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Communications

A Pronounced Axial Ligand Effect on the Reactivity of Oxoiron(IV) Porphyrin Cation Radicals

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During the catalytic action of heme-dependent enzymes such as catalases and peroxidases two oxoiron porphyrin intermediates are usually observed, commonly referred to as compound I and compound II.[1] Regarding synthetic iron porphyrins, both oxoiron(IV) porphyrins and oxoiron(IV) porphyrin cation radicals,[2] which are considered synthetic analogs of compound II and compound I, respectively, were isolated and characterized by various spectroscopic methods.[3] Most attention was given to oxoiron(IV) porphyrin cation radicals, since such species can mimic reactions mediated by P-450 monooxygenases and are considered to be the reactive intermediates in catalytic oxidation systems based on iron porphyrins.[1,4]

One important difference among the various hemoproteins is the identity of their axial ligand. The unique spectroscopic and chemical features that distinguish P-450 from the other enzymes are due to its cysteinate ligand, whose role was elucidated for most steps in the catalytic cycle of P-450.[5] The last step, which is the oxygenation of substrates by compound I, was intensively studied by model porphyrins,[6] but to our knowledge no systematic investigation was carried out for the exploration of an axial ligand effect for that reaction. Because of the extreme instability of P-450's compound I, such a study is a formidable task in natural systems. It also cannot be studied in synthetic systems under catalytic conditions, since after a few catalytic cycles the identity of the original axial ligand in the iron(III) porphyrin catalyst is lost by reaction with the solvent, the substrate, or the oxidant.[7] In the present study we have overcome these problems and found a very significant ligand effect on the reactivity of oxoiron(IV) porphyrin cation radicals toward styrene.

Oxoiron(IV) tetramesitylporphyrin cation radical ($[(\mathrm{TMP}^{+\cdot})\mathrm{Fe}^{\mathrm{IV}}{=}\mathrm{O}]^{+}$, **1**) is by far the most extensively characterized complex of its type. We have prepared a series of iron(III) tetramesitylporphyrins with different axial ligands ((TMP)Fe-X, **2-X**), oxidized them by ozone[8] to the corresponding **1-X** (X = $^{-}$F, $HOCH_3$, $^{-}$Cl, $^{-}$OAc, $^{-}OSO_2CF_3$, $^{-}OClO_3$), and examined their EPR and ^{1}H NMR spectra.[9] The typical $S = {}^3/_2$ EPR spectra[3] (that of **1-**$OClO_3$, which is representative of the spectra of all other compounds, is presented in Figure 1) served to confirm the formation of oxoiron(IV) porphyrin cation radicals by this procedure and to eliminate the possibility of other reactive oxidative species.[4b,c] Inspection of the last column of Table 1 reveals that the presence of different axial ligands in **1-X** had only a minor effect on the EPR spectra, but fortunately the NMR spectra were very indicative for that purpose. The effect of the axial ligands on the chemical shifts of the various protons in **1-X** is illustrated in the NMR spectra of Figure 1 and presented in Table 1. This clearly shows that the axial ligands from **2-X** remained intact in **1-X** after ozonolysis. In addition, we have also confirmed that after the oxidation of styrene by **1-X** the original **2-X** were regenerated (NMR and UV–vis).

Next, we have studied the reaction of the various **1-X** with excess styrene.[10] Only styrene oxide was detected (in 32–67% yield relative to **2-X** and 54–97% yield relative to **1-X**),[11] and its

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(9) Solutions of **1-X** were obtained by bubbling ozone at −78 °C for 30 s (6μmol of O_3/min, 1.1 equiv) into 2.6 μmol of the dissolved **2-X** (0.6 mL of CD_2Cl_2 for NMR and EPR measurements, 1.5 mL of CH_2Cl_2 for the kinetic experiments), followed by purging with N_2 (70 mL/min) for 1 min. The complex **1-**$HOCH_3$ was obtained by oxidation of **2-Cl** in CH_2Cl_2 (CD_2Cl_2) which contained 5% MeOH (MeOH-*d*$_4$).[2]

(10) To the preformed solutions of **1-X** at −78 °C, which contained 1 equiv of nitrobenzene as an internal standard, was added 30–400 equiv of styrene at once under a constant stream of N_2, which was kept on during the reactions. Small aliquots were removed from the reaction vessel and quenched by an excess of *n*-Bu_4NI, still at −78 °C. These aliquots were examined by GC analysis for styrene oxide relative to the internal standard. For each of the various **1-X**, 6–8 aliquots were examined at different time intervals, covering about $2t_{1/2}$. An additional aliquot was examined much later to obtain a reliable infinity point.

(11) The yield of styrene oxide relative to **1-X** can be calculated from the following equation: Yield = $100k[\text{styrene}]/k_{\text{obs}}$, where k is the second-order rate constant from Table 1 and k_{obs} is the pseudo-first-order constant for that particular concentration of styrene.

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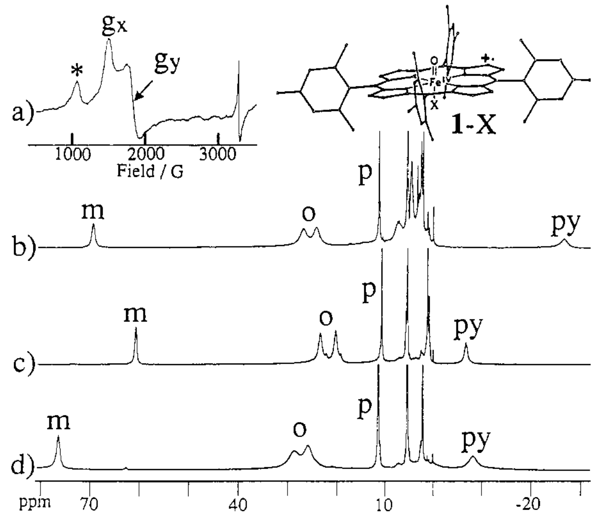

Figure 1. (a) X-band EPR spectrum of 1-$OClO_3$ in frozen CD_2Cl_2 at 15 K. The peak marked with an asterisk at $g = 6$ is due to residual iron(III), which also contributes to the $g = 2$ signal. (b–d) 200-MHz ^1H NMR spectra (CD_2Cl_2, −80 °C) of **1**-$HOCH_3$, **1**-Cl, and **1**-OAc, respectively. Key: m = *meta*-H, o = *ortho*-CH_3, p = *para*-CH_3, and py = pyrrole-H.

Table 1. NMR[a] and EPR[b] Data for the Various **1-X** Compounds and the Second-Order Rate Constants (±5%) for Their Reaction with Styrene

X in **1-X**	k^c	*m*-H	*o*-CH_3	*p*-CH_3	pyr-H	$g_x - g_y$
^-F	706	71.4	26.9, 24.1	10.7	−13.0	0.78
MeOH	196	69.4	26.7, 24.1	11.2	−26.7	0.73
^-Cl	149	60.6	23.3, 20.2	10.7	−6.7	0.51
^-OAc	114	76.2	25.7, 28.5	11.3	−8.3	0.62
$^-OSO_2CF_3$	46	68.6	26.8, 24.3	11.3	−26.2	0.77
$^-OClO_3$	*d*	65.3	26.0, 23.5	11.1	−26.9	0.76

[a] δ, ppm in CD_2Cl_2 at −80 °C. [b] *g* values at 15 K in frozen CD_2Cl_2. [c] 10^{-3} M^{-1} min^{-1}, at −78 °C. [d] Not determined, because only very low yields of styrene oxide were obtained.

formation followed excellent pseudo-first-order kinetics. The second-order rate constants for these reactions were elucidated from the linear dependence of the pseudo-first-order rate constants on the concentrations of styrene. The results which are collected in Table 1 revealed a very significant ligand effect on the reactivity of **1-X** toward styrene; the reaction of **1-F** was 15 times faster than that of **1**-OSO_2CF_3. Also presented in Table 1 are the NMR and EPR data for the various **1-X**, and apparently none of these spectroscopic features is in any correlation with their reactivities. On the other hand, there is a qualitative relationship between the effect of the ligands on the reactivity of **1-X** and on the pyrrole chemical shift in the various **2-X**, which are 81.5, 80.3, 79.6, 52.6, and 29.2 ppm (benzene-d_6) for X = ^-F, ^-Cl, ^-OAc, $^-OSO_2CF_3$, and $^-OClO_3$, respectively. It is well-known that the pyrrole chemical shifts in iron(III) (and manganese(III)) porphyrins are very sensitive to the field strengths of the axial ligands.[12,13] Thus, one can explain the kinetic ligand effect as originating from destabilization of the oxoiron(IV) moiety in **1-X**. This bond is described as a combination of one σ bond and two 3-electron dπ–pπ double bonds,[14] and we suggest that the π bonds are destabilized by the weak field, strong π-donor ligands, such as ^-F and ^-Cl.[15]

In summary, we have detected a remarkable axial ligand effect on the rate of epoxidation of styrene by **1-X**, a synthetic analog of compound I. We have also found a qualitative relationship between this effect and the field strengths of the same ligands. Whether or not this correlation is only accidental is currently under investigation by expansion of the **1-X** series and the range of organic substrates.

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Supplementary Material Available: Text giving synthetic procedures and NMR data for the various **2-X** compounds and a table of EPR data for the various **1-X** compounds (1 page). Ordering information is given on any current masthead page.

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(15) Groves and Watanabe have observed an intermediate on the pathway from **1** and olefins to the products.[1,6d] The present explanation for the kinetic ligand effect does not depend on whether or not such an intermediate was formed prior to the rate-limiting step in our reactions, since its structure is very similar to that of **1**.