Synthesis of New Five-Atom-Linked Capped Porphyrins

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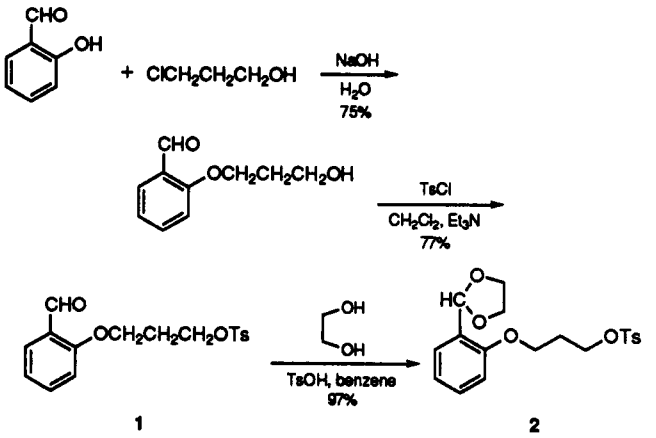
The synthesis and characterization of three new five-atom-linked "capped" porphyrins, 6, 12, and 18, are reported. The general synthetic procedure involves synthesis of a tetraaldehyde "cap" by reacting the five-atom "arm" with 1,2,4,5-tetrahydroxybenzene in DMSO solvent in the presence of KOH. The tetraaldehyde and pyrrole are reacted to form the capped porphyrin. These compounds are useful as models for the active sites of heme proteins.

Introduction

The modeling of ligand binding in heme proteins has been an active field of research over the last quarter century.[1-5] Such modeling involves the use of encumbered metalloporphyrins, in which a ligand, for example O_2 or CO, may be bound to the metal within a protected region, with the necessary base bound to the metal on the outside. While protection of bound CO is not essential, protection of bound O_2 is essential to prevent irreversible oxidation. Design of the protected region in terms of its size, shape, and polarity, in conjunction with thermodynamic and structural studies of the resultant ligand metalloporphyrins, is important in the assessment of steric and electronic factors involved in ligation. Among these encumbered porphyrins, "capped" systems, in which a cap, most often a benzene ring, is attached by means of three[6,7] or more often four[8] arms to the porphyrin core, have proved to be especially useful. The syntheses, characterization, and structures of capped porphyrin models have appeared in increasing number over the past few years.[9-18] Very recently, the syntheses of two four-atom-linked[19] benzene-capped[9] and several five-atom-linked "hydrocarbon-capped",[10] "pendant-capped",[11] and "bicyclooctane-capped"[12] porphyrins have been reported. Here, we report the design and synthesis of three new five-atom-linked benzene-capped porphyrins, H_2(OCCCOPor) (6), H_2(OCCCCPor) (12), and H_2((CO)OCCCPor) (18). Tetraphenylporphyrins with ether groups substituted on the phenyl rings are susceptible to destructive oxidation.[12] Porphyrins 12 and 18 lack such ether groups and therefore should be amenable to studies involving the binding of O_2.

Scheme I



Results and Discussion

The general methodology used in the synthesis of these porphyrins involved formation of the aldehyde arms first, linkage of these arms to 1,2,4,5-tetrahydroxybenzene to form the tetraaldehyde cap, and finally the condensation of the cap with pyyrole to form the capped porphyrin.

Synthesis of the Aldehyde Arms 2, 9, and 16. Arm 2: Alkylation of salicylaldehyde with 3-chloropropanol produced 2-(3-hydroxypropoxy)benzaldehyde in 75% yield.[20] Tosylation of the alcohol produced 2-[3-(tosyloxy)-propoxy]benzaldehyde (1) in 77% yield. The arm acetal 2 was made in 97% yield by stirring 1 in ethylene glycol and *p*-toluenesulfonic acid (Scheme I).

Arm 9: The aldehyde group in 2-bromobenzaldehyde was protected by converting it to an acetal and the Grignard reagent was formed. The Grignard reagent was reacted with 1,4-dibromobutane in the presence of cuprous bromide and HMPA–THF[12] to afford 8 in 79% yield. Compound 8 was reacted with KI in dry acetone to give arm 9 in 94% yield (Scheme II).

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(19) An n-atom-linked capped porphyrin has n atoms between the plane of the porphyrin and the plane of the cap.

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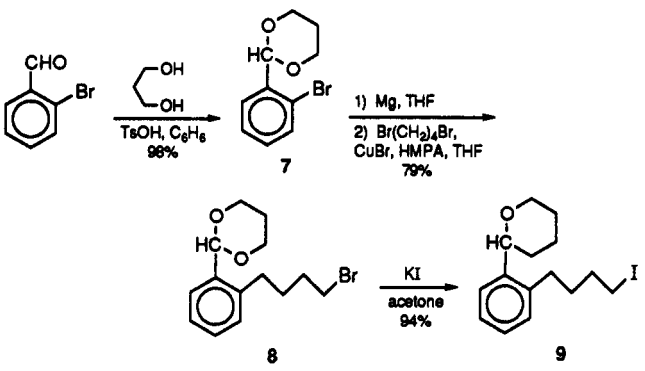
Scheme II



Arm 16: Compound 13 was obtained in 76% yield from the protection of one aldehyde group of phthalic dialdehyde with propane-1-3-diol, followed by treatment with 1 equiv of methyl triphenylphosphoranylidene acetate.[10] The carbon–carbon double bond was reduced with the use of Mg in dry methanol to give 81% yield of ester 14. Compound 14 was reduced with DIBAL to obtain the alcohol 15, which was deprotected with the use of pyridinium tosylate in wet acetone to afford arm 16 in 91% yield (Scheme III).

Synthesis of the Caps 5, 11, and 17. Caps 5 and 11: The tetraacetals 4 and 10 were obtained in 47 and 80% yield, respectively, through the nucleophilic attack of potassium tetrahydroxybenzene on the tosylate of 2 or the iodo group of 9.[9] The tetraacetals were easily deprotonated with the use of catalytic amounts of pyridinium *p*-tosylate in wet acetone to afford the tetraaldehydes 5 and 11 in 99% yield. The more common method of using H_2SO_4 in acetone to deprotect an acetal gave a mixture of products (Scheme IV).

Cap 17: The tetraaldehyde 17 was obtained in 26% yield from the reaction of pyromellitoyl chloride and 16 in NEt_3 and dry THF (Scheme III).

Synthesis of the Capped Porphyrins 6, 12, and 18. There are two procedures in general use for the synthesis of capped porphyrins by the condensation reaction of a tetraaldhyde cap and four pyrroles (Scheme V). In the procedure developed by Baldwin and co-workers[8,20] porphyrinogen formation and oxidation by air occur simultaneously. In the procedure developed by Lindsey and co-workers[21-23] the porphyrinogen is synthesized first and then in the same pot is oxidized with DDQ or *p*-chloranil. The yields of capped porphyrins by these two procedures (Baldwin, Lindsey) are 6 (13.2%, 6%); 12 (trace, 1.2%); 18 (4%, 6%) (Scheme IV).

Experimental Section

With the following exceptions all solvents and reagents were used as purchased. Toluene was distilled over sodium under N_2. THF was distilled under N_2 from sodium–benzophenone ketyl. DMSO was deoxygenated with the freeze-pump-thaw technique just prior to use. Proprionic acid was refluxed over potassium dichromate, followed by two fractional distillations. HMPA was dried over CaH_2 and distilled. Pyrrole was doubly distilled before use. 1,2,4,5-tetrahydroxybenzene was prepared by a literature method.[24] All reagents were obtained from Aldrich except Mg, KI, and Na_2SO_4, which were purchased from other commercial sources. Column chromatography was performed with the use of silica gel 60 (Baxter Healthcare Corp., 230-400 mesh).

Melting points were determined on a Mel-Temp melting point apparatus and are uncorrected. ^1H and ^{13}C NMR measurements were made with $CDCl_3$ as solvent on a Varian Gemini NMR spectrometer operating at 300 and 75.4 MHz, respectively. NMR chemical shifts are reported in parts per million with TMS as reference. EI and FAB low- and high-resolution mass spectra were recorded on a VG Analytical 70 SE quadrupole mass spectrometer. UV-visible spectra were recorded on a Cary 1E spectrophotometer.

2-[3-(Tosyloxy)propoxy]benzaldehyde (1). 2-(3-Hydroxypropoxy)benzaldehyde[8,20] (52.16 g, 289.8 mmol) and *p*-toluenesulfonyl chloride (82.88 g, 434.6 mmol) were dissolved in CH_2Cl_2 (600 mL) and cooled to 5 °C in a 1- L three-necked round-bottom flask equipped with a thermometer, N_2 inlet, and dropping funnel. Triethylamine was added dropwise into the flask, with stirring, and the temperature was carefully maintained below 10 °C for 12 h. The solution was washed with water, brine, and water, and then dried over Na_2SO_4. Solvent was removed under reduced pressure and a brown oil was obtained. Recrystallization from acetic acid and water afforded colorless prisms of 1 (74.5 g, 222.7 mmol, 77%): mp 86.5–88.0 °C; ^1H NMR δ 2.20 (m, J = 5.76 Hz, 2H, $CH_2CH_2CH_2$), 2.33 (s, 3H, $PhCH_3$), 4.08 (t, J = 6.03 Hz, 2H, $SO_2OCH_2CH_2CH_2$), 4.24 (t, J = 5.97 Hz, 2H, SO_2OCH_2), 6.88 (d, J = 7.35 Hz, 1H, ArH), 7.04 (t, J = 7.42 Hz, 1H, ArH), 7.18 (d, J = 8.25 Hz, 2H, tosyl ArH), 7.52 (m, 1H, ArH), 7.72 (d, J = 8.24 Hz, 2H, tosyl ArH), 7.80 (dd, 1H, ArH); ^{13}C NMR δ 21.64, 28.55, 63.22, 66.40, 112.16, 120.91, 124.63, 127.82, 128.32, 129.93, 132.25, 136.04, 145.14, 160.63, 189.01; MS *m/e* 334 (13.7), 213 (49.5), 162 (60.1), 155 (63.5), 91 (100); HRMS calcd for $C_{17}H_{18}O_5S$ *m/e* 334.0875, found 334.0889.

2-[2-[3-(Tosyloxy)propoxy]phenyl]-1,3-dioxolane (2). Compound 1 (33.4 g, 100 mmol), *p*-toluenesulfonic acid (250 mg), benzene (300 mL), and ethylene glycol (9.31 g, 150 mmol) were refluxed overnight, with stirring, in a 500-mL round-bottom flask equipped with a Dean–Stark trap and a condenser. The solution was cooled to room temperature and triethylamine (10 mL) and ethyl acetate (100 mL) were added. The organic layer was washed with water (2 × 200 mL) and dried over Na_2SO_4. Solvent was removed on a rotary evaporator, and remaining traces were removed under high vacuum. The light yellow oil 2 that was obtained (36.7 g, 97 mmol, 97%) was of sufficient purity for use in the next step: ^1H NMR δ 2.14 (m, J = 5.73 Hz, 2H, $OCH_2CH_2CH_2O$), 2.35 (s, 3H, $C_6H_5CH_3$), 3.98 (m, 4H, acetal CH_2), 4.10 (t, J = 5.98 Hz, 2H, $SO_2OCH_2CH_2CH_2$), 4.27 (t, J = 6.12 Hz, 2H, SO_2OCH_2), 5.93 (s, 1H, acetal H), 6.75 (t, J = 7.35 Hz, 1H, ArH), 6.85 (d, J = 7.43 Hz, 1H, ArH), 6.98 (t, J = 7.56 Hz, 1H, ArH), 7.21 (d, J = 8.24 Hz, 2H, tosyl ArH), 7.50 (dd, 1H, ArH), 7.73 (d, J = 8.25 Hz, 2H, tosyl ArH); ^{13}C NMR δ 21.46, 28.43, 65.09, 65.92, 67.89, 98.93, 112.08, 121.22, 126.44, 127.06, 127.74, 128.17, 129.74, 130.11 132.66, 144.79, 156.06; MS *m/e* 378 (50), 213 (56), 165 (100), 149 (54), 91 (80); HRMS calcd for $C_{19}H_{22}O_6S$ *m/e* 378.1137, found 378.1146.

1,2,4,5-Tetrakis{3-[2-(1,3-dioxolan-2-yl)phenoxy]propoxy}benzene (4). A 1-L three-necked round-bottom flask was equipped with a 100-mL dropping funnel, N_2 inlet, and a stirring bar. The flask was purged with N_2 and degassed DMSO (400 mL) was added. While the solution was stirred, 1,2,4,5-tetrahydroxybenzene (2.23 g, 15.7 mmol) was added, followed by powdered KOH (14.1 g, 251.6 mmol). After 5 min, tosyl acetal 2 (47.53 g, 125.60 mmol), dissolved in degassed DMSO (100 mL), was added all at once and the reaction was stirred at room temperature for 5 h under N_2. The solution was poured into saturated brine (1.5 L) and allowed to sit overnight. A clear red water layer was removed and the oily semisolid residue was dissolved in $CHCl_3$, washed with water, and dried over Na_2SO_4. The $CHCl_3$ was removed under reduced pressure and the oily product was purified by eluting through silica, first with $CHCl_3$ and then with 2% CH_3OH in $CHCl_3$. The first fraction isolated was starting material 2; the second fraction isolated, a yellow oil, was compound 4 (7.02 g, 7.26 mmol, 46.2%): ^1H NMR δ 2.15 (m, J = 5.72 Hz, 8H, $OCH_2CH_2CH_2O$), 3.88 (m, 16H, acetal CH_2), 4.15 (t, J = 5.93 Hz, 8H, $OCH_2CH_2CH_2O$), 4.24 (t, J = 6.19 Hz, 8H, $OCH_2CH_2CH_2O$), 6.52 (s, 2H, cap-ArH), 6.74 (d, J = 7.93 Hz,

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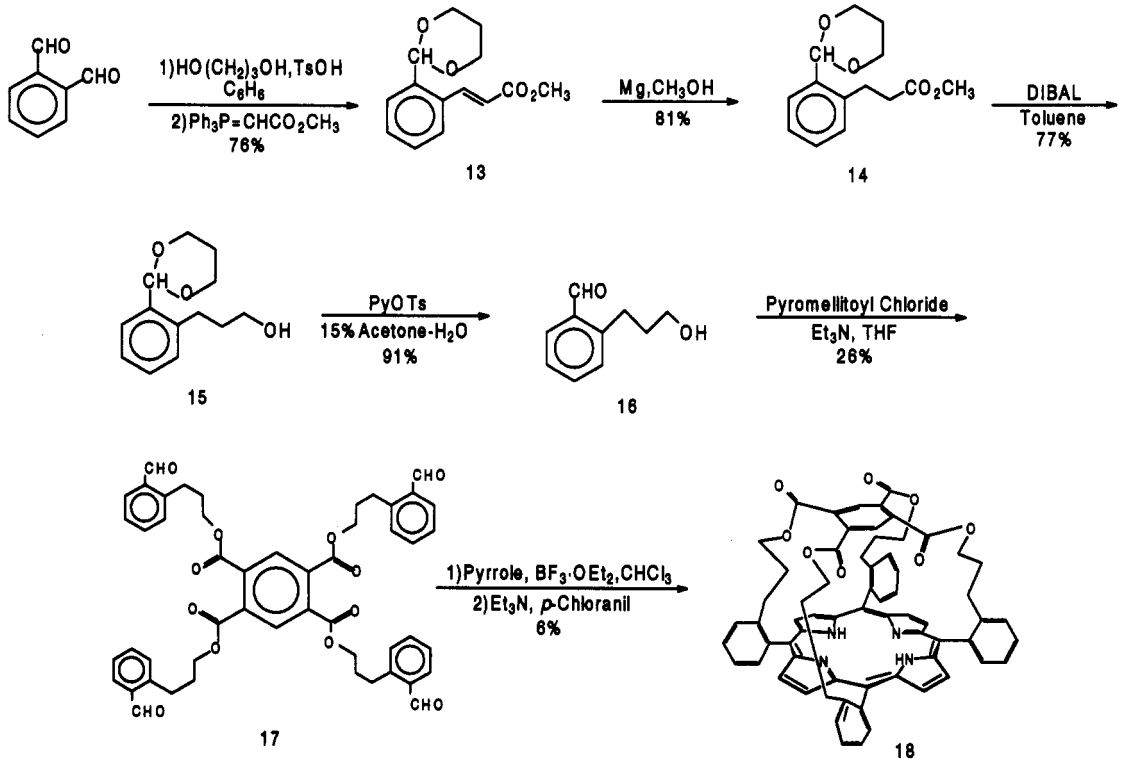
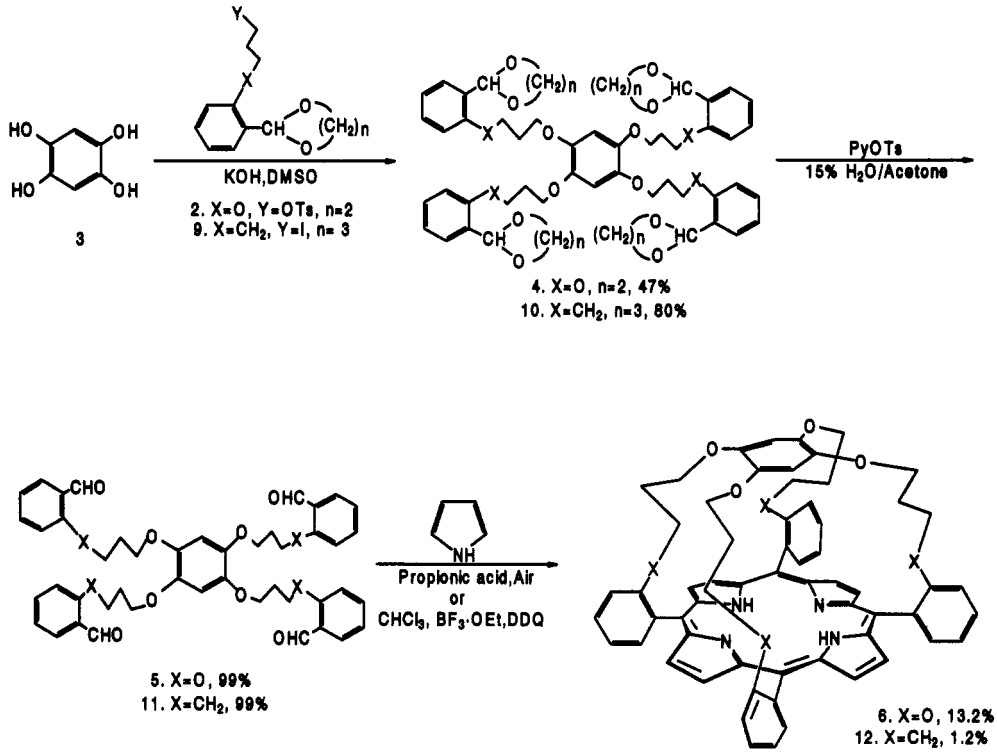
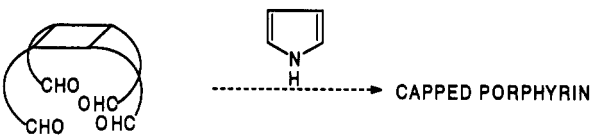
Scheme III



Scheme IV



Scheme V



4H, Ar*H*), 6.98 (t, J = 7.12 Hz, 4H, Ar*H*), 7.39 (t, J = 7.93 Hz, 4H, Ar*H*), 7.83 (d, J = 7.35 Hz, 4H, Ar*H*); ^{13}C NMR δ 29.49, 65.28, 67.00, 70.31, 99.33, 105.31, 111.84, 120.57, 126.08, 126.94, 130.36, 143.49; FAB MS (3-nitrobenzyl alcohol) m/e 968.5 (30.1), 967.5 (73.4), 966.5 (100), 922.5 (9.8), 895 (6.0); FAB HRMS calcd for $C_{54}H_{62}O_{16}$ m/e 966.4038, found 966.4067.

1,2,4,5-Tetrakis[3-(2-formylphenoxy)propoxy]benzene (5). Compound **4** (7.0 g, 7.24 mmol) and pyridinium *p*-toluenesulfonate (50 mg) were dissolved in a 15% water–acetone solution (100 mL) and refluxed overnight. Solvent was removed under reduced pressure and the solid yellow product was filtered, washed twice with water, and dried to obtain compound **5** (5.67 g, 7.17 mmol, 99%): mp 117–8 °C; ^{1}H NMR δ 2.25 (m, J = 5.88 Hz, 8H, $OCH_2CH_2CH_2O$), 4.12 (t, J = 6.00 Hz, 8H, $OCH_2CH_2CH_2O$), 4.24 (t, J = 5.97 Hz, 8H, $OCH_2CH_2CH_2O$), 6.59 (s, 2H, Cap-Ar*H*), 6.98 (d, J = 8.46 Hz, 4H, Ar*H*), 6.70 (t, J = 7.17 Hz, 4H, Ar*H*), 7.48

(t, J = 6.60 Hz, 4H, ArH), 7.80 (d, J = 7.68 Hz, 4H, ArH); ^{13}C NMR δ 29.39, 64.99, 66.85, 103.50, 105.49, 112.44, 120.81, 128.45, 136.04, 143.57, 161.21, 189.68; FAB MS (3-nitrobenzyl alcohol) m/e 790 (100), 762 (33.2); FAB HRMS calcd $C_{46}H_{46}O_{12}$ m/e 790.2989, found 790.2958.

H_2(OCCCOPor)-Capped Porphyrin (6). Compound **5** (1.085 g, 1.36 mmol), dissolved in doubly distilled propionic acid (600 mL), was added to a 1-L two-necked round-bottom flask equipped with a condenser, magnetic stir bar, and an air injection inlet. The solution was heated to reflux, and air was bubbled into the flask. Freshly distilled pyrrole (730 mg, 10.9 mmol) was added, and the mixture was refluxed, with stirring, for 1.5 h. Propionic acid was removed under reduced pressure and the dark purple–black solid residue was dissolved in $CHCl_3$ (500 mL) and Et_3N (50 mL). The solution was stirred for 1 h and filtered through Celite, and all solvent was removed with a rotary evaporator. The residue was passed through a silica column with eluent that was gradually adjusted from 100% $CHCl_3$ to 3% MeOH in $CHCl_3$. A fast-running purple fraction was collected and reeluted through two silica columns, the first with 1% MeOH in $CHCl_3$, the second with 1% acetone in $CHCl_3$. The purple band was collected, concentrated to dryness, and the solid residue was recrystallized from $CHCl_3$/MeOH to give purple microcrystals of **6** (176 mg, 0.18 mmol, 13.2%): mp > 300 °C; UV-vis λ_{max}(log ϵ) 422 (5.28), 518 (4.70), 550 (3.42), 592 (3.67), 647 (3.34); ^{1}H NMR δ −2.90 (s, 2H, NH), 1.60 (m, 8H, OCH$_2$CH_2CH$_2$O), 1.89 (q, J = 6.39 Hz, 4H, OCH_2CH$_2$CH$_2$O), 2.10(q, J = 6.48 Hz, 4H, OCH_2CH$_2$CH$_2$O), 4.10 (dq, 8H, OCH$_2$CH$_2$CH_2O), 4.54 (s, 2H, C$_6H_2$(OR)$_2$), 7.36 (d, J = 5.58 Hz, 4H, meso ArH), 7.40 (t, J = 6.48 Hz, 4H, meso ArH), 7.78 (t, J = 6.09 Hz, 4H, meso ArH), 7.99 (d, J = 5.54 Hz, 4H, meso ArH), 8.68 (s, 8H, β-pyrrole CH); ^{13}C NMR δ −45.73, 29.18, 65.88, 66.91, 104.81, 114.02, 115.40, 120.26, 129.82, 132.98, 135.59, 142.35, 158.38; FAB MS m/e 981 (100); FAB HRMS calcd for $C_{62}H_{52}N_4O_8$ 980.3785, found 980.3849. Anal. Calcd for $C_{62}H_{52}N_4O_8$: C, 75.90; H, 5.34; N, 5.71. Found: C, 75.72; H, 5.01; N, 5.90.

2-(2-Bromophenyl)-1,3-dioxane (7). To a 500-mL round-bottom flask equipped with a Dean–Stark trap and condenser was added 2-bromobenzaldehyde (50 g, 0.27 mol), 1,3-propanediol (30.8 g, 0.405 mol), p-toluenesulfonic acid (1 g), and benzene (300 mL). The mixture was stirred and refluxed overnight. Et_3N (5 mL) was added and the reaction mixture was cooled. Ethyl acetate (200 mL) was added and the organic layer was washed with NaOH, water, and brine, and dried over Na_2SO_4. Solvent was removed and **7** was obtained as a colorless solid (64.3 g, 0.265 mol, 98%): mp 44–46 °C; ^{1}H NMR δ 1.45 (d, J = 13.44 Hz, 1H, OCH$_2$CH_2CH$_2$O), 2.23 (m, J = 13.31 Hz, 1H, OCH$_2$CH_2CH$_2$O), 4.05 (t, J = 11.79 Hz, 2H, OCH_2CH$_2$CH$_2$O), 4.28 (dd, J = 11.52 Hz, 2H, OCH$_2$CH$_2$CH_2O), 5.78 (s, 1H, acetal H), 7.21 (t, J = 7.38 Hz, 1H, ArH), 7.36 (t, J = 7.71 Hz, 1H, ArH), 7.55 (d, J = 7.95 Hz, 1H, ArH), 7.70 (d, J = 7.68 Hz, 1H, ArH); ^{13}C NMR δ 25.74, 67.66, 100.92, 122.37, 127.64, 128.13, 130.43, 132.66, 137.53. MS m/e 244 (73), 243 (93), 242 (75), 241 (88), 186 (50), 185 (86), 184 (52), 183 (82), 163 (46), 105 (30), 87 (100); HRMS calcd $C_{10}H_{10}BrO_2$ m/e 240.9865, found 240.9870.

2-[2-(4-Bromobutyl)]phenyl]-1,3-dioxane (8). This compound was synthesized with the use of a method developed by Zhang et al.[12] Dry magnesium turnings (5.4 g, 0.225 mol) and 35 mg of iodine were added to a 500-mL three-necked flask under N_2. Dry THF (150 mL) was added and the mixture was warmed to 70–80 °C. One quarter of **7** (36.3 g total, 0.15 mol) was dissolved in dry THF (100 mL) and added to initiate the reaction. The remainder was added over a 1-h period to maintain a gentle reflux, and the mixture was refluxed an additional 1 h after the addition was complete to obtain the Grignard reagent. In another 1-L flask under an N_2 atmosphere, dry cuprous bromide (2.4 g, 16.8 mmol), dry THF (50 mL), dry HMPA (20 mL), and dry 1,4-dibromobutane (32.4 g, 0.15 mol) were stirred vigorously and refluxed gently. The Grignard reagent prepared above was quickly added and the reaction mixture was refluxed an additional 4–6 h. The solution was cooled to room temperature, aqueous NH_4Cl was added, and the solution was stirred overnight. The solution was extracted twice with ethyl acetate. The combined organic layers were washed with water and brine and dried over Na_2SO_4. Solvent was removed and a blue-brown oily product was isolated. The product was purified by passing it through silica with 1:10 ethyl acetate/hexanes as the eluent. The first fraction, compound **8**, was isolated as a light yellow oil (35.42 g, 0.119 mol, 79%): ^{1}H NMR δ 1.46 (d, J = 13.44 Hz, 1H, OCH$_2$CH_2-CH$_2$O), 1.75 (q, J = 7.11 Hz, 2H, ArCH$_2$CH$_2$CH_2), 1.92 (q, J = 7.58 Hz, 2H, ArCH$_2$CH_2), 2.25 (m, J = 12.78 Hz, 1H, OCH$_2$CH_2-CH$_2$O), 2.76 (t, J = 7.78 Hz, 2H, ArCH_2), 3.47 (t, J = 6.92 Hz, 2H, BrCH_2), 4.01 (t, J = 11.80 Hz, 2H, OCH_2CH$_2$CH$_2$O), 4.28 (dd, J = 11.49 Hz, 2H, OCH$_2$CH$_2$CH_2O), 5.66 (s, 1H, CH(OR)$_2$), 7.25 (m, 3H, ArH), 7.60 (d, J = 7.42 Hz, 1H, ArH); ^{13}C NMR δ 25.85, 29.94, 31.02, 31.45, 32.64, 33.91, 67.64, 100.10, 126.29, 126.49, 128.90, 129.56, 136.32, 139.49; MS m/e 301 (14.2), 300 (98.6), 299 (62.7), 298 (100), 297 (49.1), 241 (25.3), 163 (72.4), 129 (59.4), 91 (72.6); HRMS calcd for $C_{14}H_{19}BrO_2$ m/e 298.0568, found 298.0573.

2-[2-(4-Iodobutyl)]phenyl]-1,3-dioxane (9). Potassium iodide (43.3 g, 261.1 mmol), **8** (7.91 g, 26.11 mmol), and dry acetone (150 mL) were placed in a 250-mL round-bottom flask, stirred vigorously, and refluxed overnight. The solution was filtered and the filtrate was washed with ethyl acetate. The organic layer was added to ethyl acetate (100 mL), washed with water (2 × 100 mL), and dried over Na_2SO_4. Solvent was removed and **9** was obtained as a yellow oil (8.46 g, 24.44 mmol, 93.6%). If the compound was not pure enough at this stage, the mixture was passed through a silica column with 1:10 ethyl acetate/hexanes as the eluent and the pure product was isolated as the first fraction: ^{1}H NMR δ 1.49 (d, J = 13.53 Hz, 1H, OCH$_2$CH_2CH$_2$O), 1.75 (m, J = 7.5 Hz, 2H, PhCH$_2$CH_2), 1.92 (m, J = 7.14 Hz, 2H, ICH$_2$CH_2), 2.25 (m, J = 12.51 Hz, 1H, OCH$_2$CH_2CH$_2$O), 2.75 (t, J = 7.77 Hz, 2H, PhCH_2), 3.22 (t, J = 6.87 Hz, 2H, ICH_2), 4.01 (t, J = 11.82 Hz, 2H, OCH_2), 4.26 (dd, J = 11.54 Hz, 2H, OCH_2), 5.66 (s, 1H, acetal H), 7.25 (m, 3H, ArH), 7.60 (d, J = 7.44 Hz, 1H, ArH); ^{13}C NMR δ 7.10, 25.83, 31.26, 32.24, 33.36, 67.64, 100.02, 100.12, 126.47, 128.89, 129.53, 136.26, 139.42; MS m/e 347 (22.2), 346 (100), 345 (33.5), 287 (17.1), 163 (28.2), 143 (39.2), 91 (40.9), 87 (35.5); HRMS calcd $C_{14}H_{19}IO_2$ m/e 346.0430, found 346.0423.

1,2,4,5-Tetrakis[4-[2-(1,3-dioxan-2-yl)phenyl]butyloxy]-benzene (tetraacetal 10). Compound **10** was isolated as a yellow oil (8.07 g, 7.95 mmol, 79.5%) from the reaction of **9** (27.99 g, 80.8 mmol) and **3** (1.42 g, 10 mmol) with KOH (8.96 g, 160 mmol) in degassed DMSO (250 mL) by the same procedure used in the preparation of **4**: ^{1}H NMR δ 1.40 (d, J = 13.41 Hz, 4H, OCH$_2$CH_2-CH$_2$O), 1.84 (m, J = 5.1 Hz, 16H, OCH$_2$CH_2CH_2CH$_2$Ar), 2.21 (m, J = 12.4 Hz, 4H, OCH$_2$CH_2CH$_2$O), 2.78 (t, J = 7.08 Hz, 8H, OCH$_2$CH$_2$CH$_2$CH_2Ar), 3.93 (t, J = 13.23 Hz, 8H, OCH_2CH$_2$CH$_2$O), 3.98 (t, J = 5.76 Hz, 8H, OCH_2CH$_2$CH$_2$CH$_2$Ar), 4.21 (dd, J = 11.47 Hz, 8H, OCH_2CH$_2$CH$_2$O), 5.64 (s, 4H, CH(OR)$_2$), 6.60 (s, 2H, C$_6H_2$(OR)$_4$), 7.18–7.23 (m, 12H, ArH), 7.51 (d, J = 7.98 Hz, 4H, ArH); ^{13}C NMR δ 25.80, 27.95, 29.49, 31.94, 67.55, 70.38, 99.93, 105.40, 126.14, 126.29, 128.79, 129.46, 136.28, 139.82, 143.57; FAB MS (3-nitrobenzyl alcohol) m/e 1014 (100); FAB HRMS calcd $C_{62}H_{78}O_{12}$ m/e 1014.5493, found 1014.5579.

1,2,4,5-Tetrakis[4-(2-formylphenyl)butyloxy]benzene (11). Compound **10** (8.07 g, 7.95 mmol) was reacted with pyridinium p-toluenesulfonate (50 mg) in 15% water–acetone by the same procedure used in the preparation of **5**. The oily product was purified by passing it through silica with 5% MeOH in $CHCl_3$ as the eluent. The first fraction, compound **11**, was isolated as a light yellow oil (6.20 g, 7.92 mmol, 99%) that solidified when allowed to sit overnight: ^{1}H NMR δ 1.82 (m, J = 5.22 Hz, 16H, OCH$_2$CH_2CH_2CH$_2$Ar), 3.08 (t, J = 6.48 Hz, 8H, OCH$_2$CH$_2$-CH$_2$CH_2Ar), 3.96 (t, J = 6.03 Hz, 8H, OCH_2CH$_2$CH$_2$CH$_2$Ar), 6.56 (s, 2H, C$_6H_2$(OR)$_4$), 7.25 (d, J = 6.45 Hz, 4H, ArH), 7.33 (t, J = 7.47 Hz, 4H, ArH), 7.45 (t, J = 7.44 Hz, 4H, ArH), 7.81 (d, J = 7.65 Hz, 4H, ArH), 10.26 (s, 4H, CHO); ^{13}C NMR δ 28.76, 29.32, 32.24, 70.26, 105.41, 126.58, 131.07, 131.92, 133.68, 133.83, 143.52, 145.25, 192.43; FAB MS (3-nitrobenzyl alcohol) m/e 782 (100), 622 (65.5); FAB HRMS calcd $C_{50}H_{54}O_8$ m/e 782.3819, found 782.3883.

H_2(OCCCCPor)-Capped Porphyrin (12). Compound **11** (3.13 g, 4 mmol) was dissolved in $CHCl_3$ (4 L) distilled from K_2CO_3. While N_2 was bubbled through the solution pyrrole (1.07 g, 16 mmol) and BF_3·OEt (2.89 mL, 24 mmol) were added. The solution was stirred for 24 h at room temperature in the dark. DDQ (4.33 g) was added and the solution was refluxed 1 h. A second aliquot of DDQ (4.33 g) was added and the solution was refluxed an additional 2 h. The solvent was removed under reduced pressure, and the dark residue obtained was eluted

through silica with 3% MeOH in $CHCl_3$. The porphyrin, isolated as the fast-moving band, was chromatographed again with 1% CH_3OH in $CHCl_3$ followed by 1% acetone in $CHCl_3$. The solvent was removed and **12** was isolated as a purple solid (4.7 mg, 4.8 × 10^{-3} mmol, 1.2%): mp > 300 °C; UV-vis λ_{max}(log ϵ) ($CHCl_3$) 420 (5.63), 519 (3.85), 555 (4.29), 592 (3.72), 651 (3.23); ^{1}H NMR δ −2.90 (br s, 2H, pyrrole NH), 2.7–0.3 (m, 32H, butoxyl chain methylenes), 4.47 (s, 2H, $C_6H_2(OR)_4$), 7.90–7.50 (m, 16H, ArH), 8.61 (d, J = 5.49 Hz, 8H, β-pyrrole CH); ^{13}C NMR δ 22.95, 27.31, 29.77, 31.98, 34.00, 37.55, 68.10, 119.11, 124.05, 128.56, 134.82, 141.83, 142.35, 143.93; FAB MS (3-nitrobenzyl alcohol) *m/e* 975, 974, 973, 663; FAB HRMS (3-nitrobenzyl alcohol) calcd for $C_{66}H_{60}N_4O_4$ *m/e* 972.4615, found 972.4699. Anal. Calcd for $C_{66}H_{60}N_4O_4 \cdot H_2O$: C, 79.97; H, 6.30; N, 5.65. Found: C, 80.11; H, 6.29; N, 5.49.

2-[2-[2-(Methoxycarbonylethyl]phenyl]-1,3-dioxane (14). Dry Mg turnings (2.52 g, 105.5 mmol), 2-[2-[2-(methoxycarbonyl)-ethenyl]phenyl]-1,3-dioxane **13** (10.85 g, 43.75 mmol),[10] and absolute methanol (100 mL) were combined in a 250-mL flask, and the mixture was stirred vigorously overnight in a water bath. A 1 M NH_4Cl (10 mL) solution was added to quench the reaction, and the mixture was stirred for an additional 2 h. The solution was extracted with ethyl acetate (4 × 100 mL) and the combined organic layers were washed with water and dried over Na_2SO_4. Solvent was removed to give compound **14** as a yellow oil (8.90 g, 35.6 mmol, 81%). The product was pure enough to proceed with the next step. Alternatively, it can be further purified by eluting it through a silica column with 30% ethyl acetate in hexanes. The product is isolated as the first fraction: ^{1}H NMR δ 1.45 (d, J = 13.44 Hz, 1H, $OCH_2CH_2CH_2O$), 2.23 (m, J = 13.35 Hz, 1H, $OCH_2CH_2CH_2O$), 2.64 (t, J = 7.89 Hz, 2H, $ArCH_2CH_2CO_2Me$), 3.09 (t, J = 7.77 Hz, 2H, $ArCH_2CH_2CO_2Me$), 3.70 (s, 3H, CO_2CH_3), 4.01 (dt, J = 11.24 Hz, 2H, $OCH_2CH_2CH_2O$), 4.27 (dd, J = 12.20 Hz, 2H, $OCH_2CH_2CH_2O$), 5.66 (s, 1H, $CH(OR)_2$), 7.15–7.30 (m, 3H, ArH), 7.59 (d, J = 7.35 Hz, 1H, ArH); ^{13}C NMR δ 27.82, 34.01, 35.91, 51.21, 64.74, 101.68, 126.13, 126.35, 129.41, 134.85, 139.13, 173.18; MS *m/e* 250 (7.9), 249 (12.0), 219 (12.8), 191 (7.6), 163 (100), 132 (25.4), 117 (15.8), 105 (22.2); HRMS calcd for $C_{14}H_{18}O_4$ *m/e* 250.1205, found 250.1200.

2-[2-(3-Hydroxypropyl)phenyl]-1,3-dioxane (15). A 1 M diisobutylaluminum hydride solution (61.5 mL, 61.5 mmol) was slowly added to a dry toluene solution containing **14** (6.51 g, 24.6 mmol) at −60 °C. The solution was stirred for 4 h and warmed to room temperature, and MeOH (2 mL) was added. The reaction was cooled to 0 °C and aqueous potassium sodium tartrate (100 mL of a 0.2 M solution) was added slowly. The mixture was allowed to warm to room temperature and was stirred overnight. The mixture was then extracted with ethyl acetate and the combined organic layer was washed with water and dried over Na_2SO_4. The solvent was removed to obtain a yellow oily product that was purified by eluting it through a silica column with 35% ethyl acetate in hexanes. The first fraction, compound **15**, was isolated as a colorless oil (4.21 g, 18.94 mmol, 77%): ^{1}H NMR δ 1.45 (d, J = 13.05 Hz, 1H, $OCH_2CH_2CH_2O$), 1.92 (q, J = 5.19 Hz, 2H, CH_2CH_2OH), 2.25 (m, J = 12.00 Hz, 1H, $OCH_2CH_2CH_2O$), 2.88 (t, J = 5.46 Hz, 2H, $CH_2C_6H_5$), 3.57 (t, J = 5.50 Hz, 2H, CH_2OH), 4.00 (t, J = 11.80 Hz, 2H, $OCH_2CH_2CH_2O$), 4.27 (dd, J = 11.21 Hz, 2H, $OCH_2CH_2CH_2O$), 5.68 (s, 1H, acetal H), 7.32–7.19 (m, 3H, ArH), 7.57 (d, J = 6.82 Hz, 1H, ArH); ^{13}C NMR δ 25.73, 27.63, 33.93, 61.42, 67.64, 100.71, 100.79, 126.75, 129.01, 129.59, 136.22, 139.37; MS *m/e* 222 (8.2), 133 (28.1), 118 (38.5), 117 (47.9), 115 (31.2), 105 (24.6); HRMS calcd for $C_{13}H_{18}O_3$ *m/e* 222.1256, found 222.1243.

2-(3-Hydroxypropyl)benzaldehyde (16). In a 250-mL round-bottom flask a solution of **15** (21.3 g, 95.9 mmol) and pyridinium *p*-toluenesulfonate (500 mg) in 15% water–acetone was refluxed overnight. The organic solvent was removed on a rotary evaporator and the residue was extracted with ethyl acetate. The combined organic layer was washed with water and dried over Na_2SO_4. The solvent was removed and **16** was isolated as a yellow oil (14.36 g, 87.45 mmol, 91%): ^{1}H NMR δ 1.89 (q, J = 6.30 Hz, 2H, CH_2CH_2OH), 2.70 (br, 1H, OH), 3.15 (t, J = 6.77 Hz, 2H, CH_2Ar), 3.68 (t, J = 6.24 Hz, 2H, CH_2OH), 7.60–7.11 (m, 3H, ArH), 7.80 (d, J = 7.62 Hz, 1H, ArH), 10.41 (s, 1H, CHO); ^{13}C NMR δ 28.77, 31.55, 34.69, 61.70, 126.68, 132.98, 133.75, 134.02, 144.80, 193.37; MS *m/e* 164 (19.2), 163 (33.4), 147 (100), 146 (35.3), 133 (40.5), 131 (46.0), 129 (34.3), 119 (43.1), 118 (86.4), 117 (50.4), 91 (57.9); HRMS calcd for $C_{10}H_{12}O_2$ *m/e* 164.0837, found 164.0843.

1,2,4,5-Tetrakis[[3-(2-formylphenyl)propoxy]carbonyl]-benzene (17). Pyromellitoyl chloride (1.1 g, 3.32 mmol) in dry THF (5 mL) was added dropwise to a stirred solution of **16** (2.18 g, 13.28 mmol) and triethylamine (1.34 g, 13.28 mmol) in dry THF (50 mL) at 0 °C. The solution was maintained at 0 °C for 0.5 h and then allowed to stir overnight at room temperature. The reaction mixture was added to ethyl acetate (200 mL), and the organic layer was washed with water and dried over Na_2SO_4. When solvent was removed an oily gum product was obtained. The oil was eluted through silica with 1:1 ethyl acetate/hexanes to obtain compound **17** as the first fraction (0.72 g, 0.86 mmol, 26%): ^{1}H NMR δ 2.07 (q, J = 7.35 Hz, 8H, $ArCH_2CH_2$), 3.16 (t, J = 7.89 Hz, 8H, $ArCH_2$), 4.40 (t, J = 6.39 Hz, 8H, CH_2OH), 7.79–7.27 (m, 16H, ArH), 8.13 (s, 2H, capping ArH); ^{13}C NMR δ 28.71, 31.53, 34.67, 61.70, 126.68, 130.65, 132.08, 133.98, 134.11, 134.72, 140.38, 144.80, 167.01, 193.37; FAB MS *m/e* 861 (41), 838 (100), 822 (11), 691 (52); FAB HRMS calcd for $C_{50}H_{46}O_{12}$ *m/e* 838.2989, found 838.2932.

H_2((CO)OCCCPor)-Capped Porphyrin (18). Dry $CHCl_3$ (1.35 L) distilled from K_2CO_3, **17** (506.7 mg, 0.604 mmol), and freshly distilled pyrrole (0.168 mL, 2.40 mmol) were added to a 2-L three-necked round-bottom flask. Nitrogen was bubbled into the solution for 10 min and $BF_3 \cdot OEt_2$ (0.446 mL, 3.62 mmol) was added. After the solution was stirred for 20 h in the dark, NEt_3 (1 mL) was added, followed by *p*-chloranil (600 mg). After the solution was refluxed for 1 h, an additional aliquot of *p*-chloranil (600 mg) was added, and the solution was refluxed for an additional 2 h. Solvent was removed under reduced pressure and the residue was purified by eluting it through silica with 5% MeOH in $CHCl_3$. A fast-moving band was isolated and chromatographed again with 1% MeOH in $CHCl_3$, followed by 2% acetone in $CHCl_3$. A purple solid was isolated and recrystallized from MeOH/$CHCl_3$ to give **18** (39 mg, 3.79 × 10^{-2} mmol, 6%): mp > 300 °C; UV-vis λ_{max}(log ϵ) ($CHCl_3$) 422 (5.51), 518 (4.09), 550 (3.45), 590 (3.53), 652 (3.11); ^{1}H NMR δ −3.05 (br s, 2H, NH), 1.60 (m, 8H, $CH_2CH_2CH_2Ar$), 4.23–1.96 (m, 16H, $OCH_2CH_2CH_2Ar$), 5.88 (s, 2H, capping ArH), 7.76–7.23 (m, 16H, ArH), 8.58 (d, J = 5.49 Hz, 8H, β-pyrrole CH); ^{13}C NMR δ 26.52, 30.81, 67.83, 119.04, 123.95, 128.39, 128.92, 130.11, 130.65, 134.32, 136.73, 140.38, 141.32, 143.71, 193.37; FAB MS *m/e* 1029 (100), 908 (15); FAB HRMS calcd for $C_{66}H_{52}N_4O_8$ *m/e* 1028.3785, found 1028.3729. Anal. Calcd for $C_{66}H_{52}N_4O_8$: C, 77.03; H, 5.09; N, 5.44. Found: C, 77.28; H, 5.16; N, 5.66.

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Supplementary Material Available: ^{1}H NMR spectra of **1**, **2**, **5**, **7–11**, and **14–17** and ^{13}C NMR spectra of **1**, **4**, **5**, **7**, **9–11**, **14**, and **15** (21 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.