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## Cation Radicals of Tetraalkylporphyrins

Sir:

Oxidation of tetraphenyl- and octaethylmetalporphyrins leads to  $\pi$  cation radicals<sup>1-3</sup> which fall into two general categories:<sup>4-7</sup> (1) radicals where the electron presumably has been removed from the  $a_{2u}$  highest occupied orbital leading to a  ${}^2A_{2u}$  ground state ( $D_{4h}$  symmetry) and (2) those assumed to arise instead from the removal of an electron from the  $a_{1u}$  orbital resulting in a  ${}^2A_{1u}$  state.<sup>4,7,9</sup> The radicals possess characteristic optical spectra and exhibit the following esr parameters:<sup>4,7,10</sup> for  ${}^2A_{1u}$ , spectra consistent with predicted high spin density at the meso positions, nitrogen hyperfine splitting, metal hyperfine splitting, and, in solvents of low dielectric constants, hyperfine splitting from the gegenion. By comparison,  ${}^2A_{1u}$  radicals show small spin densities at the meso positions, and, to date, no nitrogen, metal, or anion splittings have been resolved. This has led to the conclusion<sup>7</sup> that the  $\alpha$  carbons of the pyrroles bear high spin densities in this ground state as theoretically predicted.<sup>4,9</sup> Recent results on zinc and magnesium tetrapropylporphyrins<sup>7,11</sup> indicate that their cation radicals fit the  ${}^2A_{2u}$  requisites, but the spin densities at the meso positions, deduced from the esr splittings, are considerably smaller than expected on the basis of SCF-MO calculations.<sup>4</sup>

We present here esr data on a series of meso tetraalkylporphyrins which confirm that these radicals fall in the  ${}^2A_{2u}$  category. The particularly well-resolved

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spectrum of zinc tetramethylporphyrin provides a direct probe of the spin density at the meso carbons *via* hyperconjugation and thus permits direct testing of MO calculations for the  ${}^2A_{2u}$  state. The apparent disparity between experimental results and theory, observed upon substitution of methyl groups by larger alkyl derivatives, is explained by restricted rotation of the alkyl groups.

Oxidations<sup>12</sup> of the zinc complexes of *meso*-tetramethyl-, -tetraethyl-, -tetrapropyl-, -tetrabutyl-, and -tetractylporphyrins<sup>13</sup> yield radicals whose esr spectra are readily analyzed in terms of interactions with four equivalent nitrogens and with four methyl (or methylene) groups (Table I). Experimental spectra and

**Table I.** Hyperfine Splitting Constants of Zinc Tetraalkylporphyrins in  $CCl_4$  at  $0^\circ$ ,  $g = 2.0026 (\pm 0.0001)$

Compound	$a_N$ , G	$a_H$ , G	Others
$Zn(CH_3)_4P^{+\cdot}$	1.72	5.90 ( $CH_3$ )	
$Zn(C_2H_5)_4P^{+\cdot}$	} 1.69 <sup>a</sup>	} 2.75 ( $CH_2$ )	0.20 ( $-CH_3$ )
$Zn(C_3H_7)_4P^{+\cdot}$			} Not resolved
$Zn(C_4H_9)_4P^{+\cdot}$			
$Zn(C_8H_{17})_4P^{+\cdot}$			

<sup>a</sup> Based on computer simulations.

computer simulations for  $Zn(CH_3)_4P^{+\cdot}$  and  $Zn(C_4H_9)_4P^{+\cdot}$  are shown in Figures 1 and 2.

The large differences between the methyl splittings observed in  $Zn(CH_3)_4P^{+\cdot}$  *vs.* the methylene couplings of the other radicals are not expected on the basis of predicted spin densities.<sup>4</sup> Similar effects have been observed<sup>15,16</sup> for alkyl substituted aromatic cations with the ratio of splitting constants  $a_{CH_3}/a_{CH_2} \sim 0.46$ . The phenomenon is explained by a restricted rotational model;<sup>15,16</sup>  $\beta$  proton splittings depend on the dihedral angle,  $\theta$ , between the proton and  $2p_z$  orbital of the  $\alpha$  carbon to which the methyl (or methylene) group is attached

$$a_{H\beta} = \rho_{C\alpha}(B_0 + B \cos^2 \theta) \quad (1)$$

where  $B$  and  $B_0$  are constants with  $B \gg B_0$  and  $\rho$  is the unpaired spin density of  $C_\alpha$ . For a freely rotating methyl group  $\cos^2 \theta \sim 1/2$  while, for locked methylene groups, the conformation of lowest energy requires  $\theta = 60^\circ$  and  $\cos^2 \theta = 1/4$ , giving rise to the observed ratio of  $\sim 0.5$  between hindered and free alkyl groups. In this work, as shown in Table I,  $a_N$  remains effectively constant when the alkyl groups are changed while  $a_{CH_3}/a_{CH_2} = 0.47$ . The difference in the splitting constants

(12) Oxidations were carried out in  $CHCl_3$  or  $CH_2Cl_2$  chemically using  $(FeTPP)_2O^+ClO_4^-$  and  $Br_2$  or electrochemically at a platinum electrode with tetrapropylammonium perchlorate as carrier electrolyte.<sup>4,6,7,10</sup> We are indebted to Dr. R. H. Felton for a generous supply of the iron compound.

(13) Porphyrins were prepared using methods previously described<sup>14</sup> by condensation of pyrrole with the appropriate aldehyde in xylene containing 0.1 M trifluoroacetic acid. Metalation was performed in dimethylformamide, and the resulting metalloporphyrins were recrystallized from heptane.

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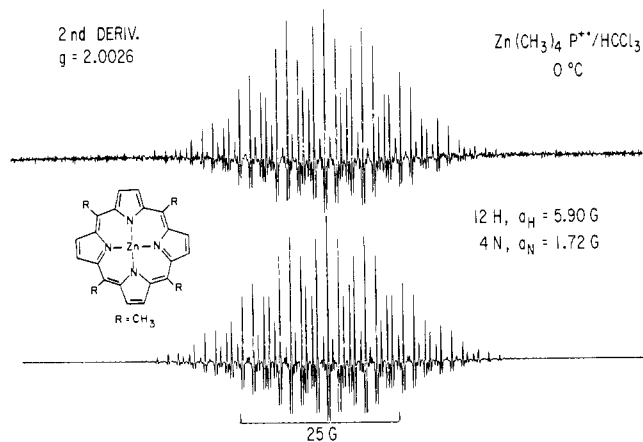


Figure 1. Second derivative esr spectrum of  $\text{Zn}(\text{CH}_3)_4\text{P}^{\cdot+}$  in  $\text{CHCl}_3$  at  $0^\circ$  (top) and a computer simulation assuming four nitrogens and four methyl groups (bottom).

is therefore assigned to restricted rotation of the alkyl groups larger than methyl caused by the adjacent pyrroles. This model is also supported by X-ray data on the structure of  $\text{H}_2(\text{C}_3\text{H}_7)_4\text{P}$  which indicate short distances between the middle group of the alkyl substituent and the adjacent  $\beta$ -carbon atom of the pyrrole ring.<sup>17</sup>

For a freely rotating methyl group on a cation radical,<sup>15,18</sup> eq 1 is simply  $a_{\text{CH}_3} \cong 39\rho_{\text{C}}$ . In  $\text{Zn}(\text{CH}_3)_4\text{P}^{\cdot+}$ ,  $a_{\text{CH}_3} = 5.90$  G, and the spin density at the meso positions is therefore 0.15. The MO values calculated<sup>4</sup> for a  ${}^2\text{A}_{2u}$  state are 0.158 before and 0.193 after configuration interaction. The narrow line widths observed in  $\text{Zn}(\text{CH}_3)_4\text{P}^{\cdot+}$  and the close agreement between the observed and simulated esr spectra exclude any significant unresolved interactions with nuclei other than the nitrogens and the methyl groups. Only negligible unpaired spin densities can therefore exist on the  $\beta$  carbons of the pyrrole rings, in accord with observations made on  ${}^2\text{A}_{2u}$  meso-tetraphenylporphyrins.<sup>7</sup> The predicted spin densities<sup>4</sup> are 0.019 before and 0.013 after configuration interaction.

Delocalization of spin onto the metal is observed in the radical of cobaltic tetrapropylporphyrin [ $\text{Co}^{\text{III}}(\text{C}_3\text{H}_7)_4\text{P}$ ] $^{\cdot 2+}$  with  $a_{59\text{Co}} = 6$  G in  $\text{CH}_2\text{Cl}_2$ , a value comparable to that observed in the radical of cobaltic tetraphenylporphyrin<sup>3,4</sup> (nuclear spin,  $I$ , of  ${}^{59}\text{Co} = 7/2$ ). Bromine oxidations of  $\text{Zn}(\text{C}_3\text{H}_7)_4\text{P}$ ,  $\text{Zn}(\text{C}_4\text{H}_9)_4\text{P}$ , and  $\text{Zn}(\text{C}_8\text{H}_{17})_4\text{P}$  yield the bromide-complexed radicals  $\text{Zn}(\text{alkyl})_4\text{P}^{\cdot+}\text{Br}^-$  with bromine splittings ( $I = 3/2$ )  $a_{59\text{Br}} = 8.8$  G and  $g$  values of 2.0045. The tetraalkylporphyrin radicals described here clearly fit the theoretical and experimental criteria for  ${}^2\text{A}_{2u}$  states, high spin density at the meso positions coupled with nitrogen, metal, and anion interactions. In addition, negligible spin density is found at the  $\beta$ -pyrrole positions.

The two radical ground states discussed above are of special interest because the oxidized forms (compounds I) of the enzymes catalase (Cat I) and horseradish peroxidase (Hrp I) exhibit optical spectra which suggest that the enzymes function *via* these radicals.<sup>5-7</sup> On

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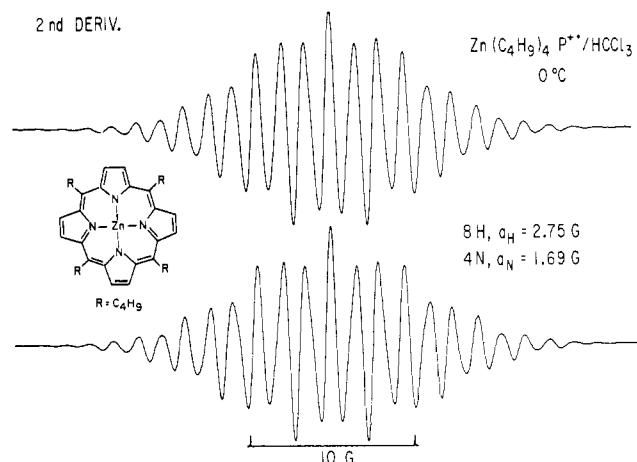


Figure 2. Second derivative esr spectrum of  $\text{Zn}(\text{C}_4\text{H}_9)_4\text{P}^{\cdot+}$  in  $\text{CHCl}_3$  at  $0^\circ$  (top) and a computer simulation assuming four nitrogens and four methylene groups (bottom).

the basis of its optical absorption spectrum, Hrp I is believed to contain the  ${}^2\text{A}_{2u}$  radical while the electronic absorption of Cat I resembles that of a  ${}^2\text{A}_{1u}$  porphyrin radical,<sup>5-7</sup> with lower spin density at the meso carbons (0.05) and most of the unpaired electron delocalized onto the  $\alpha$  carbons adjacent to the pyrrole nitrogens.<sup>4,7,9</sup> The different ground states of Hrp I and Cat I may reflect the different apoproteins<sup>19</sup> of the two enzymes since changes in anionic ligands<sup>5-7,10</sup> can switch the ground state of porphyrin radicals between  ${}^2\text{A}_{1u}$  and  ${}^2\text{A}_{2u}$ . In other words, the ground states of Hrp I and Cat I reflect their specific protein environments, but the resulting differences in spin delocalization of the ground states actually control the reactions with substrates.

Furthermore, since the sequestration of the porphyrins of cytochromes  $b_5$  and  $c$  within hydrophobic crevices<sup>20,21</sup> appears to preclude direct electron transfer between substrates and heme iron, whereas the peripheries of the porphyrins remain exposed, it is attractive to speculate that electron transfer to and from the iron<sup>5,6,22</sup> occurs *via* porphyrin radical transients with the  $\pi$ -electron configurations described here.

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### Aza Analogs of Nucleic Acid Constituents. III. The Molecular Structure of 6-Azacytidine

Sir:

6-Azacytidine is a powerful carcinostatic agent whose mode of action is postulated to be similar to