectrometer of the λ_{max} absorbance of the oxoiron(IV) porphyrin. The total volume of each reaction was 0.3 cm^3 which allowed 12–14 kinetic runs to be recorded for each pair of solutions reacted. In the kinetic analysis the data from these runs were averaged.

EPR Studies.—EPR spectra of the reaction between OFe^{IV}T2MPyP and Trolox C were obtained by loading one drive syringe, in the stopped-flow apparatus, with OFe^{IV}T2MPyP prepared from buffered solutions of Bu^tO_2H and OFe^{III}T2MPyP with $NaNO_3$, as described above. The other syringe was fitted with a buffered solution of Trolox C. The EPR spectrum was recorded over 120 s following the mixing of equal volumes of the two solutions in the EPR spectrometer cavity. The time-dependent formation and decay of the Trolox C radical was monitored using a stationary magnetic field centred on the middle peak of the EPR spectrum.

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