activation and hydrocarbon hydroxylation chemistry associated with hemoglobin, peroxidase, and cytochrome P450. To these ends we have synthesized and characterized a novel 'bis-pocket' porphyrin, meso-tetrakis(2,4,6-triphenyl)phenylporphyrin. This 'bis-pocket' porphyrin offers rigid steric protection on *both* faces of the porphyrin preventing both oxidative degradation and μ-oxo dimerization. The O_2 complexes of our model compound show remarkable thermal stability; reversible oxygenation is observed at temperatures as high as 60 °C. The effects of solvent polarity on CO and O_2 binding show that high polarity favors O_2 binding, but *disfavors* CO binding. Good correlations are found between ΔG° (O_2), ΔG° (CO), and M with empirical solvent polarity scales (*e.g.*, ET-30 or π^*). Thus, a new means of producing O_2/CO discrimination in heme systems is uncovered. These results help explain the discrepancies between other synthetic analogs and the variety of relative CO and O_2 affinities of heme proteins.

In addition, the steric hindrance offered by the 'bis-pocket' porphyrin dramatically increases the oxidative robustness of the iron complex to the presence of a wide variety of oxidants including peracids, hydroperoxides, and iodosoarenes. This provides for the first stable analogs of the high oxidation intermediates of the peroxidases and cytochrome P450. The results of the characterization of the highly oxidized intermediate observed suggest a compound I type intermediate. Studies on the shape selective hydroxylation of hydrocarbon substrates with iron and manganese 'bis-pocket' porphyrin will also be presented.

Other studies on the Mössbauer spectra of iron porphyrin complexes oxidized beyond the Fe(III) state will be related. Specifically, we have investigated the electronic structure of a series of single atom bridged dimers, $(FeTPP)_2X^{n+}$ where X = O, N, or C and TPP = meso-tetraphenylporphyrinato. In the series of complexes which are *two* oxidizing equivalents above Fe(III)–Fe(III) dimers, we find that changing the bridging atom from O to N or C shifts the site of oxidation from the porphyrin *pi* system (as in $(FeTPP)_2O^{2+}$) to the metal, yielding complexes which can be formally viewed as true Fe(IV) dimers [as in $(FeTPP)_2N^+$ and $(FeTPP)_2C$].

N15

Models for the Photosynthetic Water Oxidizing Enzyme II. Synthesis of Covalently Linked β-Cyclodextrin-Hemin

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The active center of the enzyme responsible for the water splitting reaction of photosystem II is believed to be a binuclear, or possibly a tetranuclear cluster of Mn(III) and Mn(IV) ions [1, 2]. In addition to the manganese cluster, a cytochrome-*b* is believed to play an important role in the oxidation of water by the native enzyme. According to a scheme proposed by Cramer, high-potential cytochrome-*b* 559 may function in a cycle around PSII contributing to water splitting [3]. Moreover, a heme-protein which binds two manganese ions has been isolated from spinach chloroplasts [4, 5].

We reported earlier the synthesis of a Mn(III) dimer of β-cyclodextrin [6]. In this communication we report on our efforts to synthesize a binuclear Mn(III)–β-cyclodextrin complex which is covalently attached to hemin via an ester linkage to the propionic acid side chains.

Experimental

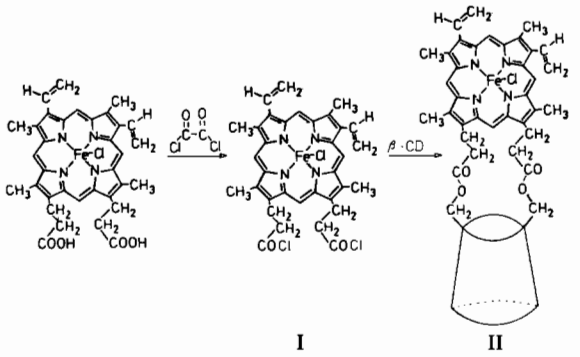
Preparation of the Acid Chloride of Hemin(I). Hemin (1 m*M*, 0.65 g) was reacted with oxalyl chloride (2.5 m*M*, 0.31 g) under Ar at 0 °C. The reaction mixture was stirred for 6 hr and then any excess of oxalyl chloride was removed under vacuum.

Preparation of Hemin derivatized with β-Cyclodextrin(II). The crude product obtained above was dissolved in freshly distilled pyridine (30 mL). β-cyclodextrin (I m*M*, I.3 g) was added to this solution and the reaction mixture stirred at room temperature for 10 hr.

Precipitation of product was induced by solvent stripping and cooling. It was washed with chloroform and isolated by column chromatography on CM cellulose. On elution with DMF: $CHCl_3$ (9:1 by volume), two bands are obtained. After solvent stripping the separated products were precipitated by the addition of acetone, and analysis for Fe was carried out. The slow moving fraction gave satisfactory Fe analysis, whereas the fast moving fraction did not show the presence of Fe.

Results and Discussion

The synthetic approach was to convert the propionic acid side chains of hemin to the acid chloride followed by reaction with the primary hydroxyls of β-CD (Scheme I). Oxalyl chloride is an



I II

Scheme 1.

efficient reagent for converting carboxylic acids to acid chlorides [7]. The acid chloride derivative was reacted with an equimolar amount of β-cyclodextrin. It has been shown previously that under these conditions it is the primary hydroxyl groups of cyclodextrin which are more reactive [9]. The whole reaction is summarized in Scheme I.

Both fractions obtained from the cellulose column were soluble in DMF and DMSO. The solubility of the Fe containing fraction in these solvents was, however, greatly reduced compared to free β-CD. Both fractions were fairly soluble in water, too, indicating that they may be precipitating as hydrochloride salts. Because only the slow moving fraction showed the presence of a significant amount of Fe, further characterization was attempted only on this sample.

The electronic spectrum of this compound and of hemin are shown in Fig. 1. The 570 nm and 600 nm bands of hemin are lost and in their place three new bands appear at 500 nm, 568 nm and 645 nm. These changes are consistent with a significant perturbation of the $\pi-\pi^*$ transitions by a nearby β-CD.

The infrared spectrum of the compound shows the presence of all the prominent bands due to cyclodextrin and the ester carbonyl stretch at 1715 cm^{-1}.

PMR of the compound in DMSO-d_6 showed that the C_1H resonance is shifted to 4.82 ppm from 5.17 ppm, for the free cyclodextrin [8]. The O_2H frequency is found to be shifted to 3.84 ppm from 4.38. The O_6H proton signal is not observed, probably due to broadening because of fast exchange between O_6H and the H^+ in the solvent. The upfield shift of 0.35 ppm in the C_1H resonance is similar to the shift observed when β-cyclodextrin is 'capped' with terephthalolyl chloride [9]. Of the seven primary hydroxyl groups of β-CD, the two which are involved in ester formation, have not been established yet.

Reaction of this derivative with Mn(II) in an attempt to isolate the manganese containing derivative is in progress. This is expected to yield the binuclear manganese adduct with a structure analogous to that reported for the free β-CD, Fig. 2 [6].

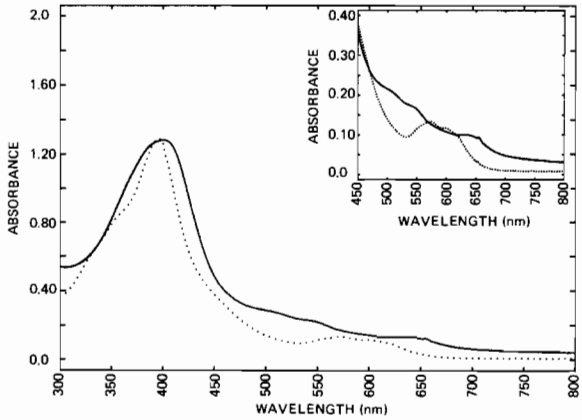


Fig. 1. Electronic spectrum of covalently linked β-cyclodextrin-hemin (——) and hemin (· · ·) in DMF.

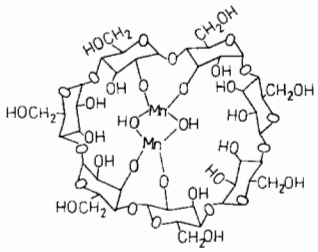


Fig. 2. Structure of the binuclear Mn adduct.

Conclusion

We have synthesized a covalently attached pair of macrocyclic ligands suitable for the coordination of a pair of Mn(III) ions via di-μ-hydroxo dimer structure and within 12 Å of the Fe(III) core of hemin. It will be interesting to compare the magnetic, spectroscopic and catalytic properties of this compound in connection with its similarity to the photosynthetic water oxidizing enzyme.

Acknowledgment. This work was supported by a grant from the U.S. Department of Energy/Solar Energy Research Institute (DE-FG 02-80CS84003) and by an award from the Chicago Community Trust/Searle Scholars (G.C.D.).

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