Four-Atom-Linked Capped Porphyrins: Synthesis and Characterization

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Received December 5, 1995[⊗]

Three new capped porphyrins, $H_2(OC_2OPor)$ (**7**), $H_2(OC(CO)NPor)$ (**13**), and $H_2(OC_2NPor)$ (**14**), to be used as heme model compounds, have been synthesized and characterized. These compounds have the shortest linkages between cap and porphyrin plane of any four-arm capped porphyrins synthesized to date. The general synthetic procedure for $H_2(OC_2OPor)$ involves the reaction of a tetraaldehyde "cap" with pyrrole to form the capped porphyrin. In the synthesis of the tetraamide-capped porphyrin, $H_2(OC(CO)NPor)$, a tetraacid chloride cap is reacted with *meso*-α,α,α,α-tetra(*o*-aminophenyl)porphyrin. The amide groups may be reduced to form $H_2(OC_2NPor)$. With the use of $FeBr_2$, Fe^{2+} may be inserted in high yield into $H_2(OC_2OPor)$ and $H_2(OC(CO)NPor)$. The crystal structures of $H_2(OC_2NPor)$, $Fe(OC_2OPor)(OMe)$, and $[Fe(OC_2OPor)]_2(\mu\text{-}O)$ provide details on the types and amounts of cap expansion necessary to accommodate small ligands of biological interest, such as O_2 and CO.

Introduction

Since the invention of the synthetic oxygen-binding hemoprotein models, the "chelated" porphyrins,[1,2] much attention has been focused on the relatively low affinity native hemoproteins show for CO compared with most such models[3,4] and with some mutagenically-altered proteins.[5] Among those factors believed to affect the binding of distal ligands, particularly CO and O_2, to models and hemoproteins alike are steric influence, hydrogen bonding, dipolar repulsion, and the proximal base.[4,5] Whereas the problem, and lack of a solution, of sterics versus electronics pervades biological chemistry it is possible to change distal steric factors in the binding of small molecules to model systems. For example, the "capped" porphyrins[6] are designed to provide a barrier above the porphyrin on the distal side. If the porphyrin-to-cap distance at maximum extension is sufficiently short, then the binding of CO to form a linear Fe−C−O linkage will be discouraged whereas the binding of O_2 to form a Fe−O−O linkage with a 120° bond angle will not. In general, capped porphyrins are derivatives of 5,10,15,20-tetraphenylporphine with three arms linked to the 1,3,5 positions of a benzene cap[7] or more commonly with four arms linked to the 1,2,4,5 positions of a benzene cap.[6,8−10] In the three-arm capped porphyrins, the so-called "pocket" porphyrins, the entire superstructure is sufficiently flexible so that the cap can move off its central position and little steric demands are placed on the nearly linear Fe−C−O linkage.[11] Previous to our work,[12−14] the known four-arm benzene-capped porphyrins had a minimum linkage of five[15] atoms between the cap and the porphyrin and showed little inhibition to CO binding.[16,17] An objective of our work has thus been to synthesize four-atom-linked capped porphyrins where inhibition of CO binding would be expected. In two previous papers,[12,13] the synthesis, structure, and binding properties of CO to the Fe derivatives of two such capped porphyrins, $H_2(OC_2OPor)$ and $H_2(OC(CO)NPor)$, were reported. Remarkable steric inhibition is achieved with these systems. $Fe(OC_2OPor)$(1-MeIm) has a $P_{1/2}^{(CO)}$[18] value of 100 Torr at 25 °C, about 10^3 times higher than is found in all but one other compound;[19] the $Fe(OC(CO)NPor)$(base) system binds neither CO nor O_2 up to pressures of 100 atm. This paper presents an expanded account of the synthesis of these systems along with the synthesis of a third four-atom-linked capped porphyrin, $H_2(OC_2NPor)$. In addition, X-ray crystallographic features of derivatives of these four-atom-linked capped porphyrins are reported.

[⊗] Abstract published in *Advance ACS Abstracts,* April 15, 1996.

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(15) An *n*-atom-linked capped porphyrin has *n* atoms connecting the *plane* of the benzene cap to each of the *ortho*-C atoms of the 5,10,15,20-tetraphenylporphyrinato base.
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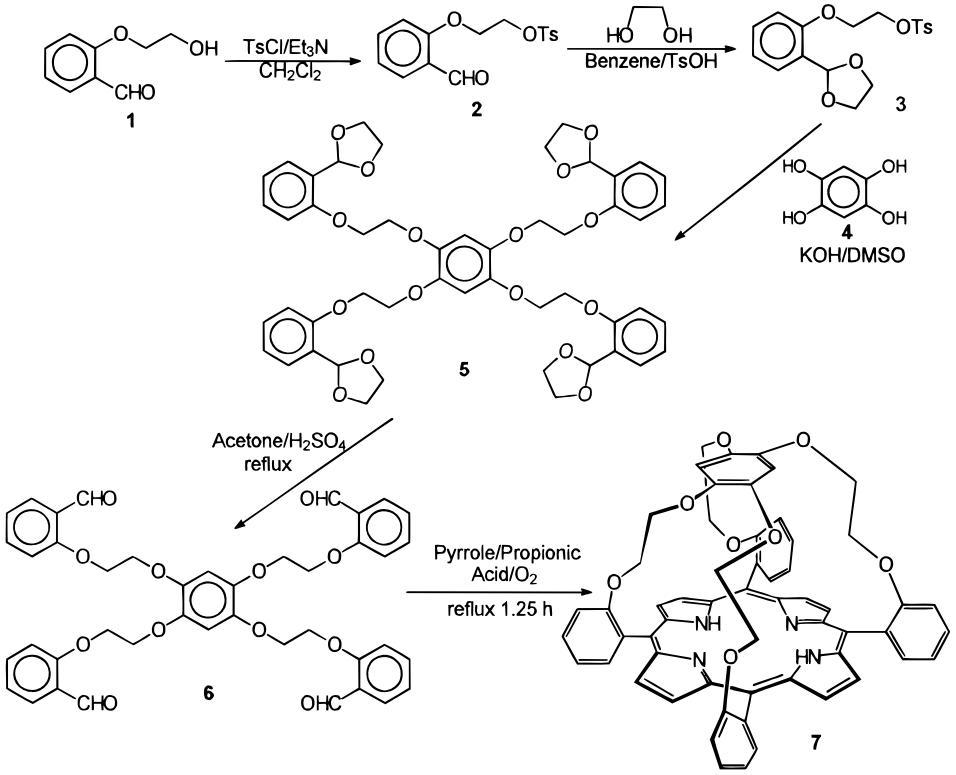
(18) $P_{1/2}^{(CO)}$ = the pressure of CO needed to carbonylate one half of the porphyrin molecules in the system.
(19) A cyclam-capped porphryin system has been reported[37] that binds O_2 normally but does not bind CO at 1 atm pressure.

S0022-3263(95)02161-X CCC: $12.00

Scheme 1



Results

Synthesis. Two different approaches were used in the synthesis of the new capped porphyrins. The porphyrin $H_2(OC_2OPor)$ (**7**) was prepared by the method of Almog et al.[6] where a tetraaldehyde is condensed with pyrrole under high dilution conditions ($\sim 5 \times 10^{-3}$ M). The porphyrin $H_2(OC(CO)NPor)$ (**13**) was synthesized by the "cap plus porphyrin" method,[7] where a cap with functional groups (acyl chlorides) is condensed with the α,α,α,α-atropisomer of a functionalized tetraphenylporphyrin (TAPP[20,21]). $H_2(OC_2NPor)$ (**14**) was synthesized by the reduction of the amide groups of $H_2(OC(CO)NPor)$ (**13**).

The synthesis of $H_2(OC_2OPor)$ (**7**) is summarized in Scheme 1. The procedure makes use of the hydroxy aldehyde **1**, first prepared by Almog et al.[6] Aldehyde **1** was treated with tosyl chloride in CH_2Cl_2/Et_3N to afford the tosyl aldehyde **2** in 52% yield. This reaction essentially halted after 20 min at 5 °C; extending reaction times up to 24 h or treating with a large excess of tosyl chloride and Et_3N or both did not force the reaction to completion. Recrystallization from methanol, followed by 20% aqueous acetic acid, gave **2**. Protection of aldehyde **2** with ethylene glycol yielded **3**. In the next step the tetraacetal **5** was obtained in about 59% yield in a one-pot reaction of 1,2,4,5-tetrahydroxybenzene (**4**) first with powdered KOH in DMSO and then with the ethylene acetal **3**. Deprotection of **5** took place readily in acetone/H_2SO_4 to give the tetraaldehyde **6**. Successful condensation of **6** with pyrrole took place in refluxing propionic acid ($\sim 5 \times 10^{-3}$ M) to give the capped porphyrin $H_2(OC_2OPor)$ (**7**) in 11% yield after extensive chromatography.

Scheme 2 describes the synthesis of $H_2(OC(CO)NPor)$ (**13**) and $H_2(OC_2NPor)$ (**14**). As in the reaction of tosyl acetal (**3**) with tetrahydroxybenzene (**4**), the reaction of ethyl bromoacetate (**8**) with **4** took place in KOH/DMSO to afford the tetraester product **9** in 31% yield after workup. A substantial amount of saponified product **10** could also be recovered from the crude reaction mixture. However, isolation of the ester followed by saponification to give **10** was cleaner and gave a higher yield. The acid **10** was readily converted to the acyl chloride **11** by treatment with oxalyl chloride/DMF (1 drop) in THF. Reaction of the acyl chloride **11** with TAPP[20] (**12**) in CH_2Cl_2/pyridine afforded the amide-capped porphyrin $H_2(OC(CO)NPor)$ (**13**) in almost 70% yield. Subsequent reduction of the amide groups of **13** with BH_3·THF reduced not only the amide carbonyl groups but also the porphyrin ring to give a chlorin that was not characterized. This chlorin was oxidized with DDQ to afford $H_2(OC_2NPor)$ (**14**) in 31% yield.

Synthesis of $Fe^{II}(OC_2OPor)$ was achieved by reacting $H_2(OC_2OPor)$ (**7**) with $FeBr_2$ in the presence of K_2CO_3 under anaerobic conditions.[13] The dimer, $[Fe(OC_2OPor)]_2(\mu\text{-O})$, was formed immediately upon exposure to air. In an attempt to obtain crystals of $Fe(OC_2OPor)(CO)(1\text{-MeIm})$ from the diffusion of CH_3OH into a $CHCl_3$ solution of $Fe(OC_2OPor)$ and 1-MeIm under 1 atm of CO pressure, crystals of $Fe(OC_2OPor)(OMe)$ were inadvertently isolated. That the compound is $Fe^{III}(OC_2OPor)(OMe)$ rather than $Fe^{II}(OC_2OPor)(HOMe)$ was established from an analysis of bond valence sums.[22-24]

Crystallographic Details. The crystal structures of $[Fe^{III}(OC_2OPor)]_2(\mu\text{-O})$, $Fe^{III}(OC_2OPor)(OMe)$, and $H_2(OC_2NPor)$ (Figure 1), in combination with the previously

(20) TAPP = *meso*-α,α,α,α-tetra(*o*-aminophenyl)porphyrin.
(21) Lindsey, J. *J. Org. Chem.* **1980**, *45*, 5215.

(22) The following r_o values were employed: $Fe^{III}-O = 1.759$, $Fe^{II}-O = 1.734$, $Fe^{III}-N = 1.855$, and $Fe^{II}-N = 1.806$ Å.[23,24] The bond valence sums for $Fe(OC_2OPor)(MeO(H?))$ are 3.03 when Fe^{III} values are used and 2.73 when Fe^{II} values are used.
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Scheme 2

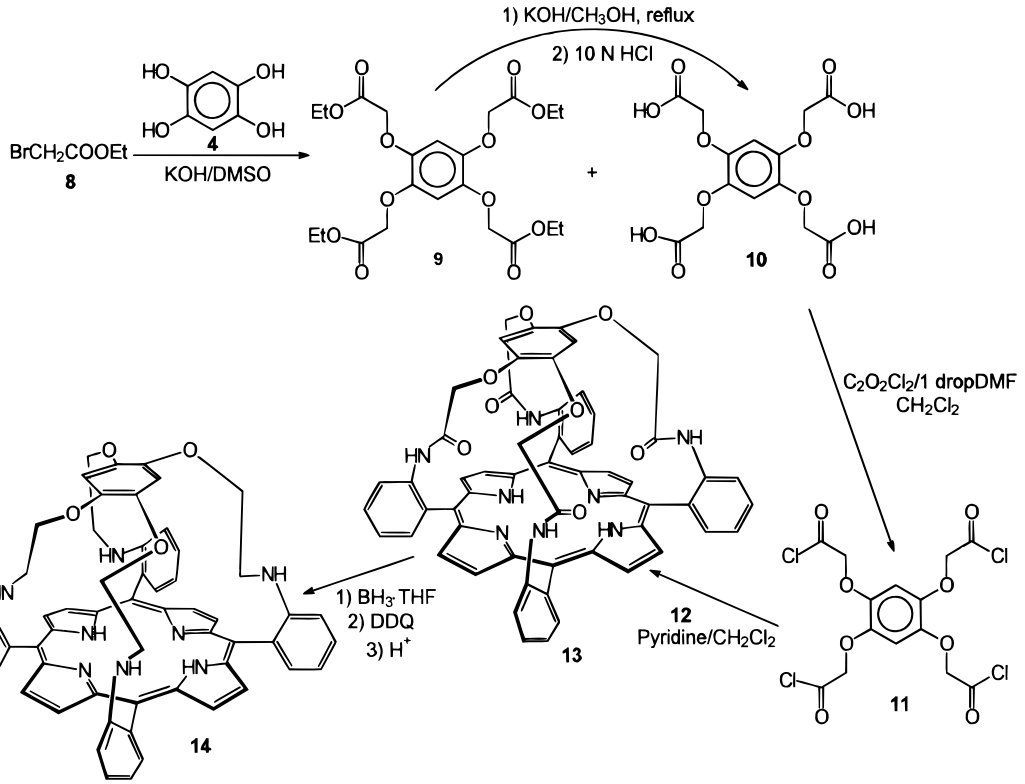

Table 1. Distortions in Crystallographically Characterized Capped Porphyrins

compd	vertl displacement[a] (Å)	horizl displacement[b] (Å)	avg displacement from mean 24 atom plane	<Fe−C−O (deg)	ref
Fe(C_2-Cap)(CO)(1-MeIm)	5.57, 5.67	0.30, 0.00	0.084, 0.085	172.9(6), 175.9(6)	25
Fe(OC_3OPor)(CO)(1-MeIm)	5.55	0.00	0.075	173.9(7)	26
H_2(OC_2OPor)	3.81	0.54	0.102		12
[Fe(OC_2OPor)]$_2$(μ-O)	3.46	0	0.053		this paper
Fe(OC_2OPor)(OMe)	3.93	0.54	0.070		this paper
H_2(OC(CO)NPor)	3.90	1.1	0.061		12
H_2(OC_2NPor)	4.02	1.21	0.074		this paper

[a] Vertical displacement is defined as the perpendicular distance of the cap centroid from the mean porphyrin plane. [b] Horizontal displacement is the horizontal distance of the cap centroid from the porphyrin centroid when the cap centroid is projected onto the plane of the porphyrin.

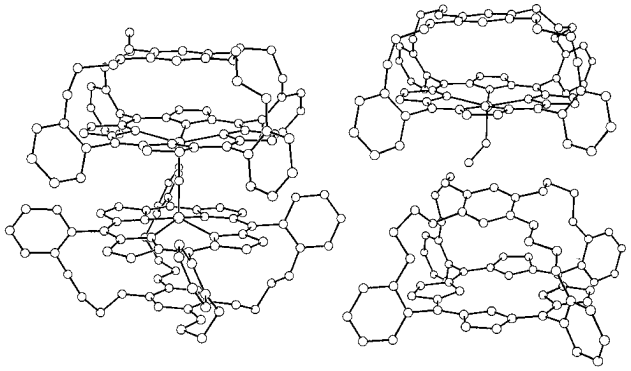

Figure 1. Views of [Fe(OC_2OPor)]$_2$(μ-O) (left), Fe(OC_2OPor)(OMe) (top right), and H_2(OC_2NPor) (bottom right).

published[12] structures of H_2(OC_2OPor) and H_2(OC(CO)NPor), provide details on the conformational changes that occur to accommodate small molecules under the cap.

Analysis of the three OC_2OPor structures and the H_2(OC(CO)NPor) structure provides an explanation for why these porphyrins show very low or no affinity for CO or O_2. Table 1 summarizes the types and amounts of distortion in these structures relative to those of the two five-atom-linked capped porphyrins Fe(C_2-Cap)(CO)(1-MeIm)[25] and Fe(OC_3OPor)(CO)(1-MeIm).[26] In these five-atom-linked capped porphyrin structures, in which there is an essentially linearly coordinated CO molecule under each cap, the average perpendicular distance from the cap to the mean porphyrin plane is ~5.6 Å. This suggests that significant amounts of distortion and steric strain are required to accommodate a linear CO molecule under the cap of a four-atom-linked capped porphyrin—either the CO must bend significantly or the cap must expand between ~1.6 and 2.1 Å to accommodate a linearly bound CO molecule. The resultant energetics are reflected in the large $P_{1/2}^{(CO)}$ value for CO binding in the OC_2OPor system (Table 2). In the H_2(OC(CO)NPor) structure the amide arms are planar, as expected, with average deviations from the mean amide plane ranging from 0.01 to 0.08 Å. The barrier to rotation about a single amide bond is 50−100 kJ/mol;[27] hence, there is a very large energy barrier to be overcome if this porphyrin is to expand and bind any small molecule. In fact, Fe(OC(CO)NPor)(1-MeIm) binds neither CO nor O_2 up to pressures of 7.7 ×

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Table 2. CO Binding to Hemoglobin and Capped Porphyrins (25 °C)

compd	$P_{1/2}^{(CO)}$ (Torr)	ref
hemoglobin	$\sim 1 \times 10^{-3}$	38, 39
Fe(C_2-Cap)(1-MeIm)	5.4×10^{-3}	16
Fe(OC_3OPor)(1-MeIm)	2.6×10^{-4}	36
Fe(OC_2OPor)(1-MeIm)	100	13
Fe(OC(CO)NPor)(1-MeIm)	$>7.7 \times 10^{4}$	13

10^4 Torr (100 atm).[13] Because H_2(OC_2NPor) is sensitive to light and air, no attempts have been made to metalate it and study CO and O_2 binding. But from the structure of H_2(OC_2NPor) (Table 1) we expect its Fe derivatives will also have very large $P_{1/2}^{(CO)}$ values.

Experimental Section

General Procedures. With the following exceptions all solvents and reagents were used as purchased. DMSO was deoxygenated with the freeze−pump−thaw technique just prior to use. Propionic acid was refluxed over $K_2Cr_2O_7$, followed by two fractional distillations. Pyrrole was distilled just prior to use. Pyridine was dried over 4 Å molecular sieves. Methylene chloride (in the synthesis of **13** only) was distilled from K_2CO_3. Literature procedures were followed in the preparation of *meso*-α,α,α,α-tetra(*o*-aminophenyl)porphyrin (TAPP) (**12**),[21,28] 2-(2′-hydroxyethoxy)benzaldehyde (**1**),[6] and 1,2,4,5-tetrahydroxybenzene (**4**).[29]

2-(2′-(Tosyloxy)ethoxy)benzaldehyde (2). A 1-L three-necked round-bottom flask was equipped with a thermometer, nitrogen inlet, and dropping funnel and was charged with CH_2Cl_2 (500 mL), hydroxy aldehyde **1** (109 g, 0.66 mol),[6] and *p*-toluenesulfonyl chloride (207.6 g, 1.0 mol). The flask was cooled to 5 °C and purged for 10 min. Triethylamine (110.2 g, 1.1 mol) was then dropped in over 20 min; the temperature of the flask was maintained at 10−15 °C with the use of an ice bath. The contents were stirred for 12 h with gradual warming to room temperature. The contents were transferred to a 2-L separatory funnel and washed with 500 mL each of water, 5% HCl, and water. The organic layer was then dried with $MgSO_4$ and concentrated on a rotary evaporator (45 °C bath). The crude product was recrystallized once from CH_3OH and once from 80%HOAc/20%H_2O to give the aldehyde **2** (110 g, 0.34 mol, 52%) as colorless prisms or flakes: mp 108−110 °C; ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H), 4.29 (m, 2H), 4.43 (m, 2H), 6.88 (d, 1H), 7.04 (t, 1H), 7.33 (d, 2H), 7.51 (m, 1H), 7.79 (d, 3H), 10.17 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.71, 65.84, 67.89, 112.33, 121.47, 124.90, 127.90, 128.32, 130.06, 132.51, 135.97, 145.44, 160.22, 189.40; MS ($CHCl_3$) *m*/*e* 320 (30), 213 (9), 199 (27), 165 (12), 155 (17), 148 (68); HRMS calcd for $C_{16}H_{16}O_5S$ *m*/*e* 320.0718, found 320.0708.

2-(2′-(Tosyloxy)ethoxy)benzaldehyde Ethylene Acetal (3). 2-(2′-(Tosyloxy)ethoxy)benzaldehyde (**2**) (20 g, 62 mmol), ethylene glycol (6.1 g, 102 mmol), *p*-toluenesulfonic acid (100 mg), and benzene (125 mL) were placed in a 500 mL round-bottom flask equipped with a magnetic stir bar, a Dean−Stark trap, and a condenser. The mixture was stirred and held at reflux for 12 h and then cooled. An additional 125 mL of benzene was added, followed by triethylamine (5 mL). The benzene solution was then transferred to a separatory funnel, washed with water (2 × 100 mL), and filtered through a Na_2SO_4 cone into a tared 500 mL round-bottom flask. The benzene was removed on a rotary evaporator, and traces of benzene were removed under high vacuum. The solid **3** so obtained (20 g, 55 mmol, 89%), mp 75−78 °C, was of sufficient purity for use in the next step: ^{1}H NMR δ 3.43 (s, 3H), 4.00 (m, 2H), 4.12 (m, 2H), 4.21 (m, 2H), 4.38 (m, 2H), 6.03 (s, 1H), 6.78 (d, 1H), 7.00 (t, 1H), 7.25 (t, 1H), 7.31 (d, 2H), 7.50 (dd, 1H), 7.80 (d, 2H); ^{13}C NMR ($CDCl_3$) δ 21.56, 65.09, 65.92, 67.89, 98.93, 112.09, 121.23, 126.44, 127.06, 127.74, 128.17, 129.74, 130.11, 132.66, 144.79, 156.06; MS ($CHCl_3$) *m*/*e* 364 (47), 199 (56), 165 (100), 149 (54), 121 (36), 91 (80); HRMS calcd for $C_{18}H_{20}O_6S$ *m*/*e* 364.0981, found 364.0965.

1,2,4,5-Tetrakis(2′-(*o*-(1″,3″-dioxolan-2″-yl)phenoxy)ethoxy)benzene (5). A 250-mL three-necked round-bottom flask was equipped with an N_2 inlet, a dropping funnel, a powder addition funnel, and a magnetic stir bar. Degassed DMSO (150 mL) was added to the flask, and the flask was purged with N_2 for 15 min. 1,2,4,5-Tetrahydroxybenzene (**4**) (0.5 g, 3.5 mmol)[29] was then dissolved with stirring, followed by finely powdered KOH (3.15 g, 56.3 mmol). After the solution was stirred for 1 min powdered acetal **3** (10 g, 27.4 mmol) was added all at once and the resultant mixture was stirred at room temperature for 1 h. Then the contents of the flask were poured into 500 mL of stirred saturated brine. The semisolid agglomerate that resulted was allowed to float to the top of the brine. Filtration through a large Büchner funnel afforded the crude product as a semisolid glass. This was purified by chromatography through a 4 × 30 cm column of silica (2% MeOH/$CHCl_3$ eluent) followed by recrystallization from $CHCl_3$/hexane to give the pure product **5** (1.88 g, 2.1 mmol, 59%) as a white microcrystalline powder: mp 123−125 °C; ^{1}H NMR ($CDCl_3$) δ 3.96 (m, 8H), 4.10 (m, 8H), 4.26 (m, 8H), 4.29 (m, 8H), 6.13 (s, 4H), 6.74 (s,2H), 6.88 (d, 4H), 6.98 (t, 4H), 7.27 (dt, 4H), 7.51 (dd, 4H); ^{13}C NMR ($CDCl_3$) δ 65.15, 67.25, 69.01, 98.99, 107.45, 112.15, 120.82, 126.24, 127.02, 130.22, 143.76, 156.79; FAB MS (3-nitrobenzyl alcohol) *m*/*e* 933 (26, Na adduct), 910 (100), 866 (7), 718 (5.2), 307 (16); FAB HRMS calcd for $C_{50}H_{54}O_{16}$ *m*/*e* 910.3412, found 910.3409.

1,2,4,5-Tetrakis(2′-(*o*-formylphenoxy)ethoxy)benzene (6). The tetraacetal **5** (720 mg, 0.79 mmol) was dissolved in refluxing acetone (50 mL). To the refluxing solution was added 1 drop of sulfuric acid. After about 2 min a precipitate formed. The suspension was refluxed for an additional 10 min. The contents of the flask were cooled to 15 °C, filtered, washed with 5% Et_3N/acetone, acetone, and ether, and then dried to give the tetraaldehyde **6** (460 mg, 0.63 mmol, 79%) as a white fluffy powder, mp 168−169 °C. Recrystallization from $CHCl_3$ increased the melting point to 173.5 °C: ^{1}H NMR (DMSO-d_6) δ 4.33 (t, 8H), 4.37 (t, 8H), 6.89 (s, 2H), 7.04 (t, 4H), 7.21 (d, 4H), 7.61 (m, 8H), 10.27 (s, 4H); ^{13}C NMR (DMSO-d_6, 70 °C) δ 67.75, 68.48, 106.90, 113.80, 120.59, 124.60, 127.11, 135.63, 143.16, 160.48, 188.71; FAB MS (3-nitrobenzyl alcohol) *m*/*e* 757 (65, Na adduct), 735 (100), 613 (30); EI MS (3-nitrobenzyl alcohol) *m*/*e* 734 (28), 434 (26), 368 (100); FAB HRMS calcd for $C_{42}H_{38}O_{12}$ *m*/*e* 734.2363, found 734.2365.

H_2(OC_2OPor) (7). A 1-L two-necked round-bottom flask equipped with a condenser, magnetic stir bar, and an air injection inlet was charged with 600 mL of doubly distilled propionic acid. The acid was brought to near reflux, whereupon the tetraaldehyde **6** (1.0 g, 1.74 mmol) was added. The mixture was heated at reflux while being stirred. When the aldehyde had all dissolved, freshly distilled pyrrole (730 mg, 10.9 mmol) was added and a trickle of air (120 mL/min) was blown through the refluxing solution. After 1.25 h the propionic acid was completely removed by distillation under reduced pressure. The dry, purple-black residue that remained was dissolved with 200 mL of hot $CHCl_3$, filtered through Celite, and loaded onto a 5 × 30 cm silica gel column. Flash chromatography (neat $CHCl_3$, increasing to 5% MeOH/$CHCl_3$) gave a fast-running fraction that was collected and reeluted through silica (2 columns: 1% MeOH/$CHCl_3$ followed by 1% acetone/CH_2Cl_2). The dark red band so obtained was collected, concentrated to dryness on a rotary evaporator, and recrystallized from CH_2Cl_2/hexane to give the product (99 mg, 0.15 mmol, 10.7%) as a lustrous purple powder: UV−vis ($CHCl_3$) λ_{max} (log ϵ) 402 (sh, 4.92), 421 (5.56), 484 (sh, 3.48), 518 (4.24), 551 (3.68), 591 (3.75), 647 (3.37); ^{1}H NMR ($CDCl_3$) δ −3.16 (s, 2H), 2.41 (m, 4H), 2.55 (m, 4H), 3.63 (s, 2H), 3.69 (m, 4H), 3.85 (m, 4H), 7.35 (d, 4H), 7.50 (t, 4H), 7.76 (t, 4H), 8.28 (d, 4H), 8.71 (s, 8H); ^{13}C NMR (DMSO-d_6, 70 °C) δ 67.76, 71.37, 106.90, 121.43, 129.05 (broad), 129.91, 131.62 (broad), 134.37, 134.52, 139.88, 160.28; FAB MS (3-nitrobenzyl alcohol) *m*/*e* 925 (100); FAB HRMS calcd for $C_{58}H_{44}O_8N_4 \cdot H^+$ *m*/*e* 925.3237, found 925.3260. Anal. Calcd for $C_{58}H_{44}N_4O_8$: C, 75.31; H, 4.79; N, 6.06. Found: C, 75.03; H, 5.01; N, 5.90.

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Benzene-1,2,4,5-tetrakis(oxyacetic acid) Tetraethyl Ester (9) and Benzene-1,2,4,5-tetrakis(oxyacetic acid) (10) (Method 1). A 1-L three-necked round-bottom flask, equipped with a paddle stirrer, N_2 inlet, thermometer, ice bath, and powder funnel, was charged with degassed DMSO (500 mL) and purged for 10 min. 1,2,4,5-Tetrahydroxybenzene (**4**) (5 g, 35 mmol)[29] was then dissolved in the stirred DMSO. Powdered KOH (30.5 g, 543 mmol) was added. The resultant pearl-colored suspension was cooled to 19 °C in an ice bath until 20−30% of the DMSO had solidified. Ethyl bromoacetate (**8**) (60 g, 279 mmol) was added over 30 s; the temperature was maintained at ≈22−25 °C with the ice bath. The mixture was stirred for an additional 35 min and then poured over cracked ice/acetic acid (2 kg/40 g) with stirring. The resulting mixture was diluted to 3.5 L with water, saturated with salt, and extracted with CH_2Cl_2 (3 × 500 mL). The CH_2Cl_2 extracts were washed with dilute KOH until the water layer no longer turned red. The CH_2Cl_2 extracts were then washed with brine until the organic layer became clear. The organic layer was dried over Na_2SO_4 and concentrated on a rotary evaporator. Residual DMSO was removed at 40−80 °C/0.25 Torr, leaving a clear oil that solidified upon standing overnight. This solid was recrystallized from CH_3OH to give pure **9** (5.33 g, 11 mmol, 31%): mp 88−91 °C; ^{1}H NMR ($CDCl_3$) δ 1.29 (t, 12H), 4.24 (q, 8H), 4.64 (s, 8H), 6.69 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 14.55, 61.63, 68.19, 108.10, 143.90, 169.38; MS ($CHCl_3$) *m*/*e* 486 (100), 399 (45); HRMS calcd for $C_{22}H_{30}O_{12}$ *m*/*e* 486.1737, found 486.1715.

The mother liquor from the aqueous workup of the above reaction contained a considerable amount of undissolved material. It was suction filtered over a 48 h period to give a muddy-white substance. This substance was placed in water (500 mL) containing NaOH (3 g), held at reflux for 1 h, and filtered while hot. The clear hot filtrate was acidified with HCl, concentrated to 200 mL on a rotary evaporator, and cooled to 10 °C. The precipitate was collected by filtration, washed (H_2O), and dried to give 3.78 g of tetraacid **10** (10 mmol, 29%), identical in all respects to the tetraacid obtained by hydrolysis of the ester: mp 280 °C dec; ^{1}H NMR (DMSO-d_6) δ 4.61 (s, 8H), 6.69 (s, 2H), 12.87 (br, 4H); ^{13}C NMR (DMSO-d_6) δ 66.45, 105.55, 142.08, 170.10; MS (glycerol) *m*/*e* 373 (29), 315 (22), 227 (60), 113 (100); HRMS calcd for $C_{14}H_{13}O_{12}^+$ *m*/*e* 373.0407, found 373.0540.

Benzene-1,2,4,5-tetrakis(oxyacetic acid) (10) (Method 2). The above tetraester (870 mg, 1.79 mmol) was dissolved in CH_3OH (200 mL). To this stirred solution was added powdered KOH (800 mg, 14.3 mmol). The stirred mixture was held at reflux overnight, during which time a white precipitate formed. This precipitate was collected by filtration and dissolved in H_2O (100 mL). The solution was heated to boiling and filtered while hot. The filtrate, when acidified while hot with 10 N HCl, deposited **10** upon cooling. Product **10** was collected, washed with water, and dried (660 mg, 1.76 mmol, 98%).

Benzene-1,2,4,5-tetrakis(oxyacetic acid chloride) (11). A mixture of the above acid (400 mg, 1.07 mmol), oxalyl chloride (3 mL), THF (30 mL), and DMF (1 drop) was held at reflux under N_2 for 20 min, during which time the acid dissolved completely. The volatile components were removed under vacuum to leave a yellow powder that was completely soluble in CH_2Cl_2. This crude acid chloride (400 mg, 0.89 mmol, 83%) was used without further purification.

H_2(OC(CO)NPor) (13). Under an N_2 atmosphere, TAPP (**12**)[21,28] (800 mg, 1.19 mmol) was dissolved in dry CH_2Cl_2 (1.6 L) that contained pyridine (4 mL); the solution was cooled to −5 °C with a dry ice bath. The tetraacid chloride **11** (1.6 g, 3.56 mmol) was dissolved in CH_2Cl_2 (50 mL) and added dropwise through a 1 × 3 cm alumina column to the solution of **12**. Reaction progress was followed by TLC. When the reaction was judged to be complete (∼5 min), the flask contents were concentrated to near dryness on a rotary evaporator. The contents were then diluted to 200 mL with 25% acetone/75% chloroform and eluted through a silica gel column (4 × 40 cm) with 25% acetone/75% chloroform as eluent. The fast-running dark band was collected and concentrated on a rotary evaporator, the solution being diluted periodically with methanol. The solid that separated was collected by filtration and triturated with hot water, then methanol, and dried under vacuum to give product **13** (786 mg, 0.80 mmol, 67.4%): UV−vis ($CHCl_3$) λ_{max} (log ϵ) 416 (5.05), 510 (3.81), 540 (3.07), 584 (3.27), 640 (2.72); ^{1}H NMR ($CDCl_3$) δ −3.01(s, 2H), 3.11 (d, 4H), 3.39 (s, 2H), 3.81 (d, 4H), 7.04 (s, 4H), 7.68 (t, 4H), 7.89 (t, 4H), 8.39 (q, 8H), 8.70 (d, 8H); ^{13}C NMR ($CDCl_3$) δ 69.03, 102.24, 114.16, 121.14, 123.77, 130.16 (broad), 132.16 (broad), 137.96, 140.19, 165.01; FAB MS (3-nitrobenzyl alcohol) *m*/*e* 977 (100); FAB HRMS calcd for $C_{58}H_{41}N_8O_8^+$ *m*/*e* 977.3047, found 977.3133. Anal. Calcd for $C_{58}H_{40}N_8O_8$: C, 71.29; H, 4.13; N, 11.47. Found: C, 71.56; H, 4.33; N, 11.77.

H_2(OC$_2$NPor) (14). A 500-mL three-necked round-bottom flask was equipped with an N_2 inlet and was purged. Dry THF (50 mL) and H_2OC(CO)NPor) (500 mg, 0.543 mmol) were added, and the flask was cooled to −50 °C. The solution was stirred and kept at −50 °C while 1 M borane−THF (80 mL, 80 mmol) was added and for 30 min thereafter. The reaction mixture was slowly warmed to room temperature and stirred for an additional 30 min. It was then quenched by the slow addition of ice−water (200 mL/100 mL THF). DDQ (500 mg, 2.42 mmol) was added to the solution, which was then stirred for an additional 1−2 min at 0−5 °C. The solution was next transferred to a round-bottom flask, and while the temperature was kept below 25 °C the THF was removed on a rotary evaporator. Chloroform was added periodically to the flask so that the porphyrin product was dissolved at all times. When the THF had all been removed, the liquids were filtered to remove boric acid. The organic layer was then separated and dried over Na_2SO_4, and with the temperature below 25 °C it was concentrated to dryness on a rotary evaporator. Purification of H_2(OC$_2$NPor) was accomplished by chromatography on silica gel (5% MeOH/$CHCl_3$). The fast-running fraction was concentrated on a rotary evaporator with continuous addition of CH_3OH at low temperature until precipitation was complete. The product was collected by filtration, washed with methanol, and dried in vacuo to give the product (155 mg, 0.169 mmol, 31%): UV−vis ($CHCl_3$) λ_{max}(log ϵ) 415 (5.11), 512 (3.79), 540 (3.05), 584 (3.29), 640 (2.71); ^{1}H NMR ($CDCl_3$) δ −2.96 (s, 2H), 1.54 (s, 2H) 2.36 (m, 4H), 2.81 (d, 4H), 3.00 (m, 8H), 3.15 (d, 4H), 3.68 (s, 2H), 7.03 (d, 4H) 7.27 (4H), 7.69 (t, 4H), 8.21 (d, 4H), 8.74 (d, 8H); ^{13}C ($CDCl_3$) δ 45.65, 68.36, 100.36, 113.69, 115.01, 117.48, 129.28 (broad), 129.80, 132.54 (broad), 140.37, 150.13; FAB HRMS calcd for $C_{58}H_{48}N_8O_4^+$ *m*/*e* 920.3798, found 920.3781. Anal. Calcd for $C_{58}H_{48}N_8O_4$: C, 75.63; H, 5.25; N, 12.17. Found: C, 75.90; H, 5.52; N, 12.34.

Fe(OC$_2$OPor). This compound was prepared by the reaction of $FeBr_2$ with **7** with the use of a literature procedure.[13]

[Fe(OC$_2$OPor)]$_2$(μ-O). This compound was prepared by exposing Fe(OC$_2$OPor) to air: UV−vis ($CHCl_3$) λ_{max} (log ϵ) 410 (5.21), 573(4.20), 610(3.69); FAB MS calcd for $C_{58}H_{42}FeN_4O_8$ (1/2 dimer − O) *m*/*e* 978.2, found 978.3.

Fe(OC$_2$OPor)(OMe). Attempts to isolate Fe^{II}(OC$_2$OPor)(CO)(1-MeIm) by diffusion of CH_3OH into a $CHCl_3$ solution of Fe(OC$_2$OPor) and 1-MeIm under 1 atm of CO pressure resulted in the isolation of Fe^{III}(OC$_2$OPor)(OMe).

Single-Crystal X-ray Studies.[30] **[Fe(OC$_2$OPor)]$_2$(μ-O)·*n*-Hexane.** Brown wedge-shaped crystals of [Fe(OC$_2$OPor)]$_2$(μ-O) were obtained by diffusion over a period of 2 months of *n*-hexane into a CH_2Cl_2 solution of [Fe(OC$_2$OPor)]$_2$(μ-O). Data from a selected crystal were collected by the ω scan method on an Enraf-Nonius CAD4 diffractometer. Unit cell dimensions were determined by least-squares refinement of 25 reflections that had been automatically centered on the diffractometer. Intensity data were processed and corrected for absorption.[31] A solution was found by direct methods. The final refinement[32] on F^2 involved an anisotropic model for all non-hydrogen atoms except for those C atoms assigned to residual electron density peaks that were presumed to result

(30) The authors have deposited atomic coordinates with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Center, 12 Union Road, Cambridge, CB2 1EZ, UK.

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from disordered hexane. The occupancies on these C atoms were refined. Crystallographic data: tetragonal; D_4^6-$P4_22_12$; $a = 15.855(3)$ Å, $c = 25.209(8)$ Å; $V = 6337(3)$ Å^3; ρ(calcd) = 1.363 g/cm^3; $Z = 2$; $\mu = 40$ cm^{-1}; Cu Kα radiation ($\lambda = 1.540\ 56$ Å); $T = 106(2)$ K; $R(F)$ ($F_o^2 > 2\sigma(F_o^2)$) = 0.080; $R_w(F^2)$ (all data) = 0.254.

Fe(OC$_2$OPor)(OMe)·4CH$_3$OH. The same procedures described above for data collection and reduction and for structure development were employed. The final refinement on F^2 involved an anisotropic model for all non-hydrogen atoms. Crystallographic data: triclinic, $C_i^1-P\bar{1}$; $a = 9.019(2)$ Å, $b = 11.651(2)$ Å, $c = 26.193(5)$ Å, $\alpha = 93.88(2)°$, $\beta = 90.52(2)°$, $\gamma = 99.71(2)°$; $V = 2706.0(9)$ Å^3; ρ(calc) = 1.392 g/cm^3; Z = 2; $\mu = 4$ cm^{-1}; Mo Kα_1 radiation ($\lambda = 0.7093$ Å); $R = 0.086$ ($F_o^2 > 2\sigma(F_o^2)$); $R_w(F^2) = 0.199$ (all data).

H$_2$(OC$_2$NPor)·*n*-Hexane. Purple bricks (~1 mm on an edge) of H$_2$(OC$_2$NPor) (**14**) were obtained by slow diffusion over a period of 1 month of CH$_3$OH into a CH$_2$Cl$_2$ solution of H$_2$(OC$_2$NPor). Crystals were cut to form a cube ~0.4 mm on a side. Unit cell parameters were determined by least-squares analysis of 37 reflections that had been automatically centered at 108(2) K on a Picker diffractometer.[33] The same procedures detailed above for data collection and reduction and for structure development were employed. The badly disordered solvent could not be modeled successfully. Consequently, the BYPASS[34] option in the program package PLATON[35] was used. In this method potential solvent regions in the crystal structure are identified from considerations of space filling, the contributions of the observed electron densities in these regions to the total structure factors are calculated by a discrete Fourier transform, and the results are incorporated into the structure factors for further least-squares refinement of the ordered part of the structure. The procedure is iterated to convergence. In the present instance electron density totaling 98 e$^-$ was subtracted, corresponding to one crystallographically independent *n*-hexane molecule. The final refinement on F^2 involved an anisotropic model for all porphyrin atoms. Crystallographic data: triclinic, $C_i^1-P\bar{1}$; $a = 8.807(4)$ Å, $b = 17.076(7)$ Å, $c = 17.825(7)$ Å, $\alpha = 83.08(2)°$, $\beta = 76.58(4)°$, $\gamma = 77.88(4)°$; $V = 2542(2)$ Å^3; ρ(calc) = 1.195 g/cm^3; μ = 0.9 cm^{-1}; MoKα_1 radiation ($\lambda = 0.7093$ Å); $R(F)$ ($F_o^2 > 2\sigma(F_o^2)$) = 0.106.

Acknowledgment. This research was supported by the National Institutes of Health (HL-13157).

Supporting Information Available: ^{1}H and ^{13}C NMR spectra of **1**–**3**, **5**, **6**, **9**, **10**, **13**, and **14** (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm edition of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO9521615

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