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SYNTHESIS AND CHEMISTRY OF AN IRON(III) TETRAPHENYLPORPHYRIN WITH A COVALENTLY-ATTACHED PHENOLATE TAIL

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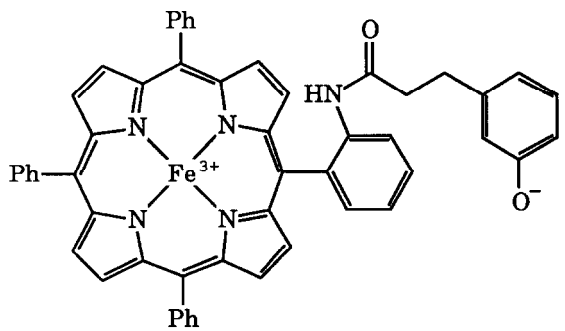
Abstract: We report the synthesis of a phenolate-tailed iron(III) tetraphenylporphyrin, **1**. The phenolate ligand is covalently-attached to the porphyrin ring and is coordinated to the iron(III) center. This phenolate ligand increases the rate of oxygen atom transfer to the metal center.

The use of iron(III) porphyrins as chemical models of the heme protein cytochrome P-450 has proven very fruitful. Groves and coworkers have studied model systems composed of an iron(III) porphyrin and an iodosylarene to characterize the high-valent iron intermediate involved in the catalytic oxidation chemistry of cytochrome P-450.[1] They have characterized this intermediate as an oxo-iron(IV) porphyrin cation radical.[2] A wide range of metalloporphyrin-oxidant systems have since been shown to catalyze similar oxidations of organic compounds.[3] A variety of oxidant, metal, and porphyrin ligand combinations have been used and have provided valuable information about the factors affecting the catalytic ability of the intermediate. Surprisingly very little work has focused on the role of the axial ligand of the metalloporphyrin in the catalytic chemistry; despite speculation about the possible unique role the axial thiolate



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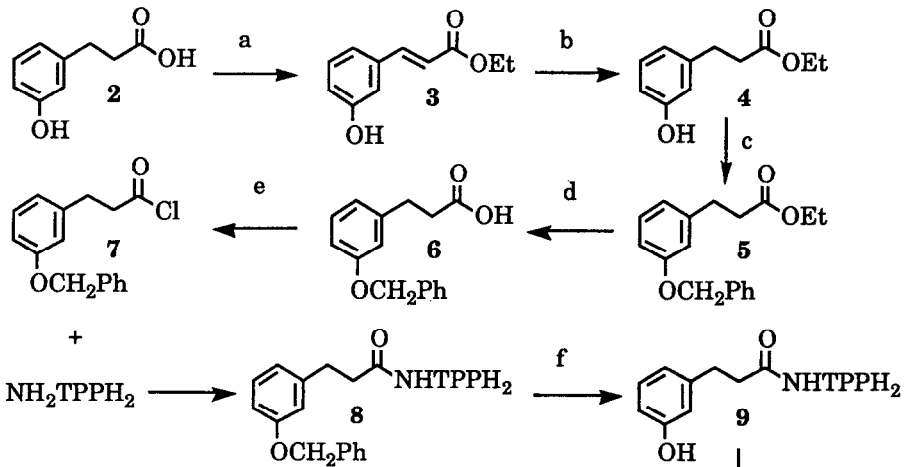
ligand in the enzymatic system.[4] Axial ligand effects have been shown to affect the oxidation chemistry catalyzed with manganese(III) tetraphenylporphyrins.[5] Changing the axial ligand on iron(III) tetraphenylporphyrin results in a change in the yield of cyclohexanol obtained from the oxidation of cyclohexane.[6] It is reasonable to expect that the axial ligand, because of its position trans to the oxo ligand, could significantly alter the electronic character of the oxo ligand and therefore the oxidation chemistry.

In order to probe the affect of the axial ligand on the catalytic chemistry of the metalloporphyrin we have synthesized an iron(III) tetraphenylporphyrin with a covalently-attached phenolate ligand. We chose the phenolate ligand for several reasons. The oxidation potential of the phenolate group could be modified by addition of electron-donating or withdrawing groups on the phenol ring. The phenolate group would act both as an axial ligand and the counterion thereby leaving the opposing face open for interaction with the oxidant. Finally, the phenolate group would not undergo oxidative dimerization like thiolate.

The synthesis of the iron(III) phenolate-tailed porphyrin is outlined in the Scheme. The phenolate tail was attached to 5-(2-aminophenyl)-10,15,20-triphenylporphyrin (NH_2TPPH_2) via an amide linkage. It was found that the phenolic group had to be protected as a benzyl ether else the amide linkage would not form. 3-(3-Hydroxyphenyl)prop-2-enoic acid, **2**, was esterified



Scheme

with ethanol and H_2SO_4 then reduced to ethyl 3-(3-hydroxyphenyl)propanoate, **3**, by treatment with Raney nickel and sodium hydroxide[7] or by hydrogenation over 10% palladium on charcoal. Treatment of **3** with benzyl bromide and sodium carbonate yielded ethyl 3-(3-benzyloxyphenyl)-propanoate, **4**.[8] The ester, **4**, was saponified to yield 3-(3-benzyloxyphenyl)propanoic acid, **5**.[8] The acid, **5**, was converted to the acyl halide, **6**, with thionyl chloride and the crude acyl halide was coupled to NH_2TPPH_2 in the presence of a catalytic amount of dry pyridine to give 5-(2-(3-(3-benzyloxyphenyl)propamido)phenyl-10,15,20-triphenylporphyrin, **7**.

Attempts to remove the benzyl ether protecting group by the standard method of hydrogenolysis with H_2 over 10% Pd on charcoal[9] yielded a complex mixture of products, a minor component of which gave spectral analysis consistent with the expected phenolic porphyrin. The benzyl ether was selectively cleaved with ethanethiol catalyzed by boron trifluoride etherate.[10] This procedure gave a clean cleavage of the benzyl ether protecting group and yielded 5-(2-(3-(3-hydroxyphenyl)propanamido)phenyl-10,15,20-triphenylporphyrin, **8**. The phenol-tailed porphyrin, **8**, was metallated using anhydrous iron(II) acetate in dimethylformamide to give 5-(2-(3-(3-oxyphenyl)propanamide)phenyl-10,15,20-triphenylporphyriniron(III), **1**.

The proton NMR spectrum of **1** showed resonances at δ +88, -28, and -99 ppm. These resonances can be assigned to the *meta* phenolate hydrogen, *meta* methylene hydrogens, and the *ortho* and *para* phenolate hydrogens. These shifts are very similar to the chemical shifts observed for proton of phenolate ligands coordinated to iron(III) porphyrins and iron(III) salen.[11] Variable temperature measurements of these signals between 290 and 230K showed that these protons obey the Curie law over that temperature range indicating that their position is the result of only the paramagnetic shift of the iron(III) center.[12] If the coordinated phenolate group were in equilibrium with the "free" phenolate, lowering the temperature would change the equilibrium population of the coordinated phenolate and a deviation from the Curie law would be expected. These observations are consistent with static coordination of the covalently-attached phenolate group to the iron center of the tailed porphyrin.

To study of the effect of the axial coordination of the phenolate ligand on the catalytic chemistry of the iron(III) porphyrin, the rate of oxygen atom transfer from *m*-chloroperoxybenzoic acid to **1** was measured using the method developed by Traylor.[13] The rate of oxygen atom transfer was monitored by trapping the high-valent oxo-iron intermediate with 2,4,6-tri-*t*-butylphenol and observing the rate of formation of the 2,4,6-tri-*t*-butylphenoxide radical. The

rate of oxygen atom transfer with **1** was approximately four times faster than with iron(III) tetraphenylporphyrin chloride ($7.4 \times 10^2\ M^{-1}\ s^{-1}$ for **1** versus $1.9 \times 10^2\ M^{-1}\ s^{-1}$ for FeTPPCl at 10°C). Traylor observed similar oxygen atom transfer rate enhancements when iron(III) porphyrins with a covalently-attached imidazole ligand were used as the catalyst.[13] The trans phenolate ligand must facilitate the cleavage of the peroxide bond of the peroxyacid. It has been suggested that the axial thiolate ligand performs a similar role in cytochrome P-450.[14] We are in the process of synthesizing the *para*-methoxy and *para*-nitro analogs of **1**. It is hoped that comparison of these phenolate tailed porphyrins will allow us to better define the electronic role of the fifth axial ligand in the catalytic chemistry of cytochrome P-450.

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