Facile Aerial Oxidation of Porphyrins. Part 16.[1] Phenolic Porphyrins Without *tert*-Butyl Substituents

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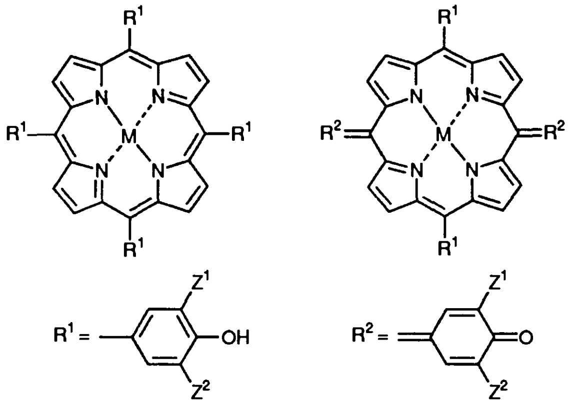
Non-*tert*-butyl-substituted phenolic porphyrins **5**, **7** and **9** undergo aerial oxidation in acidic and basic solutions. Radicals are produced whose singlet EPR spectra differ significantly from those observed for the *tert*-butyl-substituted phenolic porphyrin **1**. In the radical derived from **5a**, for example, the unpaired electron is not (as in **1**) localised on the macrocycle or the meso-substituent. Simulation of the EPR spectrum obtained for the zinc complex **7b** in basic solution, suggests two species coexisting on the EPR time-scale.

Investigations into the aerial oxidation of redox-active phenolic porphyrins, have concentrated mainly on porphyrin **1**.[2] In acidic and basic solutions, **1** undergoes two-electron oxidation to yield **2**,[3] which conproportionates[4] further with **1**, giving long-lived radical species.[5] In base, the radical's unpaired electron is localised on a meso-substituent, while in acidic solutions, the unpaired electron is restricted to the porphyrin macrocycle. The initial two-electron aerial oxidation also generates reduced-oxygen species, H_2O_2 and $OH^•$.[6]

Pyrogallyl meso-substituents similarly render the porphyrin susceptible to aerial oxidation. However, porphyrin **3** undergoes eight-electron oxidation in base, to give the tetraquinone **4**.[7] A long-lived radical is produced, which oxygen-electrode studies suggest has seven electrons fewer than **3**. The 1:2:1 triplet hyperfine splitting pattern in its EPR spectrum suggests the radical has an unpaired electron on a meso-substituent.

Previous work[3,8a] with phenolic porphyrins **5a** and **7a**, led us to expect their stability to aerial oxidation. Thus, in base, green phenoxide intermediates are formed which turn back to red on Williamson reaction with suitable substrates.[8a] This colour change has been used to determine reaction completion during the synthesis of porphyrin aryl alkyl ethers (as photosensitisers for solar-energy conversion,[8a] and as discotic liquid crystals[9]). We have found, however, that some aerial oxidation of **5a** and the zinc complexes **5b** and **7b** does indeed take place in basic solutions. We report here observation of radical intermediates whose EPR spectra [Figs. 1, 2 and 3(*a*)] differ significantly from those observed previously for **1** and **3**.

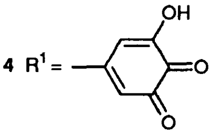


1 $Z^1 = Z^2 = Bu^t$
M = 2H

2 $Z^1 = Z^2 = Bu^t$
M = 2H

3 $Z^1 = Z^2 = OH$
M = 2H

4



5 $Z^1 = Z^2 = OMe$
a M = 2H
b M = Zn

6 $Z^1 = Z^2 = OMe$
a M = 2H
b M = Zn

7 $Z^1 = Z^2 = H$
a M = 2H
b M = Zn

8 $Z^1 = Z^2 = H$
a M = 2H
b M = Zn

9 $Z^1 = OMe$
$Z^2 = H$
M = 2H

10 $Z^1 = OMe$
$Z^2 = H$
M = 2H

Experimental

Porphyrins **5**, **7** and **9**, were synthesised by literature methods,[10] and have been reported previously.[3,8] Zinc was inserted into **5a** and **7a**, to give metalloporphyrins **5b** and **7b**, respectively, using a saturated solution of zinc acetate in methanol (MeOH).[11a]

To samples of the porphyrins and metalloporphyrins (10–15 mg) were added aerated solutions (1 cm^3) of base [1 mol dm^{-3} tetra-n-butylammonium hydroxide in methanol (1 mol dm^{-3} tnBAH–MeOH) or 1 mol dm^{-3} aqueous potassium hydroxide (KOH) solution]. For porphyrin **5a**, in order to observe the effects of porphyrin concentration on the appearance of the EPR spectrum (Fig. 1), solutions were prepared in 1 mol dm^{-3} aqueous KOH at the following molarities: 1.53×10^{-2}, 1.02×10^{-2}, 5.10×10^{-3}, 2.04×10^{-3} and 1.02×10^{-3} mol dm^{-3}. Also, one solution was prepared in trifluoroacetic acid (TFA; 10 drops) and dichloromethane (DCM; 2 cm^3).

Aliquots of these solutions were transferred to an EPR flat-cell, and placed in the cavity (at 20 °C) of a Varian E-3 EPR spectrometer (field centre = 339.5 ± 0.1 mT; microwave frequency = 9.375 ± 0.005 GHz; microwave power = 20 mW; modulation amplitude = 0.063–0.1 mT; sweep width = 5 mT; scan-time = 4 min; gain = 8×10^4).

The *g*-values obtained here were standardised against the *g* value standard, diphenylpicrylhydrazyl (DPPH; $g = 2.0037 \pm 0.0002$).[12] Using the Varian instrument, uncertainties in the measurement of field and frequency limit the accuracy of the quoted *g* values to two decimal places.

Simulations of EPR spectra were performed on a Viglen Genie Professional Workstation, using a program written and supplied by D. R. Duling of the Laboratory of Molecular Physics, NIEHS/NIH, North Carolina, USA.[2]

The spectrum shown in Fig. 3(*a*) was simulated [Fig. 3(*b*)] as two overlapping species with the same *g* value. In the first species, the unpaired electron interacts with one set of four equivalent nitrogens ($S = 1$; assumed coupling of $a_N = 0.11$ mT), with a line-width = 0.0625 mT; line shape = 100% Gaussian, and a relative area of 33%. In the second species, the unpaired electron interacts with two sets of two equivalent protons of a phenoxyl radical meso-substituent ($S = 0.5$; coupling of $a_{H(1)} = 0.0975$ mT; assumed coupling $a_{H(2)} = 0.020$ mT), with line-width = 0.0200 mT; line shape = 0% Gaussian, and relative area of 66%.

Table 1 Collected EPR data

Porphyrin	Conditions	g[a]	a(cs)[b]/mT	a_H/mT
5a	tnBAH–MeOH[c]	2.004(4)[d]	339.6(8)	—
[e]	aq. KOH[c]	2.004(6)	339.6(2)	—
	aq. KOH[c] + PO	2.003(7)[d]	339.4(3)	—
	DCM–TFA	2.002(9)[d]	339.5(8)	—
5b	tnBAH–MeOH[c] (not very soluble)	2.008(2)[d]	339.0(3)	
[f]	aq. KOH[c] (some demetallation)	2.005(7)	339.4(4)	0.0696
7a	no EPR spectrum in base or acid	—	—	—
7b[g]	aq. KOH[c]	2.010(1)	338.3(4)	0.0975
9	tnBAH–MeOH[c] (weak spectrum)	2.004(3)[d]	339.6(9)	

[a] Uncertainty = ±0.002. [b] Centre spectrum field uncertainty = ± 0.1 mT. [c] 1 mol dm^{-3}. [d] Singlet. [e] Fig. 1. [f] Fig. 2. [g] Fig. 3.

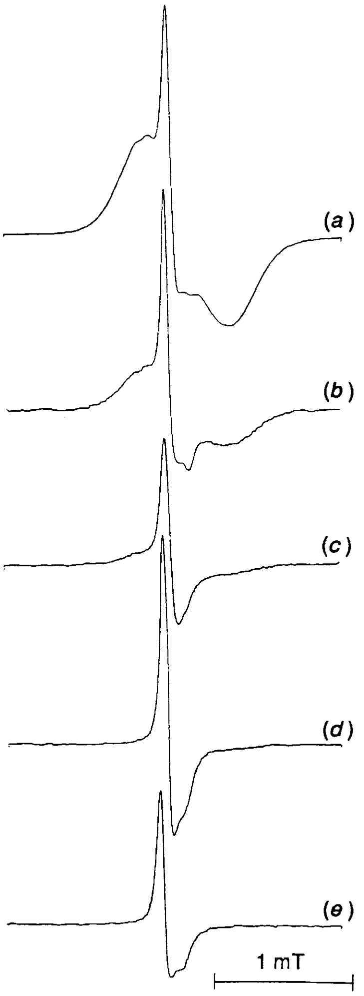


Fig. 1 EPR spectrum of porphyrin **5a** in 1 mol dm^{-3} aqueous KOH. The broad singlet disappears with increasing dilution, while the narrow unsymmetrical singlet remains: (*a*) 1.53 × 10^{-2} mol dm^{-3}; (*b*) 1.02 × 10^{-3} mol dm^{-3}; (*c*) 5.10 × 10^{-3} mol dm^{-3}; (*d*) 2.04 × 10^{-3} mol dm^{-3}; (*e*) 1.02 × 10^{-3} mol dm^{-3}.

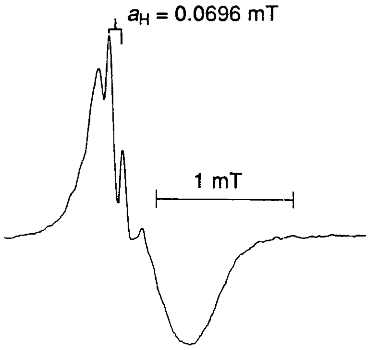


Fig. 2 EPR spectrum of porphyrin **5b** in 1 mol dm^{-3} aqueous KOH

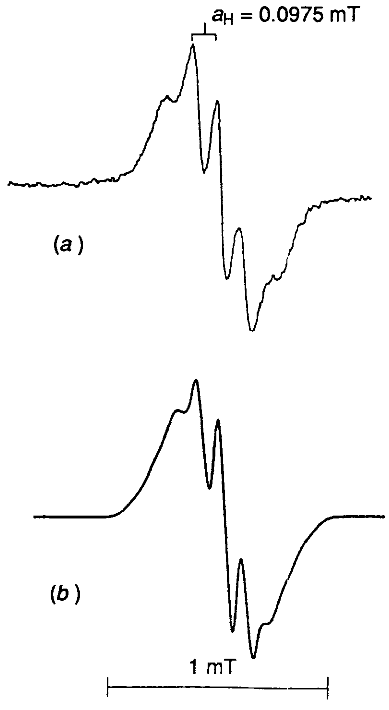


Fig. 3 (*a*) Experimental EPR spectrum for porphyrin **7b** in 1 mol dm^{-3} aqueous KOH; (*b*) simulated EPR spectrum for porphyrin **7b** as two species—a multiplet and a singlet—with the same *g* value

Results and Discussion

EPR spectral data for the porphyrins in aerated solutions are collected in Table 1, and spectra for **5a**, **5b** and **7b**, are shown in Figs. 1, 2 and 3, respectively. For all the spectra, the *g* values are similar and, within experimental error, typical for organic radicals, especially porphyrin radicals (typical *g* values ranging between 1.999 and 2.006[4b]) and semiquinone radical ions (typical *g* values between 2.003 and 2.005[13]). Simple symmetric singlet envelopes were obtained for **5a** (in 1 mol dm^{-3} tnBAH–MeOH and TFA–DCM), **5b** (weak spectrum, compound not very soluble in 1 mol dm^{-3} tnBAH–MeOH) and **9** (weak spectrum, 1 mol dm^{-3} tnBAH–MeOH). In aqueous 1 mol dm^{-3} KOH, however, compounds **5a** and **5b** gave the unsymmetrical spectra shown in Figs. 1 and 2, respectively.

Compound **5b** also showed evidence of demetallation in aqueous 1 mol dm^{-3} KOH, in which it was more soluble than in 1 mol dm^{-3} tnBAH–MeOH. For example, the usual metalloporphyrin two-banded visible Q-band spectrum[11b] of **5b** had additional bands at longer wavelength after neutralisation, indicating the presence of the metal-free porphyrin **5a**. Also, a white residue of zinc hydroxide was left on the inside of the EPR cell, which dissolved with excess base.

Compound **7a** was EPR-silent in basic and acid solutions. However, the zinc complex **7b**, in 1 mol dm^{-3} aqueous KOH, gave a symmetric EPR spectrum, consisting of a broad multiplet superimposed onto a singlet envelope [Fig. 3(*a*)].

All spectra obtained in basic solutions had decayed within 30 minutes of addition of base to the starting porphyrin. The spectrum of **5a**, obtained in DCM–TFA did not decay even after two hours, reminiscent of compound **1** under the same conditions.[4a]

The strongest EPR spectra were observed with porphyrin **5a** and no spectra were obtained if the basic or acidic solutions were degassed prior to addition to the porphyrins. This implicates oxygen in the oxidation process, as with porphyrin **1**. However, large-scale formation of oxidised porphyrins **6**, **8** and **10** (by analogy with **2**), was not observed. For example, UV–VIS spectroscopy did not show disappearance of the porphyrinic B band at 420 nm[8] (as has been observed during the aerial oxidation of **1** to **2**[3]), nor was it possible to separate oxidised porphyrins from the green solutions. This implies a substantial difference in the amount, rate and/or mechanism of the aerial oxidation undergone by porphyrins **5**, **7** and **9**, compared to **1** under similar conditions.

Degassing the basic or acidic porphyrin solutions *after* the appearance of EPR spectra, did not lead to superimposition of fine structure on the singlet envelopes, as observed with porphyrin **1** in TFA–DCM[4a] and with other porphyrin radical cations.[4b] This suggests that the unpaired electron is no longer localised on the meso-substituents or the macrocycle, as with porphyrin **1** in base and TFA–DCM, respectively.[5]

The EPR spectrum given by compound **5a** at 1.53×10^{-2} mol dm^{-3} in 1 mol dm^{-3} aqueous KOH [Fig. 1(*a*)] consists of a broad singlet on which is superimposed a narrower unsymmetrical singlet. As this solution is progressively diluted [Fig. 1(*b*), (*c*), (*d*) and (*e*)], the broad singlet disappears, leaving the narrow unsymmetrical singlet. Negatively-charged porphyrins are known to form dimers and higher aggregates in aqueous solutions,[14] at concentrations well below those used in this work. Also, it is known that, at radical concentrations above 10^{-3} mol dm^{-3}, electron-spin exchange effects lead to spectral broadening.[15] We suspect, therefore, that the form of the spectra shown in Fig. 1 is due to a combination of concentration-induced exchange effects and aggregation; the former leading to the broad singlet that disappears on dilution, while the latter gives the unsymmetrical narrower singlet.

Evidence in support of this view is that addition of a large (23-fold) molar excess of pyridine *N*-oxide (PO) to a solution of **5a** in aqueous KOH (1 mol dm^{-3}), gives an EPR spectrum with a symmetric featureless singlet envelope and EPR parameters very close to those obtained for **5a** in 1 mol dm^{-3} tnBAH–MeOH (see Table 1). Being a planar aromatic moiety, the effect of PO on the EPR spectrum of **5a** in 1 mol dm^{-3} aqueous KOH is probably due to dilution of radical concentration (so inhibiting exchange broadening), and mitigation of porphyrin aggregation.

The EPR spectrum shown for porphyrin **7b** in 1 mol dm^{-3} aqueous KOH [Fig. 3(*a*)] consists of a multiplet symmetrically superimposed on a singlet. We have simulated this spectrum [Fig. 3(*b*)] as two species (the spectrum could not be modelled on the assumption of one radical species) coexisting on the EPR time-scale, with the same *g* value (see Experimental section). In one of the species, the unpaired electron is localised on the macrocycle, while in the other, it is localised on a meso-substituent. This suggests that leakage of unpaired electron density[16] between these two locations in the molecule must be slow on the EPR timescale—a reasonable suggestion as zinc complexation is known to lock the macrocycle and the phenolic meso-substituents into near-orthogonality,[17] so inhibiting coupling of the two π-systems. The zinc cation also provides a site for binding molecules of solvent. Negatively-charged zinc porphyrins, therefore, should aggregate less in solution than the non-metallated porphyrins[18]—hence the similar EPR spectra for **5b** and **7b** in 1 mol dm^{-3} aqueous KOH.

Without the zinc cation to lock the conformation of **5a**, the unpaired electron could rapidly delocalise over the macrocycle and the meso-substituent.[16] This could explain why the EPR spectrum of **5a**, in contrast to **1**,[5] consists of a smooth singlet envelope. Alternatively, some oligomer formation by **5a** in basic methanolic solutions could lead to the unpaired electron being delocalised over more than one porphyrin molecule.[2] This again would give a smooth singlet envelope in the EPR spectrum.

The EPR spectrum of **5b** in 1 mol dm^{-3} aqueous KOH consists of a multiplet unsymmetrically superimposed on a singlet envelope (Fig. 2). Simulation of this spectrum as two different overlapping species similar to Fig. 3 but with a significant *g*-shift between them, was only partially successful. We believe this might be due to complications brought on by the demetallation. These would include the appearance of other radicals (*e.g.* from **5a**) and anisotropies introduced by the presence of zinc hydroxide in the EPR cell.

Finally, that no oxidised porphyrins could be detected made us curious about the mechanism of aerial oxidation of these non-*tert*-butyl-substituted porphyrins. We have conducted some preliminary experiments using spin-traps, ostensibly to detect the presence of reduced oxygen species[6] *e.g.* H_2O_2, $OH^{\bullet}$ or $O_2^{\bullet-}/O_2H$. Thus, detection of $OH^{\bullet}$ would indicate a two-electron aerial oxidation mechanism akin to that shown by compound **1** in basic solutions, while a different mechanism would need to be considered if superoxide were detected.* Although oxygen is clearly involved in the formation of the porphyrin radicals (without O_2 in solution radical formation is supressed), we have so far failed to find any evidence of spin-trapped reduced-oxygen species. We are continuing to investigate this aspect of aerial oxidation in these phenolic porphyrins.

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* Our previous work on the two-electron aerial oxidation of the related porphyrin **1** in the presence of spin-traps (see ref. 6) leads us not to expect a mechanism that would produce superoxide or hydroperoxide radicals *directly*.

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Paper 3/05800J
Received 27*th September* 1993
Accepted 18*th November* 1993