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PORPHYRIN-CYCLOPHANES: INCLUSION COMPLEXATION AND X-RAY CRYSTAL STRUCTURE OF A ZINC OCTAMETHYLDIPHENYLPORPHYRIN

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ABSTRACT *The synthesis, characterization, and complexation properties of two novel porphyrin-cyclophanes are reported. In the first system, one face of an octamethyldiphenylporphyrin is capped by one diphenylmethane unit. In the second system, both faces of a tetraphenylporphyrin are strapped by diphenylmethane units. The X-ray crystal structure has been determined for the singly-capped zinc octamethyldiphenylporphyrin.*

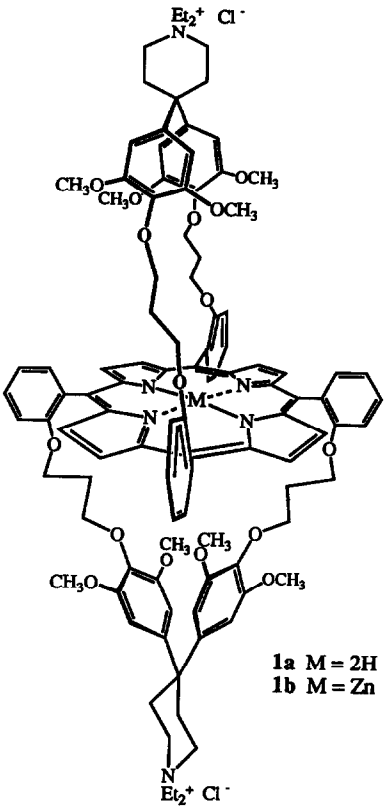
INTRODUCTION

In an effort to model the remarkable properties of heme-containing enzymes, chemists have prepared a multitude of elegant superstructured porphyrins.[1] Capped, bridged, or strapped porphyrins mimic (i) the oxygen transport and storage proteins hemoglobin and myoglobin,[2] (ii) the oxygen-reducing cytochrome C oxidase,[3] (iii) the hydrocarbon-oxidizing cytochrome P-450 enzymes,[4] and (iv) the primary electron transfer processes at photosynthetic reaction centers.[5]

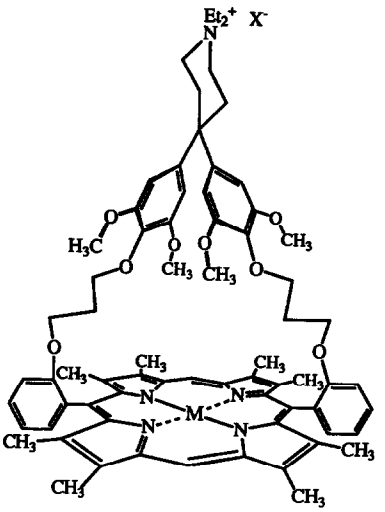
Cytochrome P-450 enzymes are heme-containing monooxygenases which bind and subsequently epoxidize or hydroxylate a great variety of unactivated aliphatic and aromatic hydrocarbons.[6] The X-ray crystal structure analysis of $P\text{-}450_{cam}$ from *pseudomonas putida* has shown that an iron porphyrin forms one side of the oxygen and substrate binding site which is deeply buried in the protein and, therefore, has a pronounced hydrophobic character.[7] As an approach to model the oxidation of aromatic hydrocarbons by P-450 cytochromes,[8] we designed porphyrin-cyclophanes capable of complexing aromatic substrates in hydrophobic cavities in close proximity to a porphyrin ring.[9] In a recent communication, we described the synthesis and catalytic properties of a porphyrin-cyclophane which forms stable complexes with large polycyclic aromatic hydrocarbons such as phenanthrene and acenapthylene in protic solvents.[10] In the presence of iodosobenzene, the corresponding iron(III) porphyrinate catalyzed the epoxidation of acenapthylene to acenaphthen-1-one with good turnovers.

Herein, we report the synthesis of the new bridged porphyrins **1** and **2** designed to incorporate smaller aromatic substrates of the size of benzene or naphthalene derivatives into cavities shaped by the porphyrin face and diphenylmethane caps.[11] In compound **1**, a tetraphenylporphyrin is doubly-bridged by two diphenylmethane units in a cross *trans*-linked fashion.[1a] In compound **2**, the same bridging unit spans only one face of an octamethyldiphenylporphyrin. The X-ray crystal structure for the zinc(II) porphyrinate **2c** shows that the potential binding cavity lacks preorganization which explains why no binding of neutral aromatic molecules was observed with **1** or **2** in either the free base or the zinc forms. However, both zinc(II) porphyrinates **1b** and **2b** form size-

selective inclusion complexes with pyridine derivatives both in protic and nonprotic solvents, and complexation occurs exclusively in the cavities created by the diphenylmethane caps.



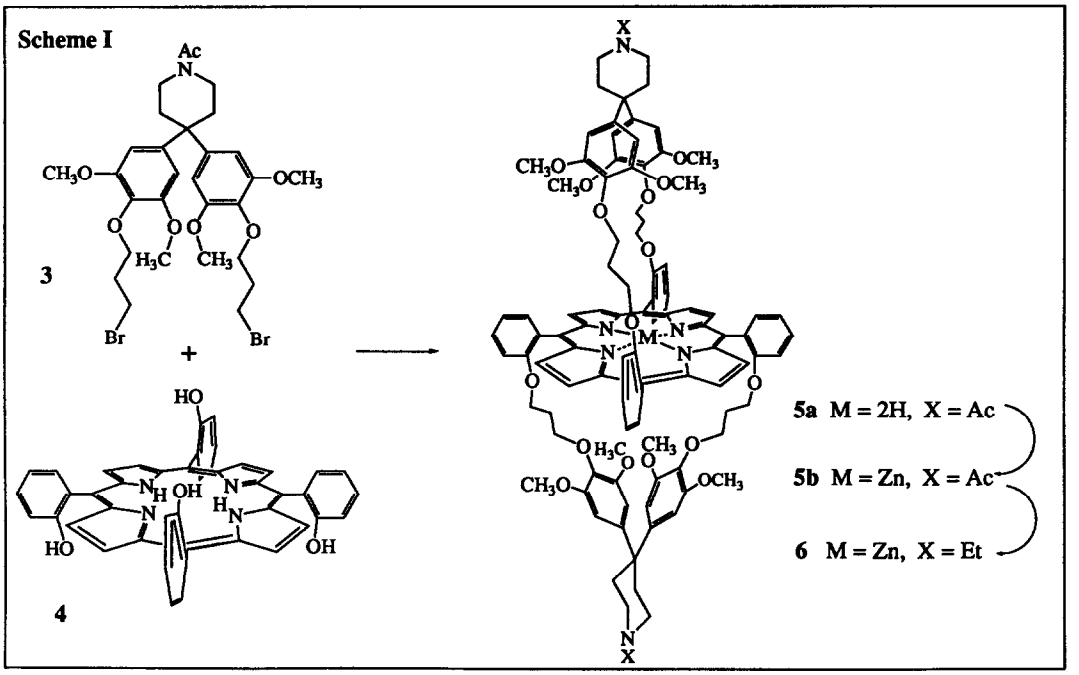
1a M = 2H
1b M = Zn



2a M = 2H, X = Cl^-
2b M = Zn, X = Cl^-
2c M = Zn, X = I^-

RESULTS AND DISCUSSION

Synthesis of Cyclophane 1. In preparing system **1**, we followed a protocol developed by Momenteau et al.[12] for the synthesis of porphyrins doubly-strapped with alkyl chains (Scheme I). The cyclization to give cyclophane **5a** was carried out by slowly adding a solution of **3** [prepared from 1-acetyl-4,4-bis(4-hydroxy-3,5-dimethoxyphenyl)piperidine][13] via syringe pump to a stirred solution of tetra(*o*-hydroxyphenyl)porphyrin **4** and K_2CO_3 in DMF at 100 °C. The desired cross *trans*-linked isomer was the predominant product, comprising 77% of the isomeric product mixture (^1H NMR integration). Pure **5a** was obtained in 5.4% yield by fractional crystallization. In order to avoid metallation of the porphyrin during reduction of the amide groups with diisobutyl aluminum hydride (DIBAL-H), the zinc(II) derivative **5b** was prepared [$Zn(OAc)_2 \cdot H_2O$, $CHCl_3$/MeOH (1:1), reflux, 99% yield]. The subsequent reduction of **5b** proceeded smoothly when a solution of **5b** was added slowly to an excess of the reducing agent at 0 °C in THF, giving **6** in 99% yield. Quaternization of **6** (EtI, acetone), followed by demetallation with concentrated HCl in MeOH, and ion exchange chromatography on Dowex furnished the bis(quaternary ammonium chloride) **1a** (76% yield). The zinc derivative **1b** was prepared by reacting **1a** with $Zn(OAc)_2 \cdot 2H_2O$ in $CHCl_3$/MeOH again followed by ion exchange chromatography.



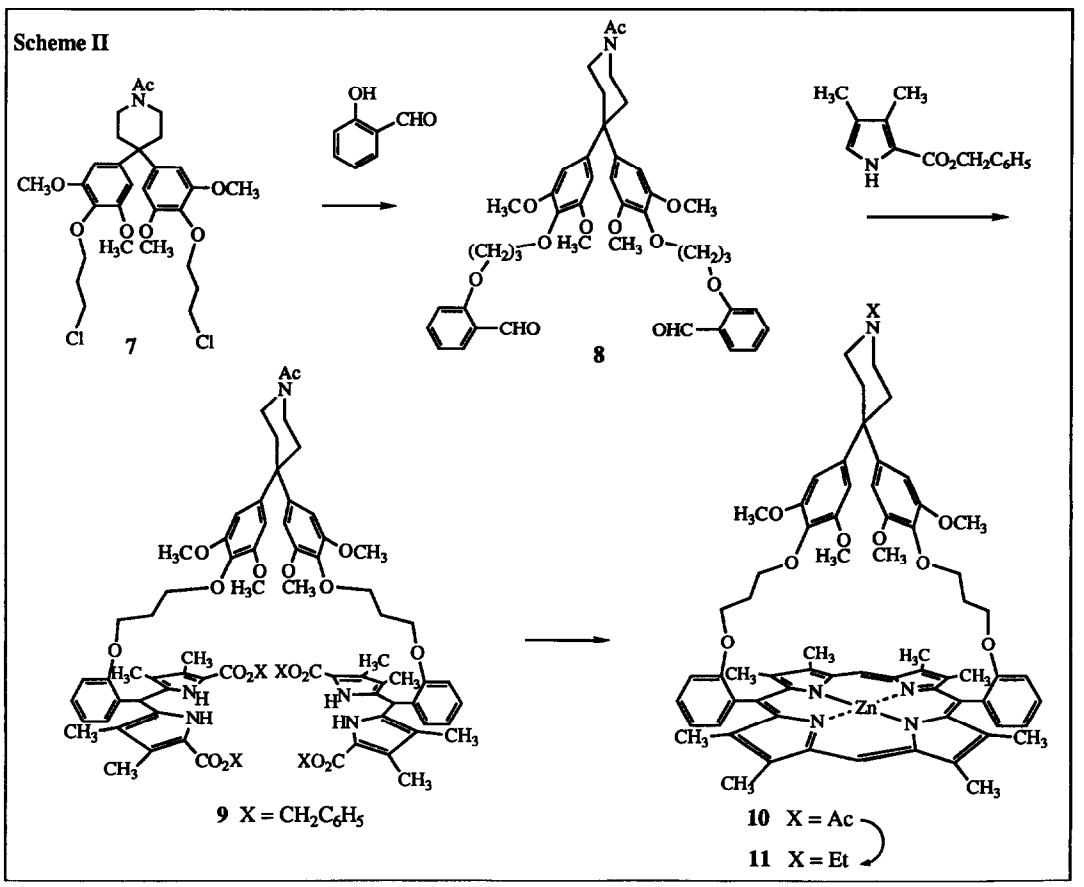
Synthesis of Cyclophane 2. For the preparation of **2**, we followed a general procedure published by Baldwin et al. (Scheme II).[14] The dialdehyde **8** was prepared in a Williamson ether synthesis between the dichloride **7** and salicylaldehyde (Cs_2CO_3, DMF, 64% yield). Subsequently, compound **8** was condensed with four equivalents of benzyl 3,4-dimethylpyrrole-2-carboxylate[15] in ethanol yielding 90% of the bis(dipyrromethane) **9**. Hydrolysis of the benzyl groups (10% Pd/C, H_2, THF) and subsequent cyclization [$HC(OMe)_3$, Cl_3CCOOH, $Zn(OAc)_2 \cdot 2H_2O$, CH_2Cl_2] led to the zinc(II) porphyrinate **10** in 17% yield. Reduction of the amide group to give **11** was effected by slowly adding a solution of **10** in toluene to a solution of DIBAL-H (10-fold excess) in toluene at 0 °C (89% yield). Quaternization (EtI, acetone, 85% yield) provided the ammonium iodide **2c**, and subsequent ion exchange chromatography afforded **2b**. The metal-free derivative **2a** was obtained by stirring **2b** in concentrated HCl/MeOH, followed by neutralization and ion exchange.

^{1}H NMR Analysis of the Porphyrin-Cyclophanes 1 and 2. The ^{1}H NMR spectra of all new porphyrin derivatives are consistent with data previously reported for similar porphyrins.[1,4] The diamagnetic ring current of the porphyrin [18]annulene perimeter causes large upfield shifts for protons situated in or near the center of the ring and downfield shifts for protons located outside of the ring. In $CDCl_3$ at 293 K, the protons in the β-pyrrole positions of the free base derivatives **1a** and **5a** appear at ≈ 8.65 ppm. A 0.1 ppm downfield shift for the same protons in the corresponding zinc(II) porphyrinates **1b** and **5b** occurs due to transfer of electron density from the porphyrin π-system onto the metal ion. In the octamethyldiphenylporphyrins **2a-c** and their precursors **10** and **11**, the β-pyrrole methyl groups resonate at about 2.5 and 3.5 ppm, while the corresponding protons appear at 1.70 (4-CH_3) and 2.18 (3-CH_3) in the nonmacrocyclic bis(dipyrromethane) derivative **9**. The ≈ 1 ppm upfield shift measured for one of the two sets of four equivalent porphyrin methyl resonances is due to the

location of these groups directly within the shielding region of the phenyl rings on the adjacent *meso*-positions. The NH-protons in the center of all free base porphyrins appear between - 2 and - 3 ppm.

Upfield shifts compared to the resonances in **3** are observed for all protons in the diphenylmethane caps of **1** and **2** and their cyclophane-precursors, confirming a position above the shielding region of the porphyrin. The methoxy group resonances in all non-porphyrin precursors, e.g., in **3** and **8**, appear between 3.65 and 3.78 ppm. At room temperature in $CDCl_3$, the methoxy signal in **1a** is shifted upfield to 2.70 ppm while that of **1b** appears at 2.77 ppm. The corresponding positions in **2a** and **2b** are 2.57 and 2.69 ppm, respectively. We had originally thought that the methoxy groups of the bridging diphenylmethane units in **1b** and **2b** might provide a fifth axial ligand to the zinc atoms. However, the downfield shifted methoxy resonances in the spectra of the zinc(II) porphyrinates **1b** and **2b** compared to their position in the spectra of the free base forms **1a** and **2a** suggest that these groups in the zinc derivatives are on average more distant from the center of the porphyrin ring.

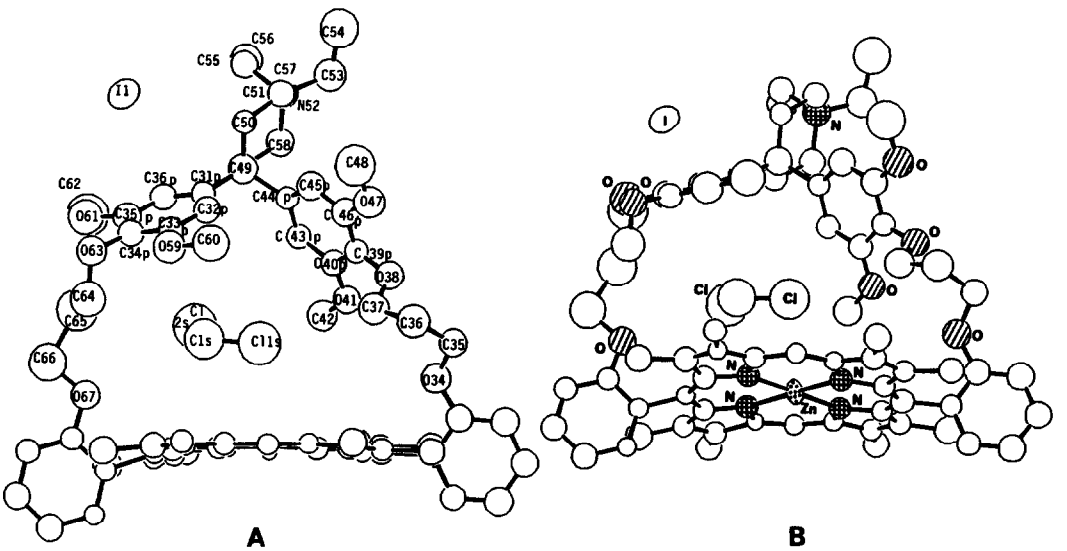
Scheme II



X-ray Crystallographic Analysis of Compound 2c. X-ray quality crystals of the zinc(II) porphyrinate **2c** were obtained by slow evaporation of a CH_2Cl_2/toluene solution. Figure 1 shows two different views of the cyclophane. Three molecules of CH_2Cl_2 were found in the crystal lattice, two of them (not shown)

located exterior to the cavity and highly disordered. The third molecule is bound within the cavity in a well-defined position. This bound solvent molecule is not centrally located over the porphyrin, nor is the diphenylmethane cap symmetrically disposed over the macroring. Instead, the cap seems to have shaped itself to best accommodate the solvent molecule. Figure 1 shows a cyclophane cavity which lacks the space to incorporate an aromatic ring. Presumably, this lack of preorganization explains the inability of both systems **1** and **2** to bind benzene or naphthalene derivatives (see below). However, inclusion complexation of pyridine, as will be discussed in the following section, demonstrates that the cavity can be shaped and organized to the size of a six-membered aromatic ring when the apolar binding event is accompanied by an additional energy-releasing process such as ligation to the metal center.

Figure 1: Two views of the X-ray crystal structure of cyclophane **2c**. Only the cavity-bound CH_2Cl_2 is shown; two other CH_2Cl_2 molecules are located exterior to the cavity and are highly disordered.



The conformation of the diphenylmethane unit in **2c** is best characterized by the two dihedral angles between the least-squares planes of the two phenyl rings and the central plane defined by C_{31p}-C_{49}-C_{44p} (Figure 1A).[11b] The crystal structure analysis shows a rather small value of 44° for the torsional angle C_{44p}-C_{49}-C_{31p}-C_{32p} and a value of 78° for the torsional angle C_{31p}-C_{49}-C_{44p}-C_{43p} in **2c**. The latter torsional angle is more consistent with the values between 70° and 90° that had previously been revealed by X-ray crystal structure analysis for the comparable angles in diphenylmethane units of other cyclophane receptors.[13a,16] The methoxy groups are all more or less aligned with the phenyl rings to which they are attached and point away from the porphyrin.[13a]

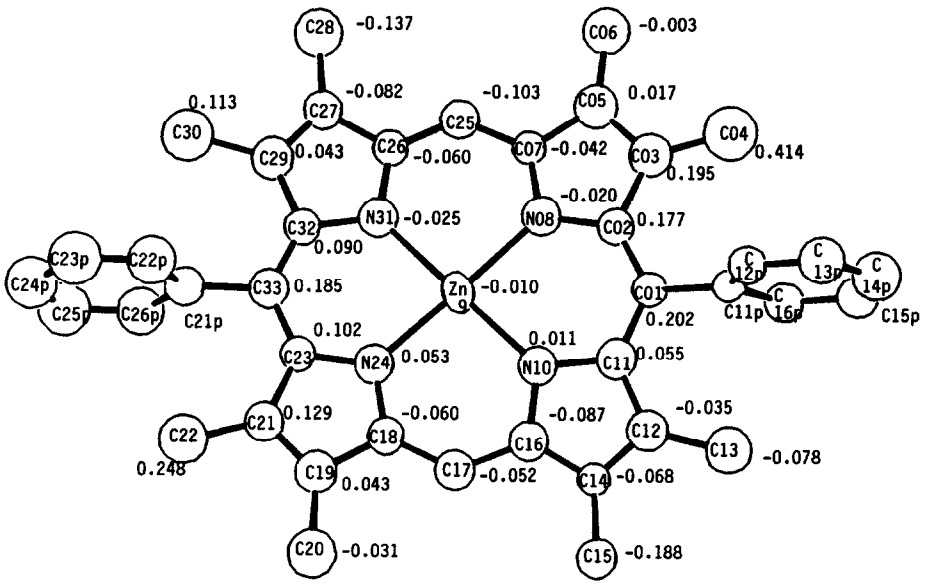
A search of the Cambridge structural data base provided no other examples of X-ray structures for octamethyldiphenylporphyrins. The only similar structures were the diporphyrin systems of Chang et al.[17] and of Collman et al.[18] The compounds prepared by Chang et al. consist of two tetraethyltetramethyl-

metalloporphyrins attached to one anthracene or one biphenylene spacer unit. Each porphyrin forms one bond from a *meso*-position to an aromatic ring of the spacer. A significant ruffling of the porphyrin surfaces in these structures was observed, the effect being greater in the anthracene-diporphyrin. Deviations of the pyrrole rings from the least-squares plane of the porphyrin are as high as 0.75 Å in the anthracenyl compound and 0.4 Å in the biphenylene structure. Puckering is more pronounced for the pyrrole rings next to the *meso*-position to which the aromatic spacer is attached.

Collman et al. reported the X-ray structure of a "face-to-face" porphyrin dimer in which two tetraethyltetramethylporphyrins are connected by two alkyl chains leaving from the *meso*-positions on opposite sides of each macroring.[18] Each porphyrin nucleus in this compound is also greatly puckered with the *meso*-carbon atoms deviating 0.35 - 0.65 Å from the least-squares plane of the porphyrin. Even with this ruffled shape, the nonbonded distance between the β–pyrrole methyl groups and the methylene unit attached to the neighboring *meso*-position is compressed to 3.02 Å.

Both the zinc(II) octaethyl-*meso*-tetraphenylporphyrinate[19] and the pyridine complex of the zinc(II) octamethyl-*meso*-tetraphenylporphyrinate[20] have been characterized by X-ray crystallography. The structure of the porphyrin skeleton is nearly identical in the two compounds, each nonplanar and severely saddle-shaped, with the β-hydrogens on adjacent pyrrole rings displaced by ≈ ± 1.0 Å relative to the plane of the four nitrogens.

Figure 2: Deviations (Å) from the least-squares plane through all atoms of the zinc(II) porphyrinate in **2c** except the β-methyl groups.



Based on these precedents, we were surprised to find that the zinc(II) octamethyldiphenylporphyrinate in **2c** is almost planar. The displacement of the four-coordinate zinc atom from a least-squares plane containing zinc and all 24 atoms of the porphyrin core (minus the β-methyl groups) is ≈ 0.010 Å (Figure 2). The average

displacement of the pyrrole nitrogens from the same least-squares plane is ≈ 0.027 Å (max. = 0.053 Å, min. = 0.011 Å), while the greatest displacement of the carbon atoms of the porphyrin skeleton is on the order of 0.2 Å. The numbers next to the atoms in Figure 2 represent their distances from the porphyrin least-squares plane, measured in Ångstroms (estimated standard deviation for all of the carbon and nitrogen atoms range between 0.021 and 0.031 Å.

The average N-Zn bond distance measured in the structure of **2c** is 2.06 Å. This is somewhat larger than the N-Zn distances found in other four-coordinate zinc(II) porphyrinates in the literature. For example, Scheidt et al. reported the structure of the toluene solvate of Zn(TPP) [TPP= *meso*-tetraphenylporphyrinate] and found compressed N-Zn bond lengths of 2.036 Å.[21] Simonis et al. have crystallized a Zn(TPP) derivative, strapped in an adjacent *trans*-linked[1a] fashion with $O(CH_2)_6O$ chains, and the X-ray crystal structure revealed an average N-Zn bond distance of 2.031 Å.[22] In both of these crystal structures, the zinc atom is precisely centered in the plane of the porphyrin ring. The only other reported structure of a porphyrin having a four-coordinate zinc is a TPP derivative in which all *para*-positions of the four *meso*-phenyl rings are occupied by n-octyl groups.[23] This molecule has a nonplanar porphyrin with the zinc atom pulled 0.15 Å out of the plane of the core, and with an average N-Zn distance of 2.024 Å.

A literature comparison shows that the metal-nitrogen bond lengths in **2c** with a four-coordinate zinc in the porphyrin plane are actually closer in length to reported values in five-coordinate zinc porphyrins (2.05-2.076 Å).[24,25] In all five-coordinate zinc porphyrins reported to date, the zinc atom is pulled out of the plane of the porphyrin by 0.2-0.4 Å. At one time, it was believed that zinc is too large to fit comfortably in the plane of the porphyrin even when four-coordinate,[25a] and the ability of zinc to take on only one additional ligand[26] strengthened that notion. Despite the overwhelming preference for penta-coordination, one example of a hexa-coordinated zinc porphyrin has been reported, that being the bis-tetrahydrofuran (THF) complex of Zn(TPP), wherein the zinc atom is also positioned in the mean plane of the porphyrin ligand.[27]

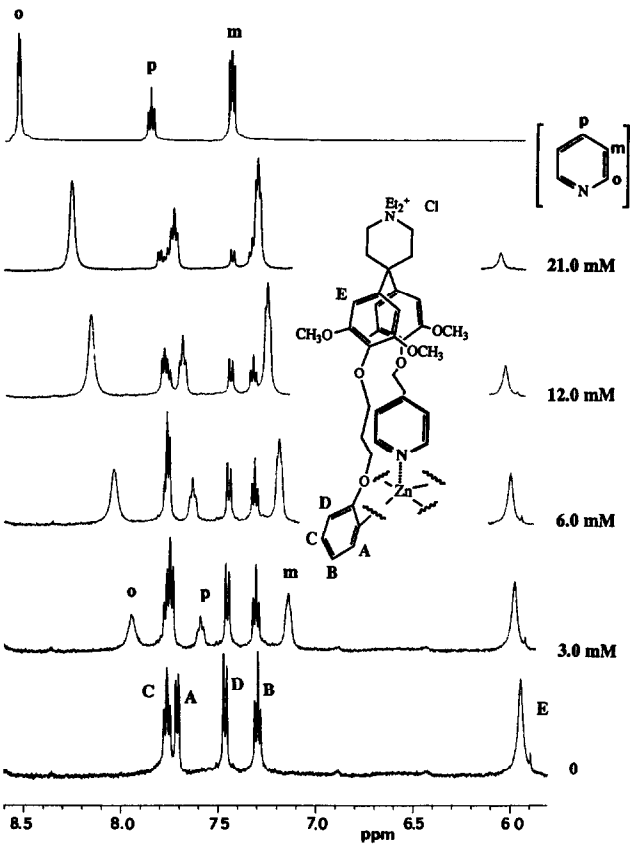
As is evident in Figure 1A, the *meso*-phenyl rings bend below the plane of the porphyrin. This bend is defined as the angle between vectors along C_{11p}-C_{15p} and the porphyrin plane (15.4°) and C_{21p}-C_{24p} and the porphyrin plane (5.1°). With values of 2.89 - 2.98 Å, the distances between the carbon atoms joining the *meso*-phenyl rings to the porphyrin and the adjacent β-methyl groups are much shorter than the sum of their van der Waals radii (≈ 3.40 Å). These nonbonded contacts are even shorter than those found in the structure of Collman et al. mentioned above.[18] Not surprisingly, the *meso*-phenyl rings are very nearly orthogonal to the plane of the porphyrin ring, with dihedral angles of 92.7° and 86.7°, a result of steric constraints imposed by the β-methyl groups.

Binding Studies with Cyclophanes 1 and 2. *Benzene and Naphthalene Derivatives.* CPK model examinations suggested that the cavities in **1** and **2**, shaped by the diphenylmethane caps and the porphyrin, adopt an energetically favorable geometry of the correct size for the inclusion of benzene and naphthalene guests. However, ^1H NMR binding studies with **1a** or **1b** in CD_3OD showed that compounds like *p*-benzodinitrile or 6-methoxy-2-naphthonitrile were not included in either cavity of the doubly-capped porphyrin. No marked shifts of the ^1H NMR resonances of the cyclophane or the aromatic substrates, indicative of complexation, were observed.

A variety of benzene and naphthalene derivatives were also tested for binding to **2a** and **2b**. Upon addition of 6-methoxy-2-naphthonitrile (5.7 mM) to a solution of **2a** (4.3 mM) in CD_3OD (T = 295 K), the proton resonances of the two components experienced small ($\Delta\delta \leq 0.1$ ppm), uncharacteristic changes in chemical shift, indicative of a very weak intermolecular association. The absence of similar shifts in solutions of **1a** suggests that this interaction arises from π-π stacking on the open face of the porphyrin.

Pyridine Derivatives. Pyridine was chosen as a possible guest for **1b** due to its propensity to form complexes with zinc porphyrins. Zinc porphyrins are known to bind only one molecule of pyridine, resulting in a five-coordinate zinc atom.[26] Since methanol can also ligate to a zinc(II) porphyrinate,[28] only weak binding of pyridine to **1b** in this solvent would be expected. Surprisingly, rather large upfield shifts of the pyridine resonances, up to ≈ 1 ppm for the ortho protons, were measured for a methanol-d_4 solution with 3 mM pyridine and 3.3 mM **1b**. Figure 3 shows a stack plot of 2.2 mM **1b** with increasing concentrations of pyridine (3 mM - 29 mM) focusing on the aromatic region of the spectrum. The shifts of both pyridine and cyclophane resonances suggest that a true inclusion complex is formed in which the pyridine nitrogen is ligated to the zinc atom.

Figure 3. 500 MHz ^{1}H NMR binding titration of 2.2 mM **1b** with 3 - 29 mM concentrations of pyridine in CD_3OD, T = 293 K.



In the titration which is illustrated in Figure 3, approximately 73% saturation binding of **1b** was observed. The aromatic protons ($\Delta\delta_{sat}$ = 0.165 ppm) and the methoxy protons ($\Delta\delta_{sat}$ = 0.092 ppm) of the diphenylmethane unit are shifted downfield with increasing concentrations of pyridine. The methylene protons of the C_3-bridges between the porphyrin and the diphenylmethane cap, however, all shift significantly upfield, which is consistent with their location within the shielding region of the pyridine guest as schematically shown in Figure 3. The greatest upfield shift is measured for the central methylene unit in the chains; for the OCH_2-resonance at the *meso*-phenyl rings, a saturation shift of $\Delta\delta_{sat}$ = 0.170 ppm was calculated. To determine the association constant K_a for the **1b**·pyridine complex in CD_3OD at 293 K, the resonances of the three protons for which saturation binding shifts are given were evaluated in a nonlinear least-squares curve-fitting procedure. A value of $K_a = 98 \pm 5$ L mol^{-1} was obtained for the 1:1 complex, which gives a ΔG^o of - 2.67 kcal mol^{-1} (Table 1). In the presence of **1b**, all pyridine protons are shifted upfield, with the protons *ortho* to the nitrogen moving the most and the ones *para* shifting the least. For saturation binding, the following upfield complexation shifts were calculated: H_o: $\Delta\delta_{sat}$ = 3.97 ppm, H_m: $\Delta\delta_{sat}$ = 1.99 ppm, H_p: $\Delta\delta_{sat}$ = 1.71 ppm.[29]

The major stabilization of the pyridine complex formed by **1b** clearly occurs as a result of nitrogen-Zn coordinative binding. However, it was of interest to us to evaluate the contribution of apolar binding interactions to the stability of the complex. Cole et al.[30] have reported thermodynamic data for binding of several nitrogen bases to Zn(TPP) in benzene and in chloroform. The measured free energy for pyridine binding in benzene is about 1 kcal mol^{-1} larger than in chloroform (4.9 vs 3.8 kcal mol^{-1}, T = 298 K). They proposed that the free porphyrin interacts more favorably with $CHCl_3$ than with benzene molecules, and that the disruption of a more favorable solvation upon pyridine ligation leads to weaker binding in the more polar solvent. Nardo and Dawson[28] evaluated the ligation strength between a number of oxygen donor ligands and Zn(TPP). For methanol binding in benzene, they calculated an association constant of K_a = 9.6 L mol^{-1} (ΔG^o = - 1.3 kcal mol^{-1}, T = 298 K). Hence, in our study, pyridine has to compete with the solvent as a weaker binding ligand which is present in a very large excess. The displacement of methanol from the zinc atom in **1b** by the incoming pyridine is an energetically unfavorable process, and, therefore, the **1b**·pyridine complex in methanol is less stable than the corresponding complex formed by Zn(TPP) in non-coordinating, aprotic solvents. No data could actually be found in the literature concerning binding of pyridine to simple zinc porphyrins in polar protic solvents but we felt that such complexes, if formed, would be very weak. The low solubility of Zn(TPP) in methanol does not permit a meaningful analysis of weak pyridine coordination in this solvent. However, the lutidine binding studies with **2b** described below provide very strong evidence that pyridine coordination in methanol to an open-faced zinc porphyrin is not an energetically favorable process. Therefore, we thought that the hydrophobic cavity of **1b** must be imparting a significant stabilization to the complex with pyridine in methanol.

To further examine this possibility, we performed a ^{1}H NMR titration in $CDCl_3$ using compound **5b** (1.01 mM) and pyridine (0.2 - 1.9 mM). Shifts of the host protons are in the same direction as those described above for **1b** in the methanol titration. The calculated K_a from this titration was 4700 L mol^{-1} (ΔG^o = - 4.9 kcal mol^{-1}). Therefore, the driving force for formation of the **5b**·pyridine complex in $CDCl_3$ is approximately 1.1 kcal mol^{-1} higher than for the corresponding Zn(TPP) complex in this solvent. This result demonstrates that inclusion complexation is also imparting additional stabilization to the complex formed in $CDCl_3$. A precedent for such a ligand stabilization had been reported by Collman et al.[31] in studies of a capped ruthenium porphyrin [Ru(c-porph)] axially ligated to CO and pyridine (Pyr). In the equilibrium between $Ru(c\text{-}porph)(CO)_{out}(Pyr)_{in}$

Table 1: Thermodynamic data for the complexation of pyridine derivatives by porphyrin-cyclophanes, T = 293 K.

Host	Guest	Solvent	K_a (L mol^{-1})[a]	$-\Delta G^o$ (kcal mol^{-1})	Titration
1b	pyridine	CD_3OD	98	2.7	NMR
5b	pyridine	$CDCl_3$	4700	4.9	NMR
2b	pyridine	CD_3OD	90	2.6	NMR
		CH_3OH	70	2.5	UV/Vis
2b	3,5-lutidine	CD_3OD	< 10	< 1.3	NMR, UV/Vis

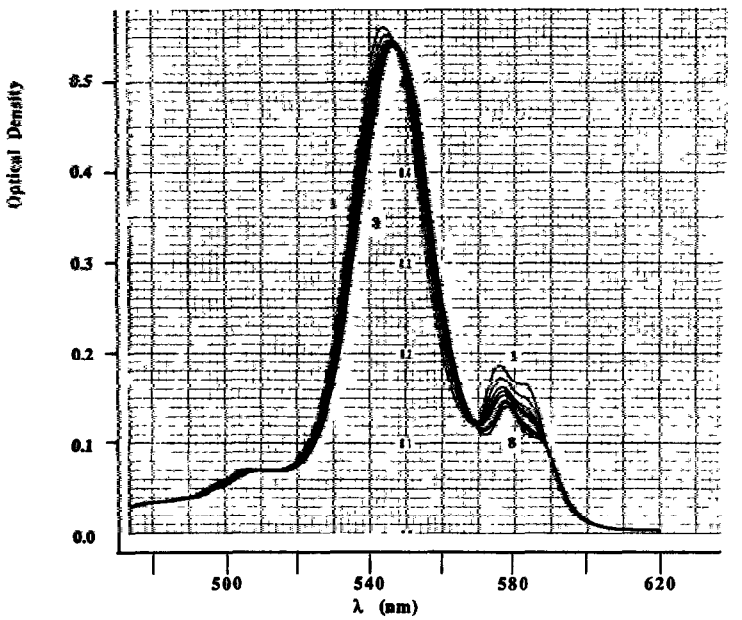
[a] accuracy in K_a: ± 5 %.

and Ru(c-porph)$(CO)_{in}(Pyr)_{out}$ in $CDCl_3$ under 1 atmosphere CO, the regioisomer with the cavity-bound pyridine $(Pyr)_{in}$ is preferred by a factor of > 50:1.

An interesting binding selectivity was encountered when pyridine and 3,5-lutidine were examined as guests with **2b** in methanol. Figure 4 shows an electronic absorption titration of 0.16 mM **2b** with 5 - 100 mM pyridine in methanol at 293 K. At least 4 isosbestic points are observed in this titration. The evaluation of the changes in optical density at λ = 584 and 555 nm as a function of pyridine concentration gave an association constant of K_a = 70 L mol^{-1}, consistent with the value obtained in a ^{1}H NMR titration (Table 1). Pyridine binding by singly-capped **2b** closely resembles the binding of this ligand by doubly-capped **1b**. Similar complexation-induced shifts of both host and guest resonances are observed in ^{1}H NMR binding titrations, and the association constants calculated for the two complexes are almost identical (Table 1). These data suggest that when pyridine is given a choice between binding within the cavity and binding to the open face of the porphyrin in **2b**, the inclusion complex is the predominant species present.

These conclusions were further supported by using 3,5-lutidine (3,5-dimethylpyridine) as a guest in ^{1}H NMR and optical titrations. Previously reported binding studies with Zn(TPP) and various substituted pyridines in $CDCl_3$ and in benzene had shown that electron-donating groups in the *meta* and *para*-positions increase the association constants for the complexes of pyridine derivatives while electron-withdrawing groups weaken the ligation.[29,30] For example, both 3- and 4-methylpyridine bind to Zn(TPP) about 0.3 kcal mol^{-1} more strongly than does pyridine itself. Although data for 3,5-lutidine ligation were not reported, one would assume that its assocation would be even stronger. However, both optical and ^{1}NMR titrations showed that 3,5-lutidine forms a much weaker complex with **2b** than pyridine. Characteristic shifts of the diphenylmethane bridge resonances in **2b** suggest that the small amount of complexation that is observed is occurring within the hydrophobic cavity. From the high concentration ranges in which spectral changes occurred (e.g., 0.17 mM **2b** and 0.025 - 0.5 M 3,5-lutidine in optical titrations), a small association constant of K_a < 10 L mol^{-1} must be assumed. Apparently, the methyl groups of 3,5-lutidine render the pyridine derivative too bulky for adopting a stable inclusion conformation within the cavity of **2b**. This data strongly implies that in methanol, pyridine coordination to simple zinc porphyrins, e.g., Zn(TPP), is not an energetically very favorable process.

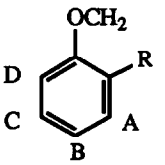
Figure 4. Optical titration of 0.16 mM **2b** with 5 - 100 mM pyridine in CH_3OH at 293 K, d = 0.2 cm.



Conclusions. In this paper, we have described the preparation of two novel porphyrin-cyclophanes that are singly (system **2**) or doubly (system **1**) strapped by diphenylmethane units. The X-ray crystal structure quite unexpectedly shows that the porphyrin in the singly capped zinc octamethyldiphenylporphyrin **2c** is nearly planar. The crystal structure also reveals that **2** and presumably also **1** possess flexible, poorly preorganized binding sites created by the diphenylmethane caps and the porphyrin. Benzene and neutral derivatives do not form inclusion complexes with the two cyclophanes. Such complexes would be stabilized by apolar interactions only, which apparently is not sufficient to pay for the costly reorganization of the binding sites for guest inclusion. In contrast, pyridine forms inclusion complexes with both systems **1** and **2**. This suggests that the cavities of the porphyrin-cyclophanes, in agreement with the original design, can adopt the right size for inclusion of substrates which have the size of a benzene ring. In the pyridine complexes, nitrogen-zinc coordination provides the major stabilizing interaction in addition to significant apolar binding in the cavity. The two forces together apparently are strong enough to stabilize the inclusion complexes while providing the energy for the reorganization of the cavities into favorable binding conformations. When given the choice between coordinating to zinc within the cavity and binding to the open face of the porphyrin in **2b**, pyridine clearly prefers the inclusion mode which provides an extra-stabilization of $\approx \geq 1.1$ kcal mol^{-1} through apolar interactions. Finally, to accomplish the binding of benzene and neutral derivatives, the porphyrin-cyclophane cavities will have to be made more rigid so that the complexation processes need not be accompanied by a costly reorganization of the cavity.

EXPERIMENTAL SECTION

General. ^{1}H NMR spectra were recorded on Bruker AF200, AM360, and AM500 instruments. The aromatic protons of *meso*-phenyl rings are assigned as follows:



Aromatic coupling patterns were enhanced through Gaussian multiplication of the FIDs. UV/Vis spectra were performed using a Varian Cary 2300 spectrophotometer. Mass spectra were carried out on a AEI MS902 high resolution mass spectrometer at UCLA or on VG-ZAB2FHF or VG-7070EHF instruments at UC Riverside. EI mass spectra were done at 70 eV, and FAB spectra were run in a *m*-nitrobenzyl alcohol matrix. Melting points were recorded on a Büchi apparatus (Dr. Tottoli), and are uncorrected. IR spectra were recorded on a Perkin Elmer 1600 Series FTIR or on a Perkin Elmer 520B instrument. E. Merck silica gel 60, 0.04-0.063 mm and 0.063-0.200 mm, was employed for gravity chromatography. Analytical thin layer chromatography (TLC) was done using plates precoated with E. Merck silica gel F-254. Elemental analyses were done by Spang Microanalytical Laboratory, Eagle Harbor, MI. CAS Registry Services provided the names for the macrocyclic compounds.

Materials. All chemicals were reagent grade, and were used as received. Dichloromethane (CH_2Cl_2) was purified by distilling from calcium hydride under argon (Ar). Tetrahydrofuran (THF) and toluene were distilled from sodium benzophenone ketyl under Ar. Acetone was dried by standing over potassium carbonate (K_2CO_3). Dimethylformamide (DMF) was dried by standing over basic alumina (E. Merck, Activity I) followed by filtration through celite. Millipore water was employed in ion-exchange chromatography and in all manipulations involving the quaternized ammonium compounds.

Binding studies. UV/Vis titrations were performed on a Varian Cary 2300 spectrophotometer thermostated at T = 293 K using 0.2 cm quartz cuvettes. Samples of **2b** were weighed using a Sartorius 4503 microbalance, and all solution preparations were done with Eppendorf micropipettes. Aliquots of a stock solution of pyridine or 3,5-lutidine were added to a stock solution of the host, and methanol was added to give a final volume of 2.0 mL. Quantitative binding data (K_a, ΔG°, and $\Delta\, OD_{sat}$) were calculated from the UV/Vis titrations by measuring the changes in optical density (OD) at two separate wavelengths, plotting these against the total concentration of the guest, and subsequently analyzing the data by using a nonlinear least-squares curve-fitting routine.

Samples for ^{1}H NMR titrations were obtained in an analogous manner, and the runs were carried out on a Bruker AM500 spectrometer at T = 293 K. For titrations in CD_3OD, chemical shift values were measured versus the solvent quintet at 3.30 ppm, and in $CDCl_3$ they were measured versus the solvent singlet at 7.26 ppm. To calculate thermodynamic data, the changes in chemical shift of 3 separate host resonances as a function of guest concentration were evaluated as described above. The reported K_a and ΔG° values are averages of those calculated.

X-ray Crystal Structure of Cyclophane 2c. *Summary of Crystallographic Data Collection.* Compound **2c** ($C_{71}H_{80}N_5O_8ZnI$), M_r = 1323.74, crystallized in the triclinic space group P1, Z = 2, with a (Å) = 10.1048 (7), b (Å) = 15.712 (1), and c (Å) = 26.698 (2), α (°) = 93.647 (2), β (°) = 92.123 (2), γ(°) = 103.343 (2), and V (Å^3) = 4110. Data were collected on a Huber diffractometer constructed by Professor C. E. Strouse, UCLA, using MoKα radiation, to a maximum 2 θ = 45 °, giving 10734 unique reflections, and the structure was solved by heavy atom methods. The final discrepancy index was R = 0.100 and R_w = 0.122 for 2966 independent reflections with $I > 3\sigma(I)$.

Collection and Reduction of X-ray Data. A red crystal of **2c**, obtained by slow evaporation of a solution in CH_2Cl_2/toluene, was sealed in a capillary with solvent and mounted on the Huber diffractometer. These crystals quickly changed to powder when removed from solvent. Unit cell parameters were determined from a least-squares fit of 77 accurately centered reflections (7.5° < 2θ < 17.7°). Data were collected at 25 °C in the θ - 2θ scan mode. Three intense reflections (3 1 2, 1 0 -7, 0 3 2) were monitored every 97 reflections to check stability. Intensities of these reflections decayed less than 4% during the course of the experiment (106.5 hours). Of the 10734 unique reflections measured, 2966 were considered observed ($I > 3\ \sigma(I)$) and were used in the subsequent structure analysis. Data were corrected for Lorentz, polarization, and absorption effects. Programs used in this work include locally modified versions of the following programs: CARESS (Broach, Coppens, Becker, and Blessing) peak profile analysis, Lorentz and polarization corrections, ORFLS (Busing, Martin, and Levy) structure factor calculation and full-matrix least-squares refinement, ABSCOR absorption correction based on psiscan, SHELX76 (Sheldrick) crystal structure package, and ORTEP (Johnson) figure plotting.

Solution and Refinement. Atoms were located by use of heavy atom methods. All calculations were performed on the VAX 3100 crystallographic computer. Final refinement was in two blocks, one containing solvent molecules and the other containing the cyclophane. The heavy atoms Zn and I were refined with anisotropic parameters. All other non-hydrogen atoms were refined isotropically. All phenyl rings were refined as rigid groups, C-C = 1.395 Å. All H atoms were included in calculated positions, C-H = 1.0 Å. H atoms were assigned u values based on those of the attached C. Scattering factors for H were obtained from Stewart et al.[32] and for other atoms were taken from the International Tables for X-ray Crystallography.[33] Anomalous dispersion terms were applied to the scattering for Zn and I. The largest peak on a final difference electron density map was 1.0 e Å^{-3} and was in the region containing disordered solvent. The rather high value of agreement, R = 0.100, can be attributed to the lack of data from the small crystal and to the disorder in the solvent regions. The disordered interstitial solvent has not been fully characterized. The cyclophane contains one molecule of CH_2Cl_2 in a well-defined location in its cavity. Tables of the atomic coordinates, equivalent isotropic thermal parameters, bond angles and bond lengths, and tables of observed and calculated structure factors have been submitted to the Cambridge Crystallographic Data Centre.

Synthesis

1-Acetyl-4,4-bis(4-hydroxy-3,5-dimethoxyphenyl)piperidine.[13] Concentrated sulfuric acid (50 mL) was added portionwise over a period of two hours to a solution of 43.7 g (0.283 mol) of 2,6-dimethoxyphenol and 20.0 g (0.142 mol) of 1-acetyl-4-piperidone in 11.3 mL of water. The temperature was kept below 15 °C throughout. After standing at room temperature overnight, the viscous red liquid was taken up in 150 mL of boiling ethanol. The solution was neutralized by the addition of 2N Na_2CO_3 and diluted with 500 mL of

water. After overnight refrigeration, the white solid was filtered, washed with water, and dried at 80 °C in a vacuum oven, giving 50.9 g (83%) of colorless product: mp 220-223 °C; IR (KBr) ν (OH) 3230, (C=O) 1614 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.11 (s, 3H, $COCH_3$), 2.25-2.4 (m, 4H, $AcNCH_2CH_2$), 3.45-3.55 (m, 2H, $AcNCH_2$), 3.6-3.7 (m, 2H, $AcNCH_2$), 3.82 (s, 12H, OCH_3), 5.49 (br s, 2H, OH), 6.43 (s, 4H, ArH); MS (EI, 16 eV), *m/z* (relative intensity) 431 (M^+, 100); Anal. Calcd for $C_{23}H_{29}NO_7$ (431.6): C, 64.01; H, 6.78; N, 3.25. Found: C, 63.93; H, 6.82; N, 3.34.

1-Acetyl-4,4-bis[4-(3-bromopropoxy)-3,5-dimethoxyphenyl]piperidine (3). A total of 18.2 g (42 mmol) of 1-acetyl-4,4-bis(4-hydroxy-3,5-dimethoxyphenyl)piperidine was stirred with 128 g (0.634 mmol) of 1,3-dibromopropane and 29 g (0.21 mol) of anhydrous potassium carbonate in 100 mL of refluxing acetone under nitrogen until the reaction was complete by TLC (about 8 hours). The reaction mixture was filtered through celite, and the solvent was removed *in vacuo*. Purification was achieved by column chromatography on silica gel. First, pure CH_2Cl_2 was used to elute residual 1,3-dibromopropane, and then the desired compound was eluted with CH_2Cl_2:MeOH (97:3). A light yellow oil weighing 25.8 g (91%) was obtained: IR (CH_2Cl_2) ν (C=O) 1637 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 2.11 (s, 3H, CH_3CO), 2.2-2.3 (m, 4H, $CH_2CH_2CH_2$), 2.3-2.35 (m, 4H, $AcNCH_2CH_2$), 3.5-3.55 (m, 2H, $AcNCH_2CH_2$), 3.65-3.7 (m, 2H, $AcNCH_2CH_2$), 3.71 (t, J = 6.5 Hz, 4H, CH_2Br), 3.78 (s, 12H, OCH_3), 4.08 (t, J = 5.7 Hz, 4H, OCH_2), 6.42 (s, 4H, ArH); MS (EI, 20 eV) *m/z* (relative intensity) 675 (M^+ + 4, 54), 673 (M^+ + 2, 100), 671 (M^+, 43); HRMS *m/z* (M^+, $C_{29}H_{39}Br_2NO_7$) calcd 671.1094, obsd 671.1104.

Dispiro[piperidine-4,24'-[20,23:25,28:53,56:58,61]tetraetheno[6,9:39,42]diimino-[5,38:10,43]di[2]pyrrolyl[5]ylidene[16H,24H,30H,49H,57H,63H]tetrabenz[t,b_1,w_1,e_2]-[1,5,15,19,30,34,44,48]octaoxacyclooctapentacontin-57',4''-piperidine], 1,1''-diacetyl-17', 18',31',32',50',51',64',65'-octahydro-21',27',54',60',67',70',82',85'-octamethoxy- (5a). A solution of 25.5 g of the dibromide **3** (37.9 mmol) in dry DMF (160 mL) was added over a period of 5 hours *via* syringe pump to a stirred mixture of 6.43 g (9.47 mmol) of the tetra(*o*-hydroxyphenyl)porphyrin **4** and anhydrous potassium carbonate (16 g, 0.116 mol) at 100 °C in DMF. The reaction was then stirred for an additional four hours at this temperature. The cooled reaction mixture was filtered through celite, and the solvent was removed *in vacuo*. The three product isomers were partially purified by flash chromatography on silica gel using CH_2Cl_2/MeOH (98:2) as eluant. An oily purple residue was obtained, weighing 4.4 g. ^1H NMR indicated that the desired cross *trans*-linked isomer **5a** made up approximately 77% of the mixture, and that some non-porphyrinic material was also present. Slow evaporation of a solution of this material in CH_2Cl_2/MeOH yielded 403 mg of the desired isomer in a pure state. Further fractional crystallization lead to an additional 495 mg of this isomer, an overall yield of 5.4%: mp >310 °C (dec.); IR (KBr) ν (NH) 3321, (C=O) 1646 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log ε) 646 (3.30), 591 (3.64), 547 (3.66), 514 (4.16), 484 (3.33), 419 (5.56), 401 (4.76, sh); ^1H NMR (500 MHz, $C_2D_2Cl_4$, 383K) δ -2.49 (s, 2H, NH), 1.55-1.65 (m, 8H, $CH_2CH_2CH_2$), 2.0-2.1 (m, 8H, $AcNCH_2CH_2$), 2.03 (s, 6H, CH_3CO), 2.58 (s, 24H, OCH_3), 3.26 (t, J = 6.4 Hz, 8H, $Ar(OMe)_2OCH_2$), 3.4-3.55 (m, 8H, $AcNCH_2CH_2$), 4.15 (t, J = 6.1 Hz, 8H, $Ar(porph)OCH_2$), 5.76 (s, 8H, $Ar(OMe)_2H$), 7.34 (ddd, $J_{BA} \approx J_{BC} \approx$ 7.5 Hz, J_{BD} = 1.1 Hz, 4H, H_B), 7.44 (dd, J_{DC} = 8.5 Hz, J_{DB} = 1.1 Hz, 4H, H_D), 7.80 (ddd, J_{CD} = 8.5 Hz, J_{CB} = 7.5 Hz, J_{CA} = 1.9 Hz, 4H, H_C), 7.85 (dd, J_{AB} = 7.5 Hz, J_{AC} = 1.9 Hz, 4H, H_A), 8.71 (s,

8H, β-H); MS (FAB) *m/z* (relative intensity) 1704 (M^+ + 3, 46), 1703 (M^+ + 2, 83), 1702 (M^+ + 1, 100), 1701 (M^+, 68); Anal. Calcd for $C_{102}H_{104}N_6O_{18}$ (1702.0): C, 71.98; H, 6.16; N, 4.94. Found: C, 71.61; H, 6.05; N, 4.82.

Zinc, [1,1''-diacetyl-17',18',31',32',50',51',64',65'-octahydro-21',27',54',60',67',-70',82',85'-octamethoxydispiro[piperidine-4,24'-[20,23:25,28:53,56:58,61]tetraetheno-[6,9:39,42]diimino[5,38:10,43]di[2]pyrrolyl[5]ylidene[16H,24H,30H,49H,57H,63H]-tetrabenz[t,b_1,w_1,e_2][1,5,15,19,30,34,44,48]octaoxacyclooctapentacontin-57',4''-piperidinato](2-)-$N^{72'}$,$N^{76'}$,$N^{78'}$,$N^{86'}$]-, (SP-4-1)- (5b). Porphyrin **5a** (310 mg, 0.182 mmol) and zinc acetate dihydrate (250 mg, 1.14 mmol) were refluxed in 20 mL of a 1:1 mixture of chloroform and methanol for five minutes. Completion of the reaction was verified by visible spectroscopy. The solution was concentrated *in vacuo*, and the residue was partitioned between CH_2Cl_2 and H_2O. The organic solution was dried over sodium sulfate and the solvent removed to yield 318 mg (99%) of purple crystals: mp 245 °C (dec); IR (KBr) ν (C=O) 1645 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log ε) 616 (2.54), 584 (3.34), 548 (4.27), 513 (3.37), 485 (2.95, sh), 421 (5.61), 401 (4.47, sh); ^1H NMR (500 MHz, $C_2D_2Cl_4$, 383K) δ 1.5-1.6 (m, 8H, $CH_2CH_2CH_2$), 2.0-2.1 (m, 8H, $AcNCH_2CH_2$), 2.03 (s, 6H, CH_3CO), 2.70 (s, 24H, OCH_3), 3.17 (t, J = 6.4 Hz, 8H, $Ar(OCH_3)_2OCH_2$), 3.4-3.5 (m, 8H, $AcNCH_2CH_2$), 4.13 (t, J = 6.2 Hz, 8H, Ar(porph)OCH_2), 5.76 (s, 8H, $Ar(OMe)_2H$), 7.35 (ddd, $J_{BA} \approx J_{BC} \approx 7.3$ Hz, J_{DB} = 1.3 Hz, 4H, H_B), 7.45 (dd, J_{DC} = 8.6 Hz, J_{DB} = 1.3 Hz, 4H, H_D), 7.80 (ddd, J_{CD} = 8.6 Hz, J_{CB} = 7.3 Hz, J_{CA} = 1.7 Hz, 4H, H_C), 7.85 (dd, J_{AB} = 7.3 Hz, J_{AC} = 1.7 Hz, 4H, H_A), 8.83 (s, 8H, β-H); MS (FAB) *m/z* (relative intensity) 1768 (M^+ + 5, 58), 1767 (M^+ + 4, 78), 1766 (M^+ + 3, 90), 1765 (M^+ + 2, 100), 1764 (M^+ + 1, 94), 1763 (M^+, 72); Anal. Calcd for $C_{102}H_{102}N_6O_{18}Zn$ (1765.4): C, 69.40; H, 5.82; N 4.76. Found: C, 69.11; H, 5.77; N, 4.63.

Zinc, [1,1''-diethyl-17',18',31',32',50',51',64',65'-octahydro-21',27',54',60',67',-70',82',85'-octamethoxydispiro[piperidine-4,24'-[20,23:25,28:53,56:58,61]tetraetheno-[6,9:39,42]diimino[5,38:10,43]di[2]pyrrolyl[5]ylidene[16H,24H,30H,49H,57H,63H]-tetrabenz[t,b_1,w_1,e_2][1,5,15,19,30,34,44,48]octaoxacyclooctapentacontin-57',4''-piperidinato](2-)-$N^{72'}$,$N^{76'}$,$N^{78'}$,$N^{86'}$]-, (SP-4-1)- (6). A solution of 278 mg (0.158 mmol) of **5b** in 10 mL of dry THF at 0 °C under nitrogen was added *via* syringe to a solution of DIBAL-H in hexanes (1.3 mL of a 1.0 M solution; 1.3 mmol), and the reaction was stirred for 15 minutes. After quenching with water, the mixture was diluted with CH_2Cl_2, washed twice with 15% NaOH, twice with water, and once with saturated NaCl. After drying over sodium sulfate, the solvent was evaporated *in vacuo*. A total of 274 mg (99%) of **6** was obtained as a purple solid: mp 235 °C (dec.); MS (FAB) $C_{102}H_{106}N_6O_{16}Zn$ (1734.69) *m/z* (relative intensity) 1739 (M^+ + 4, 55), 1738 (M^+ + 3, 67), 1737 (M^+ + 2, 77), 1736 (M^+ + 1, 100), 1735 (M^+, 49). The zinc derivative **6** gave a ^1H NMR spectrum in which all peaks were extremely broadened, and the compound was better analyzed by ^1H NMR in the free-base form which was obtained by stirring the zinc porphyrin in a mixture of MeOH and concentrated HCl. The solution was neutralized with saturated Na_2CO_3 and the free porphyrin extracted into CH_2Cl_2. The organic phase was washed once with water and dried with magnesium sulfate. Evaporation of the solvent yielded pure metal-free porphyrin-cyclophane: ^1H NMR (360 MHz, $CDCl_3$, 323K) δ -2.67 (s, 2H, NH), 1.04 (t, J = 7.2 Hz, 6H, CH_2CH_3), 1.5-1.55 (m, 8H, $CH_2CH_2CH_2$), 2.1-2.2 (m, 8H, NCH_2CH_2), 2.31 (q, J =

7.2 Hz, 4H, CH_2CH_3), 2.35-2.5 (m, 8H, NCH_2CH_2), 2.48 (s, 24H, OCH_3), 3.18 (t, J = 6.3 Hz, 8H, Ar(porph)OCH_2), 4.13 (t, J = 6.1 Hz, 8H, Ar$(OMe)_2OCH_2$), 5.71 (s, 8H, Ar$(OMe)_2H$), 7.25 (m, 4H, H_B), 7.37 (m, 4H, H_D), 7.7-7.8 (m, 8H, H_A and H_C), 8.65 (s, 8H, β-H); MS (FAB) $C_{102}H_{108}N_6O_{16}$ (1672.76) *m/z* (relative intensity) 1677 (M^+ + 4, 41), 1676 (M^+ + 3, 39), 1675 (M^+ + 2, 100), 1674 (M^+ + 1, 81), 1673 (M^+, 43).

Dispiro[piperidine-4,24'-[20,23:25,28:53,56:58,61]tetraetheno[6,9:39,42]diimino [5,38:10,43]di[2]pyrrolyl[5]ylidene[16H,24H,30H,49H,57H,63H]tetrabenz[t,b_1,w_1,e_2][1,5,-15,19,30,34,44,48]octaoxacyclooctapentacontin-57',4''-piperidinium], 1,1,1'',1''-tetraethyl-17',18',31',32',50',51',64',65'-octahydro-21',27',54',60',67',70',82',85'-octamethoxy-, dichloride (1a). The zinc(II) porphyrinate **6** (224 mg, 0.129 mmol) was dissolved in a mixture of freshly distilled iodoethane (5 mL) and dry acetone (5 mL) and was stirred at 20 °C until ^{1}H NMR showed the reaction to be complete. The solvent was evaporated, and the residue was treated with a mixture of concentrated HCl and MeOH to remove the zinc ion. The solution was then made basic with 2N NaOH, and the metal-free porphyrin was extracted into CH_2Cl_2. The CH_2Cl_2 solution was washed once with water, with saturated NaCl, and dried over sodium sulfate. After the solvent was evaporated *in vacuo*, elution of the residue (247 mg) through a Dowex ion exchange column (Cl^-) using H_2O/MeOH (60:40) as eluant provided a purple solid weighing 177 mg (76% yield). Crystallization leading to pure **1a** was achieved by slow evaporation of a CH_2Cl_2/EtOAc solution: mp > 310 °C (dec.); UV/Vis (CH_2Cl_2) λ_{max} (log ε) 646 (3.36), 591 (3.71), 548 (3.76), 512 (4.16), 482 (3.55), 419.2 (5.47), 370 (sh, 4.26); UV/Vis (MeOH) λ_{max} (log ε) 644 (3.34), 589 (3.68), 546 (3.71), 513 (4.13), 480 (3.52), 416 (5.45), 369 (4.26); ^{1}H NMR (360 MHz, $CDCl_3$, 323K) δ -2.77 (s, 2H, NH), 1.04 (t, J = 6.7 Hz, 12H, CH_2CH_3), 1.55-1.6 (m, 8H, $CH_2CH_2CH_2$), 2.25-2.35 (m, 8H, NCH_2CH_2), 2.74 (s, 24H, OCH_3), 3.15 (t, J = 6.2 Hz, 8H, Ar$(OCH_3)_2OCH_2$), 3.15-3.25 (m, 8H, NCH_2CH_2), 3.31 (br q, J = 6.7, 8H, CH_2CH_3), 4.14 (t, J = 5.8 Hz, 8H, Ar(porph)OCH_2), 5.75 (s, 8H, Ar$(OMe)_2H$), 7.30 (ddd, $J_{BA} \approx J_{BC} \approx$ 7.4 Hz, J_{BD} = 1.1 Hz, 4H, H_B), 7.38 (dd, J_{DC} = 7.4 Hz, J_{DB} = 1.1 Hz, 4H, H_D), 7.69 (dd, J_{AB} = 7.4 Hz, J_{AC} = 1.8 Hz, 4H, H_A), 7.76 (ddd, $J_{CA} \approx J_{CB} \approx$ 7.4 Hz, J_{CA} = 1.8 Hz, 4H, H_C), 8.66 (s, 8H, β-H); $C_{106}H_{118}Cl_2N_6O_{16}$ (1803.0).

Zinc, [1,1,1'',1''-tetraethyl-17',18',31',32',50',51',64',65'-octahydro-21',27',54',60',67',70',82',85'-octamethoxydispiro[piperidinium-4,24'-[20,23:25,28:53,56:58,61]-tetraetheno[6,9:39,42]diimino[5,38:10,43]di[2]pyrrolyl[5]ylidene[16H,24H,30H,49H,57H,-63H]tetrabenz[t,b_1,w_1,e_2][1,5,15,19,30,34,44,48]octaoxacyclooctapentacontin-57',4''-piperidiniumato](2-)-$N^{72'}$,$N^{76'}$,$N^{78'}$,$N^{86'}$]-, (SP-4-1)-, dichloride (1b). The zinc(II) porphyrinate **1b** was prepared by refluxing the free base derivative **1a** with $Zn(OAc)_2$ in a mixture of $CHCl_3$ and MeOH until the UV/Vis spectrum indicated complete reaction. Ion exchange chromatography on Dowex (Cl^-), eluting with MeOH/H_2O (1:1) followed by crystallization from EtOAc/CH_2Cl_2 gave a red solid: mp 235 °C (dec.); UV/Vis (CH_2Cl_2) λ_{max} (log ε) 643 (3.13), 586 (3.49), 549 (4.20), 513 (3.58), 482 (3.47), 421 (5.57), 402 (4.51); UV/Vis (MeOH) λ_{max} (log ε) 626 (3.21), 595 (3.65), 557 (4.18), 517 (3.54), 423.8 (5.63), 404 (4.56); ^{1}H NMR (500 MHz, Me_2SO-d_6, 383K) δ 1.09 (t, J = 7.1 Hz, 12H, CH_2CH_3), 1.45-1.5 (m, 8H, $CH_2CH_2CH_2$), 2.35-2.4 (m, 8H, NCH_2CH_2), 2.95 (s, 24H, OCH_3), 3.05-3.1 (m, 8H, NCH_2CH_2), 3.06 (t, J = 6.4 Hz, 8H,

$Ar(OCH_3)_2OCH_2$), 3.27 (q, J = 7.1 Hz, 8H, CH_2CH_3), 4.04 (t, J = 6.0 Hz, 8H, Ar(porph)OCH_2), 6.04 (s, 8H, Ar(porph)*H*), 7.33 (ddd, $J_{BA} \approx J_{BC} \approx$ 7.4 Hz, J_{BD} = 1.1 Hz, 4H, H_B), 7.48 (dd, J_{DC} = 8.5 Hz, J_{DB} = 1.1 Hz, 4H, H_D), 7.73 (dd, J_{AB} = 7.4 Hz, J_{AC} = 1.8 Hz, 4H, H_A), 7.76 (ddd, J_{CD} = 8.5 Hz, J_{CB} = 7.4 Hz, J_{CA} = 1.8 Hz, 4H, H_C), 8.57 (s, 8H, β-H); MS (FAB) $C_{106}H_{116}N_6O_{16}Cl_2Zn$ (1862.70) *m/z* (relative intensity) 1794 (M^+ + H - 2Cl, 14), 1765 (M^+ + H - 2Cl - C_2H_5, 100), 1764 (M^+ + H - 2Cl - C_2H_5, 100).

1-Acetyl-4,4-bis[4-(3-chloropropoxy)-3,5-dimethoxyphenyl]piperidine (7). A total of 10.0 g (0.0232 mol) of 1-acetyl-4,4-bis(4-hydroxy-3,5-dimethoxyphenyl)piperidine was heated at 90 °C in dry DMF in the presence of 1,3-dichloropropane (40.0 g; 0.354 mol) and cesium carbonate (30.5 g; 0.0936 mol) under Ar. When TLC indicated complete reaction (≈ 12 hours), the reaction mixture was cooled and filtered through celite, and the DMF was removed *in vacuo*. The deep red oil was purified by column chromatography on silica gel, eluting first with CH_2Cl_2 to remove residual 1,3-dichloropropane then gradually changing to CH_2Cl_2:MeOH (97:3) to elute the desired compound as a light brown oil weighing 12.8 g (94%): IR (CH_2Cl_2) ν (C=O) 1636 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 2.10 (s, 3H, CH_3CO), 2.1-2.2 (m, 4H, $CH_2CH_2CH_2$), 2.3-2.4 (m, 4H, $AcNCH_2CH_2$), 3.5-3.6 (m, 2H, $AcNCH_2CH_2$), 3.65-3.7 (m, 2H, $AcNCH_2CH_2$), 3.78 (s, 12H, OCH_3), 3.83 (t, J = 6.5 Hz, 4H, CH_2Cl), 4.09 (t, J = 5.8 Hz, 4H, OCH_2), 6.44 (s, 4H, ArH); HRMS (EI) *m/z* (M^+, $C_{29}H_{39}Cl_2NO_7$) calcd 583.2103, obsd 583.2114.

1-Acetyl-4,4-bis{4-[3-(2-formylphenoxy)propoxy]-3,5-dimethoxyphenyl}piperidine (8). A solution of 3.0 g (5.13 mmol) of **7** and 6.26 g (51.3 mmol) of salicylaldehyde was heated at 90 °C under argon in dry DMF with 12.0 g (37.0 mmol) of anhydrous cesium carbonate. After completion of the reaction (≈ 8 hours), the mixture was filtered through celite, and the solvent was removed *in vacuo*. The residue was dissolved in CH_2Cl_2, and the solution was extracted twice with 2N NaOH, once with water, and once with brine. The organic layer was dried over sodium sulfate, concentrated *in vacuo*, and applied to a silica gel column, eluting with ethyl acetate. A white foam was obtained, weighing 2.5 g (64%): IR (KBr) ν (C=O) 1725, 1685, 1640 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 2.10 (s, 3H, CH_3CO), 2.2-2.35 (m, 8H, $AcNCH_2CH_2$, $CH_2CH_2CH_2$), 3.45-3.55 (m, 2H, $AcNCH_2CH_2$), 3.55-3.7 (m, 2H, $AcNCH_2CH_2$), 3.65 (s, 12H, OCH_3), 4.15 (t, J = 5.8 Hz, 4H, $(Ar(OCH_3)_2OCH_2)$, 4.37 (t, J = 5.9, 4H, Ar(CHO)OCH_2), 6.37 (s, 4H, Ar(CHO)OCH_2), 7.01 (dddd, J_{BA} = 7.7 Hz, J_{BC} = 7.3 Hz, J_{BD} = 0.8 Hz, $J_{B\text{-}CHO}$ = 0.5 Hz, 2H, H_B), 7.05 (dd, J_{DC} = 8.4 Hz, J_{DB} = 0.8 Hz, 2H, H_D), 7.54 (ddd, J_{CD} = 8.4 Hz, J_{CB} = 7.3 Hz, J_{CA} = 1.8 Hz, 2H, H_C), 7.81 (dd, J_{AB} = 7.7 Hz, J_{AC} = 1.8 Hz, 2H, H_A), 10.46 (d, $J_{CHO\text{-}B}$ = 0.5 Hz, 2H, CHO); MS (EI, 20 eV) *m/z* (relative intensity) 757 (M^+ + 2, 15), 756 (M^+ + 1, 49), 755 (M^+, 100); HRMS (EI) *m/z* (M^+, $C_{43}H_{49}NO_{11}$) calcd 755.3305, obsd 755.3326.

1H-Pyrrole-2-carboxylic acid, 5,5',5'',5'''-[(1-acetyl-4-piperidinylidene)bis[(2,6-dimethoxy-4,1-phenylene)oxy-3,1-propanediyloxy-2,1-phenylenemethylidyne]]-tetrakis(3,4-dimethyl)-, tetrakis(phenylmethyl) ester (9). The dialdehyde **8** (1.39 g, 1.84 mmol) and benzyl 2,3-dimethylpyrrole-2-carboxylate[15] (1.69 g, 7.35 mmol) were heated to reflux in absolute ethanol under nitrogen. Concentrated hydrochloric acid (0.025 mL) was added *via* syringe, and the dark solution was stirred for 30 minutes. The cooled reaction mixture was diluted with CH_2Cl_2, washed with 10% $NaHCO_3$, water, and concentrated NaCl, dried over sodium sulfate, and concentrated *in vacuo*. A short silica column was first eluted

with pure CH_2Cl_2 followed by CH_2Cl_2/MeOH (95:5), affording 2.7 g (90%) of a light yellow foam: IR (KBr) ν (N-H) 3447, (C=O) 1690, 1650 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 1.70 (s, 12H, pyr-4-CH_3), 2.0-2.05 (m, 4H, $CH_2CH_2CH_2$), 2.08 (s, 3H, CH_3CO), 2.18 (s, 12H, pyr-3-CH_3), 2.3-2.4 (m, 4H, NCH_2CH_2), 3.45-3.55 (m, 2H, NCH_2CH_2), 3.6-3.7 (m, 2H, NCH_2CH_2), 3.64 (s, 12H, OCH_3), 3.89 (t, J = 5.8 Hz, 4H, OCH_2), 4.16 (t, J = 6.1, 4H, $Ar(OCH_3)_2OCH_2$), 5.23 (s, 8H, $BnCH_2$), 5.71 (s, 2H, methine-CH), 6.41 (s, 4H, ArH), 6.85-6.95 (m, 6H, ArH), 7.2-7.45 (m, 22H), 8.44 (s, 4H, NH); MS (FAB) $C_{99}H_{105}N_5O_{17}$ (1635.75) *m/z* (relative intensity) 1638 (M^+ + 2, 12), 1637 (M^+ + 1, 17), 1636 (M^+, 16), 1547 (M^+ + 2 - Bn, 31%), 1546 (M^+ + 1 - Bn , 55), 1545 (M^+ - Bn, 54).

Zinc, [1'-acetyl-7,8,21,22-tetrahydro-11,17,52,55-tetramethoxy-30,31,35,36,42,43,48,-49-octamethylspiro[46H-10,13:15,18-dietheno-34,37-imino-29,32-nitrilo-28,38-([2,5]-endo-pyrrolometheno[2]pyrrolyl[5]ylidene)-6H,14H,20H,32H-dibenzo[t,g_1][1,5,15,19]tetraoxa - cyclotetratriacontin-14,4'-piperidinato](2-)-N^{40},N^{46},N^{50},N^{51}]-, (SP-4-1)- (10). The tetrapyrrole **9** (2.7 g, 1.6 mmol) was treated with H_2 (3 bar) in dry THF (150 mL) in the presence of triethylamine (0.85 mL, 6.1 mmol) and 5% Pd on C (2 g) for 2 hours in a Parr apparatus. Filtration through Celite, followed by evaporation of the solvent, gave a yellow foam which was thoroughly dried on the vacuum pump. The residue (2.6 g) was stirred with trimethyl orthoformate (3.7 mL, 34 mmol) and trichloroacetic acid (16.8 g, 0.10 mol) in dry CH_2Cl_2 (640 mL), protected from light and from moisture. After 4 hours, a slurry of zinc acetate dihydrate (0.80 g, 37 mmol) in dry methanol (5 mL) was added and the reaction stirred a further 46 hours. The black solution was washed with 2N Na_2CO_3 and with water, dried over sodium sulfate, and the solvent was removed *in vacuo*. The residue was dissolved in CH_2Cl_2 (325 mL), a slurry of $Zn(OAc)_2 \cdot 2H_2O$ (800 mg; 3.7 mmol) was added, and the mixture was heated to reflux for 10 min. The solvent was removed *in vacuo*, and the residue was purified by chromatography on silica gel, eluting with CH_2Cl_2/MeOH (98:2). The material was still impure by ^1H NMR, so it was recrystallized twice by slow evaporation from a CH_2Cl_2/MeOH solution, giving 337 mg (17%) of a red powder: mp >310 °C (dec.); IR (KBr) ν (C=O) 1648 cm^{-1}; UV/Vis (CH_2Cl_2) λ_{max} (log ε) 390 (4.63, sh), 410 (5.57), 501 (3.33), 538 (4.23), 574 (3.97); ^1H NMR (360 MHz, $CDCl_3$) δ 1.55-1.65 (m, 4H, $CH_2CH_2CH_2$), 1.85-1.95 (m, 4H, NCH_2CH_2), 1.92 (s, 3H, CH_3CO), 2.51 (s, 24H, OCH_3 and β-CH_3), 3.1-3.2 (m, 6H, NCH_2CH_2 and $Ar(OCH_3)_2OCH_2$), 3.35-3.4 (m, 2H, NCH_2CH_2), 3.49 (s, 12H, β-CH_3), 4.26 (t, J = 5.9 Hz, 4H, Ar(porph)OCH_2), 5.54 (s, 4H, $Ar(OMe)_2H$), 7.31 (ddd, J_{BC} = 7.5 Hz, J_{BA} = 7.3 Hz, J_{BD} = 1.0 Hz, 2H, H_B), 7.34 (dd, J_{DC} = 8.4 Hz, J_{DB} = 1.0 Hz, 2H, H_D), 7.65 (dd, J_{AB} = 7.3 Hz, J_{AC} = 1.8 Hz, 2H, J_A), 7.76 (ddd, J_{CD} = 8.4 Hz, J_{CB} = 7.5 Hz, J_{CA} = 1.8 Hz, 2H, H_C), 10.06 (d, J = 2.3 Hz, 2H, *meso*-H); MS (FAB) *m/z* (relative intensity) 1184 (M^+ + 5, 43), 1183 (M^+ + 4, 62), 1182 (M^+ + 3, 81), 1181 (M^+ + 2, 100), 1180 (M^+ + 1, 92), 1179 (M^+, 96); Anal. Calcd for $C_{69}H_{73}N_5O_9Zn$ (1181.8): C, 70.13; H, 6.23; N, 5.93. Found: C, 70.11; H, 6.15; N, 5.98.

Zinc, [1'-ethyl-7,8,21,22-tetrahydro-11,17,52,55-tetramethoxy-30,31,35,36,42,43,48,-49-octamethylspiro[46H-10,13:15,18-dietheno-34,37-imino-29,32-nitrilo-28,38-([2,5]-endo-pyrrolometheno[2]pyrrolyl[5]ylidene)-6H,14H,20H,32H-dibenzo[t,g_1][1,5,15,19]tetraoxa-cyclotetratriacontin-14,4'-piperidinato](2-)-N^{40},N^{46},N^{50},N^{51}]-, (SP-4-1)- (11). A solution of 227 mg (0.192 mmol) of **10** in dry toluene (11 mL) was added slowly to a stirred solution of DIBAL-H (2.0 mL

of a 1.0 M solution in hexanes, 2.0 mmol) in dry toluene (8.0 mL) at 0 °C under nitrogen. After stirring for thirty minutes, the reaction was quenched with water, and the toluene solution was treated with 15% NaOH, washed twice with water, dried over sodium sulfate, and the solvent was removed *in vacuo* to give 200 mg (89% yield) of a fine red powder: mp >310 °C (dec.); ^{1}H NMR (500 MHz, $CDCl_3$, 323K) δ 0.95 (t, J = 7.2 Hz, 3H, CH_2CH_3), 1.5-1.6 (m, 4H, $CH_2CH_2CH_2$), 1.95-2.0 (m, 4H, NCH_2CH_2), 2.19 (q, J = 7.2 Hz, 2H, CH_2CH_3), 2.25-2.3 (m, 4H, NCH_2CH_2), 2.48 (br s, 12H, OCH_3), 2.53 (s, 12H, pyr-CH_3), 3.15 (t, J = 6.4 Hz, 4H, $Ar(OMe)_2OCH_2$), 3.49 (s, 12H, pyr-CH_3), 4.24 (t, J = 6.0 Hz, 4H, Ar(porph)OCH_2), 5.60 (s, 4H, $Ar(OCH_3)_2H$), 7.31 (ddd, $J_{BA} \approx J_{BC} \approx 7.4$ Hz, J_{BD} = 1.1 Hz, 2H, H_B), 7.34 (dd, J_{DC} = 8.5 Hz, J_{DB} = 1.1 Hz, 2H, H_D), 7.68 (dd, J_{AB} = 7.4 Hz, J_{AC} = 1.8 Hz, 2H, H_A), 7.76 (ddd, J_{CD} = 8.5 Hz, J_{CB} = 7.4 Hz, J_{CA} = 1.8 Hz, 2H, H_C), 10.06 (s, 2H, *meso*-H); MS (FAB) $C_{69}H_{75}N_5O_8Zn$ (1165.50) *m/z* (relative intensity) 1170 (M^+ + 5, 51), 1169 (M^+ + 4, 65), 1168 (M^+ + 3, 83), 1167 (M^+ + 2, 94), 1166 (M^+ + 1, 100), 1165 (M^+, 60).

Zinc, [1',1'-diethyl-7,8,21,22-tetrahydro-11,17,52,55-tetramethoxy-30,31,35,36,42,-43,48,49-octamethylspiro[46H-10,13:15,18-dietheno-34,37-imino-29,32-nitrilo-28,38-([2,5]-endo-pyrrolometheno[2]pyrrolyl[5]ylidene)-6H,14H,20H,32H-dibenzo[t,g$_1$][1,5,15,19] - tetraoxacyclotetratriacontin-14,4'-piperidiniumato](2-)-N^{40},N^{46},N^{50},N^{51}]-, iodide, (SP-4-1)-(2c). The tertiary amine **11** (180 mg; 0.154 mmol) was dissolved in a mixture of acetone (10 mL) and iodoethane (10 mL) and was stirred at room temperature overnight. The solvent was removed in vacuo yielding a red oil which was taken up in a small amount of CH_2Cl_2. Diethyl ether was added to precipitate 175 mg of a fine red solid (85% yield): mp 244 °C; UV/Vis (CH_2Cl_2) λ_{max} (log ε) 390 (4.61, sh), 410 (5.56), 501 (3.29), 538 (4.15), 574 (3.89); ^{1}H NMR (500 MHz, $CDCl_3$, 323K) δ 1.05 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.55-1.65 (m, 4H, $CH_2CH_2CH_2$), 2.2-2.3 (m, 4H, NCH_2CH_2), 2.53 (s, 12H, β-CH_3), 2.75 (s, 12H, OCH_3), 3.05-3.15 (m, 4H, NCH_2CH_2), 3.11 (t, J = 6.2 Hz, 4H, $Ar(OCH_3)_2OCH_2$), 3.20 (br q, J = 7.1 Hz, CH_2CH_3), 3.50 (s, 12H, β-CH_3), 4.23 (t, J = 5.8 Hz, Ar(porph)OCH_2), 5.66 (s, 4H, $Ar(OCH_3)_2H$), 7.32 (ddd, $J_{BA} \approx J_{BC} \approx 7.4$ Hz, J_{BD} = 1.1 Hz, 2H, H_B), 7.34 (dd, J_{DC} = 8.5 Hz, J_{DB} = 1.1 Hz, 2H, H_D), 7.70 (dd, J_{AB} = 7.4 Hz, J_{AC} = 1.8 Hz, 2H, H_A), 7.76 (ddd, J_{CD} = 8.5 Hz, J_{CB} = 7.4 Hz, J_{CA} = 1.8 Hz, 2H, H_C), 10.06 (s, 2H, *meso*-H); MS (FAB) *m/z* (relative intensity) 1199 (M^+ + 4 - I, 63), 1198 (M^+ + 3 - I, 67), 1197 (M^+ + 2 - I, 86), 1196 (M^+ + 1 - I, 86), 1195 (M^+ - I, 100); Anal. Calcd for $C_{71}H_{80}N_5O_8ZnI$ (1323.7): C, 64.42; H, 6.09; N, 5.29. Found: C, 64.13; H, 6.04; N, 5.30.

Zinc, [1',1'-diethyl-7,8,21,22-tetrahydro-11,17,52,55-tetramethoxy-30,31,35,36,42,-43,48,49-octamethylspiro[46H-10,13:15,18-dietheno-34,37-imino-29,32-nitrilo-28,38-([2,5]-endo-pyrrolometheno[2]pyrrolyl[5]ylidene)-6H,14H,20H,32H-dibenzo[t,g$_1$][1,5,15,19]-tetraoxacyclotetratriacontin-14,4'-piperidiniumato](2-)-N^{40},N^{46},N^{50},N^{51}]-,chloride, (SP-4-1)- (2b). The quaternary ammonium chloride salt **2b** was prepared by eluting **2c** through a Dowex ion exchange column with CH_3CN/H_2O (1:1): mp 241 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 323K) δ 1.11 (t, J = 7.0 Hz, 3H, CH_2CH_3), 1.55-1.65 (m, 4H, $CH_2CH_2CH_2$), 2.2-2.3 (m, 4H, NCH_2CH_2), 2.53 (s, 12H, β-CH_3), 2.69 (s, 12H, OCH_3), 3.12 (t, J = 6.3 Hz, 4H, $Ar(OCH_3)_2OCH_2$), 3.2-3.3 (m, 4H, NCH_2CH_2), 3.39 (br q, J = 6.8, CH_2CH_3), 3.49 (s, 12H, β-CH_3), 4.24 (t, J = 5.9 Hz, Ar(porph)OCH_2), 5.63 (s, 4H, $Ar(OCH_3)_2H$), 7.32 (ddd, $J_{BA} \approx J_{BC} \approx 7.4$ Hz, J_{BD} = 1.1 Hz, 2H, H_B), 7.34 (dd, J_{DC} = 8.5 Hz, J_{DB} = 1.1 Hz, 2H, H_D), 7.69 (dd,

J_{AB} = 7.4 Hz, J_{AC} = 1.8 Hz, 2H, H_A), 7.76 (ddd, J_{CD} = 8.5 Hz, J_{CB} = 7.4 Hz, J_{CA} = 1.8 Hz, 2H, H_C) 10.06 (s, 2H, *meso*-H); MS (FAB) $C_{71}H_{80}N_5O_8ZnCl$ (1229.50) *m/z* (relative intensity) 1194.8 (M^+ - Cl, 100).

Spiro[46H-10,13:15,18-dietheno-34,37-imino-29,32-nitrilo-28,38-([2,5]-endo-pyrrolo-metheno[2]pyrrolyl[5]ylidene)-6H,14H,20H,32H-dibenzo[t,g_1][1,5,15,19]tetraoxacyclo-tetratriacontin-14,4'-piperidinium], 1',1'-diethyl-7,8,21,22-tetrahydro-11,17,52,55-tetra-methoxy-30,31,35,36,42,43,48,49-octamethyl-, chloride (2a). The metal-free porphyrin-cyclophane **2a** was made by stirring the zinc derivative **2c** in a mixture of concentrated HCl and MeOH, followed by ion exchange on Dowex exchange resin (Cl^-): mp >310 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 323K) δ -2.36 (br s, 2H, NH), 0.88 (t, J = 6.9 Hz, 6H, CH_2CH_3), 1.55-1.65 (m, 4H, $CH_2CH_2CH_2$), 2.1-2.2 (m, 4H, NCH_2CH_2), 2.55 (s, 12H, β-CH_3), 2.61 (s, 12H, OCH_3), 3.0-3.1 (m, 4H, NCH_2CH_2), 3.11 (q, J = 6.9 Hz, 4H, CH_2CH_3), 3.18 (t, J = 6.4 Hz, 4H, $Ar(OCH_3)_2OCH_2$), 3.50 (s, 12H, β-CH_3), 4.25 (t, J = 5.8 Hz, 4H, Ar(porph)OCH_2), 5.62 (s, 4H, $Ar(OCH_3)_2H$), 7.32 (ddd, $J_{BA} \approx J_{BC} \approx$ 7.3 Hz, J_{BD} = 1.3 Hz, 2H, H_B), 7.35 (dd, J_{DC} = 8.6 Hz, J_{DB} = 1.3 Hz, 2H, H_D), 7.68 (dd, J_{AB} = 7.3 Hz, J_{AC} = 1.7 Hz, 2H, H_A), 7.77 (ddd, J_{CD} = 8.6 Hz, J_{CB} = 7.3 Hz, J_{CA} = 1.7 Hz, 2H, H_C) 10.09 (s, 2H, *meso*-H); MS (FAB) $C_{71}H_{82}N_5O_8Cl$ (1167.58) *m/z* (relative intensity) 1132 (M^+ - Cl, 100).

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REFERENCES

[1] (a) Morgan, B.; Dolphin, D. *Struct. Bonding (Berlin)* **1987**, *64*, 115-203. (b) Baldwin, J. E.; Perlmutter, P. *Top. Curr. Chem.* **1984**, *121*, 181-220.

[2] (a) Traylor, T. G. *Acc. Chem. Res.*, **1981**, *14*, 102-109. (b) Momenteau, M. *Pure Appl. Chem.* **1986**, *58*, 1493-1502.

[3] Collman, J. P.; Anson, F. C.; Barnes, C. E.; Bencosme, C. S.; Geiger, T.; Evitt, E. R.; Kreh, R. P.; Meier, K.; Pettman, *J. Am. Chem. Soc.* **1983**, *105*, 2694-2699.

[4] (a) Battersby, A. R.; Howson, W.; Hamilton, A. D. *J. Chem. Soc. Chem. Commun.* **1982**, 1266-1268. (b) Powell, M. F.; Pai, E. F.; Bruice, T. C. *J. Am. Chem. Soc.* **1984**, *106*, 3277-3285. (c) Mansuy, D.; Battioni, P.; Renaud, J.-P.; Guerin, P. *J. Chem. Soc. Chem. Commun.* **1985**, 155-156. (d) Lecas, A.; Renko, Z.; Rose, E. *Tetrahedron. Lett.* **1985**, *26*, 1019-1022. (e) Cook, B. R.; Reiner, T. J.; Suslick, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 7281-7286. (f) Renaud, J.-P.; Battioni, P.; Mansuy, D. *New. J. Chem.* **1987**, *11*, 279-290. (g) Mansuy, D.; *Pure Appl. Chem.* **1987**, *59*, 759-770. (h) Collman, J. P.; Brauman, J. I.; Fitzgerald, J. P.; Hampton, P. D.; Naruta, Y.; Michida, T. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 47-57. (i) Groves, J. T.; Viski, P. *J. Org. Chem.* **1990**, *55*, 3628-3634. (j) Stäubli, B.; Fretz, H.; Piantini, U.; Woggon, W.-D. *Helv. Chim. Acta* **1987**, *70*, 1173-1193.

[5] (a) Krieger, C.; Weiser, J.; Staab, H. A.; *Tetrahedron Lett.* **1985**, *26*, 6055-6058. (b) Lindsey, J. S.; Delaney, J. K.; Mauzerall, D. C.; Linschitz, H.; *J. Am. Chem. Soc.* **1988**, *110*, 3610-3621. (c) Mauzerall, D.; Weiser, J.; Staab, H. *Tetrahedron* **1989**, *45*, 4807-4814.

[6] For reviews of cytochrome P-450 see: (a) Ortiz de Montellano, P. R. *Cytochrome P-450*; Plenum: New York, 1986. (b) Black, S. D.; Coon, M. J. *Adv. Enzym.* **1987**, *60*, 35-87. (c) Guengerich, F. P.; Macdonald, T. L. *Acc. Chem. Res.* **1984**, *17*, 9-16. (d) White, R. E.; Coon, M. J. *Ann. Rev. Biochem.* **1980**, *49*, 315-356.

[7] (a) Poulos, T. L.; Finzel, B. C.; Howard, A. J. *Biochemistry* **1986**, *25*, 5314-5322. (b) Poulos, T. L.; Finzel, B. C.; Howard, A. J. *J. Mol. Biol.* **1987**, *195*, 687-700. (c) Poulos, T. L.; Finzel, B. C.; Gunsalus, I. C.; Wagner, G. C.; Kraut, J. *J. Biol. Chem.* **1985**, *260*, 16122-16130. (d) Poulos, T. L.; Howard, A. J. *Biochemistry* **1987**, *26*, 8165-8174. (e) Raag, R.; Poulos, T. L. *Biochemistry* **1989**, *28*, 917-922.

[8] Model studies of cytochrome P-450 activity: (a) Groves, J. T. *J. Chem. Educ.* **1985**, *62*, 928-931. (b) Collman, J. P.; Kodadek, T.; Brauman, J. I. *J. Am. Chem. Soc.* **1986**, *108*, 2588-2594. (c) Meunier, B. *Bull Soc. Chim. France* **1986**, 578-594. (d) Ostovic, D.; Bruice, T. C. *J. Am. Chem. Soc.* **1989**, *111*, 6511-6517. (e) Traylor, T. G.; Miksztal, A. R. *J. Am. Chem. Soc.* **1989**, *111*, 7443-7448. (e) Mansuy, D.; Battioni, P.; Battioni, J.-P. *Eur. J. Biochem.* **1989**, *184*, 267-285. Model studies of arene hydroxylation by cytochromes P-450: (f) Chang, C. K.; Kuo, M.-S. *J. Am. Chem. Soc.* **1979**, *101*, 3413-3415. (g) Chang, C. K.; Ebina, F. *J. Chem. Soc. Chem. Commun.* **1981**, 778-779. (h) Lindsay Smith, J. R.; Sleath, P. R. *J. Chem. Soc. Perkin Trans. 2* **1982**, 1009-1015. (i) Tabushi, I.; Morimitsu, K. *Tetrahedron Lett.* **1986**, *27*, 51-54. (j) Hanzlik, R. P.; Ling, K.-H. J. *J. Org. Chem.* **1990**, *55*, 3992-3997.

[9] Synthetic porphyrin-receptors: (a) Kobayashi, N.; Akiba, U.; Takatori, K.; Ueno, A.; Osa, T. *Heterocycles* **1982**, *19*, 2011-2014. (b) Gonzalez, M. C.; McIntosh, A. R.; Bolton, J. R.; Weedon, A. C. *J. Chem. Soc. Chem. Commun.* **1984**, 1138-1140. (c) Gonzalez, M. C.; Weedon, A. C. *Can. J. Chem.* **1985**, *63*, 602-608. (d) Hamilton, A.; Lehn, J.-M.; Sessler, J. L. *J. Am. Chem. Soc.* **1986**, *108*, 5158-5167. (e) Aoyama, Y.; Yamagishi, A.; Asagawa, M.; Toi, H.; Ogoshi, H. *J. Am. Chem. Soc.* **1988**, *110*, 4076-4077. (f) Lindsey, J. S.; Kearney, P. C.; Duff, R. J.; Tjivikua, P. T.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 6575-6577. (g) Breslow, R.; Brown, A. B.; McCullough, R. D.; White, P. W. *J. Am. Chem. Soc.* **1989**, *111*, 4517-4518. (h) Aoyama, Y.; Motomura, T.; Ogoshi, H. *Angew. Chem.* **1989**, *101*, 922-923. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 921-922. (i) Kuroda, Y.; Hiroshige, T.; Sera, T.; Shiroiwa, Y.; Tanaka, H.; Ogoshi, H. *J. Am. Chem. Soc.* **1989**, *111*, 1912-1913. (j) Sasaki, T.; Kaiser, E. T. *J. Am. Chem. Soc.* **1989**, *111*, 380-381. (k) Groves, J. T.; Neumann, R. *J. Am. Chem. Soc.* **1989**, *111*, 2900-2909. (l) Eshima, K.; Matsushita, Y.; Hasegawa, E.; Nishide, H.; Tsuchida, E. *Chem. Lett.* **1989**, 381-384. (m) Sutherland, I. O. *Pure & Appl. Chem.* **1989**, *61*, 1547 - 1554. (n) Hunter, C. A.; Meah, M. N.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5773 - 5780. (o) Anderson, H. L.; Hunter, C. A.; Meah, M. N.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5780-5789.

[10] Benson, D. R.; Valentekovich, R.; Diederich, F. *Angew. Chem.* **1990**, *102*, 213-216; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 191-193.

[11] (a) Diederich, F. *Angew. Chem.* **1988**, *100*, 372-396; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 362-386. (b) Dharanipragada, R.; Ferguson, S. B.; Diederich, F. *J. Am. Chem. Soc.* **1988**, *110*, 1679-1690.

[12] Momenteau, M.; Mispelter, J.; Loock, B.; Bisagni, E. *J. Chem. Soc. Perkin Trans 1* **1983**, 189-196.

[13] (a) Ferguson, S. B.; Seward, E. M.; Diederich, F.; Sanford, E. M.; Chou, A.; Inocencio-Szweda, P.; Knobler, C. B. *J. Org. Chem.* **1988**, *53*, 5593-5595. (b) Diederich, F.; Dick, K.; Griebel, D. *Chem. Ber.* **1985**, *118*, 3588-3619.

[14] Baldwin, J. E.; Crossley, M. J.; Klose, T.; O'Rear (III), E. A.; Peters, M. K. *Tetrahedron* **1982**, *38*, 27-39.

[15] Badger, G. M.; Jones, R. A.; Laslett, R. L. *Aust. J. Chem.* **1964**, *17*, 1157-1163.

[16] Krieger, C.; Diederich, F. *Chem. Ber.* **1985**, *118*, 3620-3631.

[17] Fillers, J. P.; Ravichandran, K. G.; Abdalmuhdi, I.; Tulinsky, A.; Chang, C. K. *J. Am. Chem. Soc.* **1986**, *108*, 417-424. For structures of octaalkylporphyrins with formyl and alkenyl groups on only one *meso*-position see: (a) Fuhrhop, J.-H.; Witte, L.; Sheldrick, W. S. *Liebigs Ann. Chem.* **1976**, 1537-1559. (b) Sheldrick, W. S. *Acta Cryst. B* **1978**, *B34*, 663-665.

[18] Collman, J. P.; Chong, A. O.; Jameson, G. B.; Oakley, R. T.; Rose, E.; Schmittou, E. R.; Ibers, J. A. *J. Am. Chem. Soc.* **1981**, *103*, 516-533.

[19] Barkigia, K. M.; Chantranupong, L.; Smith, K. M.; Fajer, J. *J. Am. Chem. Soc.* **1988**, *110*, 7566-7567.

[20] Dr. Jack Fajer, Brookhaven National Laboratory, personal communication.

[21] (a) Scheidt, W. R.; Kastner, M. E.; Hatano, K. *Inorg. Chem.* **1978**, *17*, 706-710. (b) Scheidt, W. R.; Reed, C. A. *Inorg. Chem.* **1978**, *17*, 710-714.

[22] Simonis, U.; Walker, F. A.; Lee, P. L.; Hanquet, B. J.; Meyerhoff, D. J.; Scheidt, W. R. *J. Am. Chem. Soc.* **1987**, *109*, 2659-2668.

[23] Chiaroni, P. A.; Riche, C.; Bied-Charreton, C.; Dubois, J. C. *Acta Cryst.* **1988**, *C44*, 429-432.

[24] Structure of H_2O-ligated Zn(TPP): Glick, M. D.; Cohen, G. H.; Hoard, J. L. *J. Am. Chem. Soc.* **1967**, *89*, 1996-1998.

[25] Some structures of pyridine-ligated zinc porphyrins: (a) Collins, D. M.; Hoard, J. L. *J. Am. Chem. Soc.* **1970**, *92*, 3761-3771. (b) Cullen, D. L.; Meyer, E. F., Jr. *Acta Cryst.* **1976**, *B32*, 2259-2269. (c) Bobrik, M. A.; Walker, F. A. *Inorg. Chem.* **1980**, *19*, 3383-3390. (d) Hatano, K.; Kawasaki, K.; Munakata, S.; Iitaka, Y. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 1985-1992.

[26] (a) Hambright, P. *J. Chem. Soc. Chem. Commun.* **1967**, 470-471. (b) Miller, J. R.; Dorough, G. D. *J. Am. Chem. Soc.* **1952**, *74*, 3977-3981.

[27] Schauer, C. K.; Anderson, O. P.; Eaton, S. S.; Eaton, G. R. *Inorg. Chem.* **1985**, *24*, 4082-4086.

[28] Nardo, J. V.; Dawson, J. H. *Inorg. Chim. Acta* **1986**, *123*, 9-13.

[29] Kirksey, C. H.; Hambright, P.; Storm, C. B. *Inorg. Chem.* **1969**, *8*, 2141-2144.

[30] Cole, S. J.; Curthoys, G. C.; Magnusson, E. A.; Phillips, J. N. *Inorg. Chem.* **1972**, *11*, 1024-1028.

[31] Collman, J. P.; Brauman, J. I.; Fitzgerald, J. P.; Hampton, P. D.; Naruta, Y.; Sparapany, J. W.; Ibers, J. A. *J. Am. Chem. Soc.* **1988**, *110*, 3477-3486.

[32] Stewart, R. F.; Davidson, E. R.; Simpson, W. T. *J. Chem. Phys.* **1965**, *42*, 3175-3187.

[33] International Tables for X-ray Crystallography; Kynoch Press: Birmingham, England, 1974; Vol IV.