Facile Entry to 5,10,15,20-Tetra-*C*-glycosylporphyrins

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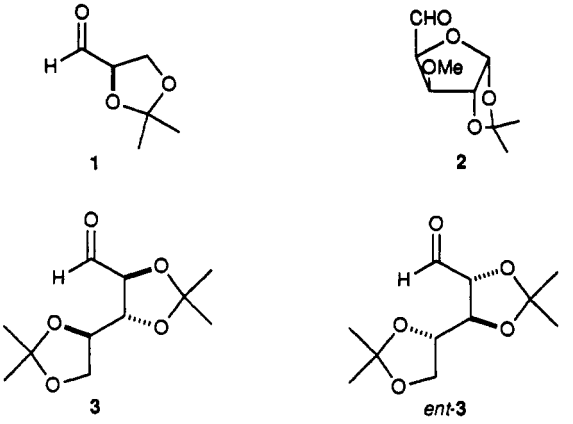
The porphyrin macrocycle, the core element of fundamental bioconjugates, has been extensively exploited by covalent association with carbohydrates,[1] peptides,[2] steroids,[3] nucleobases,[4] and other rationally engineered fragments[5] to create a variety of superstructural assemblies[6] to be employed in different realms, including molecular recognition, catalysis, and medicinal chemistry. Among all possible ways with which a functional subunit can be attached to the porphyrin core, conjugation via carbon–carbon bonds would have the decisive advantage of providing molecules with improved chemical and enzymatic resistance and bioavailability. Close to this subject, we report here that both lipophilic and water-soluble *meso*-tetraglycosylated porphyrins of type **4**–**10** (Table 1) can be constructed simply by reacting pyrrole with aldehydo sugars **1**–**3** (Chart 1).[7]

Results and Discussion

Synthesis. Pyrrole was first condensed with enantiopure 2,3-*O*-isopropylidene-D-glyceraldehyde (**1**) according to a slightly modified version of the classical Lindsey's procedure.[8] Using 1.0×10^{-3} M BF_3 etherate and 1.0×10^{-2} M pyrrole and aldehyde in CH_2Cl_2, the reaction went to completion in 6 h at room temperature providing, after oxidation of the porphyrinogen intermediates by DDQ (2.8 mmol, rt, 18 h), two major atropoisomeric porphyrins, namely the $\alpha,\beta,\alpha,\beta$- and $\alpha,\alpha,\alpha,\beta$-configured compounds **4** and **5** in 3 and 4% yields, respectively.[9,10] Owing to well-differentiated R_f values (0.45 and 0.13, respectively), purification of these protected compounds was easily attained by flash chromatography on silica eluting with a CH_2Cl_2/ethyl acetate (85:15, v/v) solvent mixture. The progress of the ring-forming reaction and the chromatographic workup were conveniently monitored by visualizing the porphyrin materials on TLC plates as green-emerald spots, by using a selective and very sensitive reagent mixture based on Ce(III) sulfate, ammonium molybdate, and sulfuric acid.

Chart 1



Having thus established that BF_3-promoted condensation of pyrrole with sugar aldehydes at high dilution can indeed provide a quick entry to *C*-glycosylated porphyrins, we next considered the suitability of this reaction as applied to 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-pentodialdofuranose (**2**) and both the enantiomers of 2,3:4,5-di-*O*-isopropylidenearabinose **3** and *ent*-**3**. In an analogous reaction, dialdose **2** also resulted in the porphyrin formation, providing $\alpha,\beta,\alpha,\beta$-configured porphyrin **6** in 6% isolated yield as the sole detectable isomer.[11] Treatment of *aldehydo*-D-arabinose **3** with pyrrole afforded three major porphyrin compounds; they were easily separated by flash chromatography (SiO_2) using a mixture of CH_2Cl_2/ethyl acetate (50:50, v/v) as an eluant. The three compounds were identified (vide infra) as the expected fully protected $\alpha,\beta,\alpha,\beta$-porphyrin **7** (2%, R_f 0.72), monodeprotected porphyrin **8** (1%, R_f 0.28), and bis-deprotected porphyrin **9** (4%, R_f 0.03). Obviously, adaptation of this procedure to L-arabinose *ent*-**3** resulted in formation of the enantiomeric compound *ent*-**7** (and *ent*-**8**, *ent*-**9**) in comparable yield.

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(9) Under comparable conditions (BF_3 etherate, 2,5-dimethylpyrrole, rt, 6 h), 2,3-*O*-isopropylidene-D-glyceraldehyde does not undergo appreciable racemization; this was checked by ^1H NMR in the presence of chiral shift reagent Eu(hfc)$_3$.

(10) Trace amounts of two additional red-brown compounds (R_f = 0.58 and 0.17, respectively) were also isolated during the chromatographic workup, showing porphyrin-consistent UV-vis spectral characteristics. The scarcity and low purity of the samples, however, precluded more informative analytical and structural measurements. Mainly based on R_f values, $\alpha,\alpha,\alpha,\alpha$ (less polar) and $\alpha,\alpha,\beta,\beta$ (more polar) configurations have been tentatively assigned to these compounds.

(11) Under the employed mild thermodynamic conditions, the $\alpha,\beta,\alpha,\beta$-configurated atropoisomer, which suffers the least steric interactions between the four carbohydrate residues, largely predominates over the other more congested isomers.

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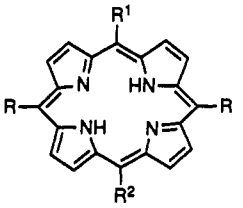
Table 1. Structures of Porphyrin Derivatives 4–10



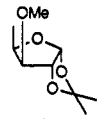
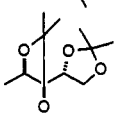
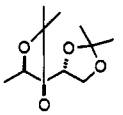
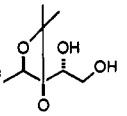
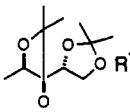
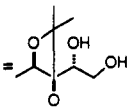
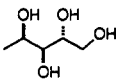
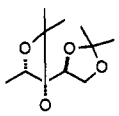
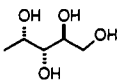
porphyrins	substituents	stereo-disposition	symmetry
4	$R = R^1 = R^2 =$ 	$\alpha,\beta,\alpha,\beta$	D_2
5	$R = R^1 = R^2 =$ 	$\alpha,\alpha,\alpha,\beta$	C_1
6	$R = R^1 = R^2 =$ 	$\alpha,\beta,\alpha,\beta$	D_2
7	$R = R^1 = R^2 =$ 	$\alpha,\beta,\alpha,\beta$	D_2
8	$R = R^1 =$  $R^2 =$ 	$\alpha,\beta,\alpha,\beta$	C_1
9	$R =$  $R^1 = R^2 =$ 	$\alpha,\beta,\alpha,\beta$	C_2
10	$R = R^1 = R^2 =$ 	$\alpha,\beta,\alpha,\beta$	D_2
ent-7	$R = R^1 = R^2 =$ 	$\alpha,\beta,\alpha,\beta$	D_2
ent-10	$R = R^1 = R^2 =$ 	$\alpha,\beta,\alpha,\beta$	D_2

Table 2. UV-vis Data for Porphyrins 4–10[a]

porphyrin	Soret	Q_1	Q_2	Q_3	Q_4	concn ($M \times 10^{-4}$)
4	417 (117.1)	519 (7.7)	552 (1.4)	595 (2.6)	650 (0.2)	0.33
5	418 (86.8)	518 (5.1)	554 (1.3)	593 (1.7)	649 (0.2)	0.42
6	419 (137.7)	523 (8.9)	560[b] (1.8)	595 (3.1)	652 (2.1)	0.27
7	415 (22.8)	516 (1.8)	549 (0.4)	595 (0.6)	650 (0.09)	1.71
8	417 (49.5)	517 (3.8)	549 (1.0)	595 (1.4)	649 (0.3)	0.80
9	417 (21.8)	518 (1.5)	556 (0.5)	595 (0.6)	650 (0.2)	1.94
10	418 (28.2)	514 (1.7)	556 (1.7)	*c*	*c*	1.06

[a] λ, nm ($\epsilon = 10^{-3}$ cm^{-1} M^{-1}); 4–9 in $CHCl_3$; 10 in H_2O. [b] Shoulder. [c] Very weak.

Complete deprotection of all the acetonide groups in 7 and *ent*-7 (or the corresponding partially deprotected derivatives 8 and 9) was easily attained by treatment with 50% aqueous trifluoroacetic acid in CH_2Cl_2 at room temperature under ultrasonic irradiation (2 h). Following neutralization with aqueous ammonia, water soluble D_2-symmetric porphyrins 10 and *ent*-10 bearing four carbon–carbon linked tetritolyl units were obtained in almost quantitative yields. These porphyrins were insoluble in most organic solvents such as chloroform, diethyl ether, ethyl acetate, and acetone. They were proven soluble in ethanol and methanol and freely soluble in water at room temperature.

Characterization of Glycosylated Porphyrins. The porphyrins 4–10 were characterized by low- and high-resolution CIMS, UV-vis, CD, ^1H, and ^{13}C NMR spectroscopies. Low-resolution CIMS of 4–10 gave molecular weights which are those expected of the corresponding formulas, while high-resolution measurements gave rise to exact $(M + 1)^+$ masses. The electronic spectra of lipophilic compounds 4–9 in $CHCl_3$ (Table 2) were similar to each other with pronounced Soret bands at 415–419 nm, accompanied by four less intense Q bands near 520, 555, 595, and 650 nm. The spectra are of phyllo type with $\epsilon_{555}/\epsilon_{595} < 1$.[12] The UV-vis spectrum of deprotected porphyrin 10 in H_2O showed a slightly different profile with

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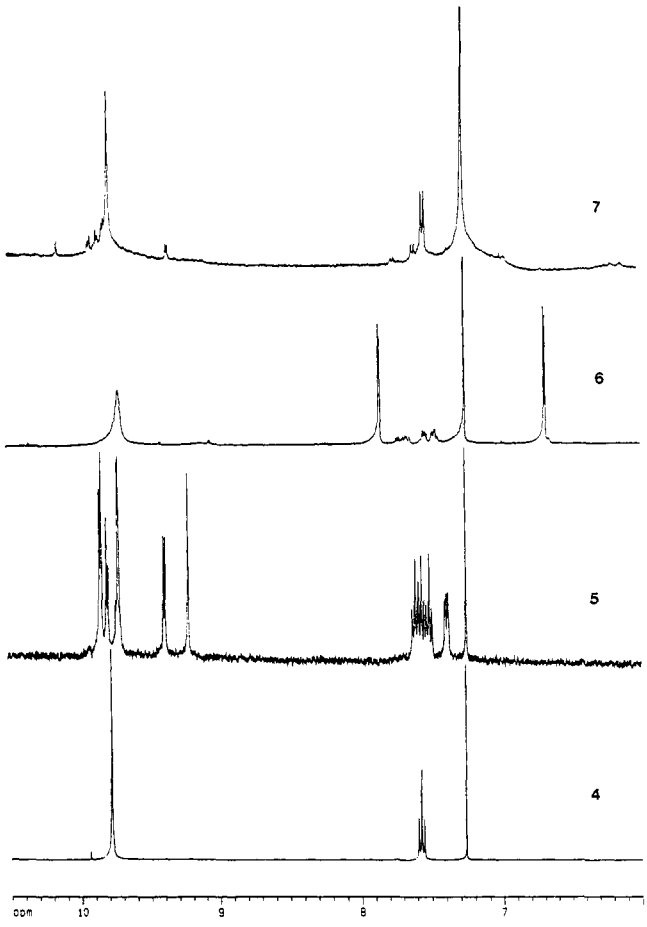

Figure 1. Partial ^1H NMR spectra of compounds 4–7 in $CDCl_3$ at room temperature in the region 7–10 ppm: $CHCl_3$ signal at 7.23 ppm; TMS = 0.0 ppm.

an intense Soret band at 418 nm and two significant Q bands of equal intensity at 514 and 556 nm.

The $CHCl_3$ solutions of **4–9** as well as the aqueous solutions of **10** were CD active at room temperature. We found induced CD at both the Soret band and Q band regions indicating that the chirality resident in the sugar moieties has been transmitted to the porphyrin chromophore in substantial amount. The opposite chirality of **7** and *ent*-**7** was clearly demonstrated by their circular dichroism spectra in $CHCl_3$, which show completely symmetric Cotton effects. Spectra of **10** and *ent*-**10** in H_2O show the same behavior in the region of the Soret bands.

The ^1H NMR spectra of porphyrins **4–9** were measured at 400 MHz in $CDCl_3$, while the ^1H NMR analysis of free-base porphyrin **10** was performed in CD_3OD. The detailed resonance assignments were obtained by 2D COSY experiments.

The two atropoisomeric porphyrins **4** (less polar) and **5** (polar) were determined to possess $\alpha,\beta,\alpha,\beta$- and $\alpha,\alpha,\alpha,\beta$-configuration, respectively.[13] The spectrum of **4** (Figure 1) reflects its D_2 symmetry with one singlet β-pyrrolic resonance, three apparent triplets each integrating to 4 H assigned to the protons of the carbohydrate residues, two singlets each integrating to 12 H assigned to isopropylidene methyls, and one broad singlet resonating at −2.43 ppm attributed to NH. At the contrary, reflecting the C_1 symmetry of the molecule, each proton of **5** has its own resonance resulting in six doublets and two singlets for the eight β-pyrrole protons and three triplets and one double doublet for the four nonequivalent H-1′ protons. D_2-Symmetric porphyrins **6** and **7** showed relatively simple spectra with one singlet resonance for the β-pyrrole protons and one resonance system corresponding to four equivalent protons of the sugar moieties; by analogy to the spectrum of **4**, the disposition of the four carbohydrate fragments relative to the mean porphyrin plane was assigned as $\alpha,\beta,\alpha,\beta$. Partially deprotected porphyrins **8** and **9**[14] showed split proton resonances in both the carbohydrate and pyrrole regions of the spectra, due to diminished symmetry. Dissymmetric compound **8** showed two 1:1 singlets for the β-pyrrole protons and three well-resolved doublets (1:1:2 ratios) assigned to H-1′ of the four sugar legs. C_2-Symmetric porphyrin **9**, instead, displayed only partially resolved resonances for the same protons. The ^1H NMR spectrum of **10** in CD_3OD showed poorly resolved resonances in all the regions resulting in two broad singlets corresponding to β-pyrrole and H-1′ carbohydrate chain protons and three multiplets assigned to H-2′, H-3′, and H-4′ protons of the residue sugar moieties.

Conclusion. Adaptation of the conventional acid-catalyzed pyrrole–aldehyde macrocyclization to suitably protected aldehydo sugar derivatives, according to the improved Lindsey's protocol,[8] allowed straightforward preparation of novel *C-meso*-glycosylated porphyrins. Removal of all the OH protecting groups of the sugar moieties resulted in formation of neutral compounds (*e.g.* **10** and *ent*-**10**) which are freely soluble in water. They might have expanded capabilities in the areas of chiral recognition and asymmetric catalysis in aqueous solution.

Experimental Section

General. 2,3-*O*-Isopropylidene-D-glyceraldehyde (**1**) was obtained from 1,2;5,6-di-*O*-isopropylidene-D-mannitol according to literature.[15] 2,3:4,5-Di-*O*-isopropylidene-D- and -L-arabinose (**3** and *ent*-**3**) were prepared from the corresponding aldoses according to known protocols.[16] 1,2-*O*-Isopropylidene-3-*O*-methyl-α-D-*xylo*-pentodialdofuranose (**2**) was from Fluka. Flash chromatography was performed on Florisil, Carlo Erba 100–200 mesh, using the indicated solvent mixtures. Analytical thin-layer chromatography was performed on E. Merck silica gel 60 F_{254} plates (0.25 mm). Porphyrinic compounds were visualized as green-emerald spots by dipping the plates in a solution of Ce(III) sulfate (1.0 g), ammonium molybdate (21 g), 96% sulfuric acid (31 mL), and distilled water (500 mL). ^1H NMR spectra were obtained on a Bruker AMX-400 and are reported in ppm (δ) relative to tetramethylsilane (0.0 ppm) as an internal reference, with coupling constants in hertz (Hz). Low-resolution mass spectra were obtained on a Finnigan 1020 6c mass spectrometer, and high-resolution mass spectra were obtained on a Kratos MSO8RFA mass spectrometer. Rotations were measured on a Rudolph Autopol III polarimeter, while circular dichroism spectra were performed on a Jasco 500 apparatus. Molar elipticity [θ] is reported in deg cm^2 $dmol^{-1}$. Ultraviolet-visible spectra were

(13) The assumption that porphyrins **4** and **5** were indeed atropoisomeric compounds was evidenced, *inter alia*, by thermal isomerization experiments at 383 K (boiling toluene) by starting with analytically pure **4** and **5**. After 5 h, equilibrium ratios of **4**:**5** = *ca.* 25:75 were reached. Two additional spots were also detected on TLC, which might be attributed to the $\alpha,\alpha,\alpha,\alpha$- and $\alpha,\alpha,\beta,\beta$-isomers, respectively. Thanks are due to the reviewers for drawing this point to our attention.

(14) Controlled deprotection of compound **7** with 50% aqueous AcOH at room temperature giving **8** and **9** substantiated the configurational correlation between these substances.

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obtained on a Kontron Uvicon 860 spectrophotometer. Elemental analyses were performed by The Microanalytical Laboratory of University of Parma (Dipartimento Farmaceutico).

The following procedure is typical.

5α,10β,15α,20β- and 5α,10α,15α,20β-Tetrakis-[(1*S*)-1,2-*O*-isopropylidene-1,2-dihydroxyethyl]porphyrins (4 and 5). To a solution of pyrrole (263 μL, 3.8 mmol) and 2,3-*O*-isopropylidene-D-glyceraldehyde (1) (500 mg, 3.8 mmol) in 385 mL of CH_2Cl_2 was added BF_3 etherate (47 μL, 0.38 mmol) while a stream of pure argon was passing. The reaction vessel was carefully shielded from light, and stirring was continued for 6 h. Then, triethylamine (53 μL, 0.38 mmol) and dichlorodicyanobenzoquinone (DDQ) (640 mg, 2.8 mmol) were added, and the reaction mixture was stirred at room temperature for additional 18 h. The solvent was evaporated under vacuum and the resulting dark-violet solid was dissolved in CH_2Cl_2 (2 mL). Florisil (1 g) was added and the solvent evaporated to give a powder which was charged at the top of a 20-mm i.d. silica gel column. Elution with a CH_2Cl_2/ethyl acetate (85:15, v/v) solvent mixture allowed the separation of pure porphyrins 4 and 5 [20.2 mg (3%) and 27.0 mg (4%), respectively] as brown-fluorescent red powders. Compound 4: R_f 0.45 (85:15 CH_2Cl_2/ethyl acetate); $[\alpha]^{23}_{546}$ +476.2° (*c* 0.005, $CHCl_3$); UV-vis ($CHCl_3$) λ_{max} 417 nm (ϵ = 117058 cm^{-1} M^{-1}), 519 (ϵ = 7729), 552 (ϵ = 1432), 595 (ϵ = 2561), 650 (ϵ = 152); CD ($CHCl_3$) $[\theta]_{415}$ = +31534, $[\theta]_{425}$ = −13210; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 8H, H-β), 7.57 (dd, *J* = 7.7, 7.8 Hz, 4H, H-1′), 5.00 (dd, *J* = 7.9, 7.7 Hz, 4H, H-2′A), 4.87 (dd, *J* = 7.9, 7.8 Hz, 4H, H-2′B), 2.13 (s, 12H, CH_3), 1.92 (s, 12H, CH_3), −2.43 (s, 2H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) CH_3 δ 26.9 (4), 24.7 (4), CH_2 78.3 (4), CH 129.4 (8), 112.2 (4), quaternary carbons 145.6 (8), 113.5 (4), 104.5 (4); HRMS (CI, CH_4) exact mass calcd for $C_{40}H_{47}N_4O_8$ 711.3396 (MH^+), found 711.3417. Anal. Calcd for $C_{40}H_{46}N_4O_8$: C, 67.59; H, 6.52; N, 7.88. Found: C, 67.71; H, 6.48; N, 7.67. Compound 5: R_f 0.13 (85:15, CH_2Cl_2/ethyl acetate); $[\alpha]^{23}_{546}$ +485.1° (*c* 0.004, $CHCl_3$); UV-vis ($CHCl_3$) λ_{max} 418 nm (ϵ = 86800 cm^{-1} M^{-1}), 518 (ϵ = 5136), 554 (ϵ = 1254), 593 (ϵ = 1704), 649 (ϵ = 166); CD ($CHCl_3$) $[\theta]_{418}$ = +88778; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (d, *J* = 5.1 Hz, 1H, H-β), 9.85 (d, *J* = 5.2 Hz, 1H, H-β), 9.84 (s, 1H, H-β), 9.74 (d, *J* = 5.2 Hz, 1H, H-β), 9.71 (d, *J* = 5.2 Hz, 1H, H-β), 9.39 (d, *J* = 5.1 Hz, 1H, H-β), 9.22 (s, 1H, H-β), 7.61 (t, *J* = 7.7 Hz, 1H, H-1′), 7.57 (t, *J* = 7.7 Hz, 1H, H-1′), 7.51 (t, *J* = 7.7 Hz, 1H, H-1′), 7.38 (dd, *J* = 3.4, 8.1 Hz, 1H, H-1′), 5.03 (m, 4H, H-2′), 4.91 (dd, *J* = 7.7, 9.3 Hz, 1H, H-2′), 4.87 (dd, *J* = 7.3, 8.1 Hz, 1H, H-2′), 4.65 (dd, *J* = 3.4, 11.7 Hz, 1H, H-2′), 4.00 (dd, *J* = 8.1, 11.7 Hz, 1H, H-2′), 2.40, 2.17, 2.15, 2.14, 2.13, 2.10, 1.93, and 1.91 (8s, each 3H, CH_3), −2.34 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) CH_3 δ 31.0, 30.0, 29.9, 27.0 (3), 24.9 (2), CH_2 75.4 (2), 75.0, 71.1, CH 130.5 (3), 128.8, 128.4, 128.1, 126.1, 120.0, 111.2 (4), quaternary carbons 148.5 (4), 143.2 (2), 138.2 (2), 114.2, 113.0, 112.5, 111.0, 110.0, 108.9, 107.5, 103.0; HRMS (CI, CH_4) exact mass calcd for $C_{40}H_{47}N_4O_8$ 711.3396 (MH^+), found 711.3401. Anal. Calcd for $C_{40}H_{46}N_4O_8$: C, 67.59; H, 6.52; N, 7.88. Found: C, 67.57; H, 6.62; N, 7.81.

The following porphyrins were obtained by adopting a quite similar procedure.

5α,10β,15α,20β-Tetrakis(1,2-*O*-isopropylidene-3-*O*-methyl-β-L-threofuranos-4-yl)porphyrin (6). From 2 and pyrrole in 6% yield: dark violet powder; R_f 0.57 (80:20, CH_2Cl_2/ethyl acetate); $[\alpha]^{23}_{546}$ −104.2°, $[\alpha]^{23}_{589}$ +135.4° (*c* 0.009, $CHCl_3$); UV-vis ($CHCl_3$) λ_{max} 419 nm (ϵ = 137677 cm^{-1} M^{-1}), 523 (ϵ = 8945), 560 (ϵ = 1840), 595 (ϵ = 3100), 652 (ϵ = 2130); CD ($CHCl_3$) $[\theta]_{414}$ = −57745; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (bs, 8H, H-β), 7.87 (d, *J* = 3.0 Hz, 1H, H-4′), 6.69 (d, *J* = 4.0 Hz, 1H, H-1′), 5.16 (d, *J* = 4.0 Hz, 1H, H-2′), 4.61 (d, *J* = 3.0 Hz, 1H, H-3′), 2.48 (s, 12H, OCH_3), 1.90 (s, 12H , CH_3), 1.60 (s, 12H, CH_3), −2.62 (s, 2H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) CH_3 δ 58.8 (4), 27.4 (4), 26.6 (4), CH 129.9 (8), 104.9 (4), 90.0 (4), 88.4 (8), quaternary carbons 145.4 (8), 112.0 (4), 109.8 (4); HRMS (CI, CH_4) exact mass for $C_{52}H_{63}N_4O_{16}$ 999.4241 (MH^+), found 999.4363. Anal. Calcd for $C_{52}H_{62}N_4O_{16}$: C, 62.51; H, 6.26; N, 5.61. Found: C, 62.63; H, 6.23; N, 5.52.

5α,10β,15α,20β-Tetrakis(1,2:3,4-di-*O*-isopropylidene-D-*arabino*-tetritol-1-yl)porphyrin (7), 5α,10β,15α-Tris(1,2;3,4-di-*O*-isopropylidene-D-*arabino*-tetritol-1-yl)-20β-(1,2-*O*-isopropylidene-3,4-dihydroxy-D-*arabino*-tetritol-1-yl)-porphyrin (8), and 5α-15α-Bis(1,2;3,4-di-*O*-isopropylidene-D-*arabino*-tetritol-1-yl)-10β-20β-bis(1,2-*O*-isopropylidene-3,4-dihydroxy-D-*arabino*-tetritol-1-yl)porphyrin (9). From 3 and pyrrole in 2, 1, and 4% yields, respectively. Compound 7: brown-red powder; R_f 0.72 (50:50 CH_2Cl_2/ethyl acetate); $[\alpha]^{23}_{589}$ −10.5° (*c* 0.019, $CHCl_3$); UV-vis ($CHCl_3$) λ_{max} 415 nm (ϵ = 22790 cm^{-1} M^{-1}), 516 (ϵ = 1758), 549 (ϵ = 410), 595 (ϵ = 602), 650 (ϵ = 88); CD ($CHCl_3$) $[\theta]_{412}$ = −14254; ^{1}H NMR δ 9.78 (s, 8H, H-β), 7.53 (d, *J* = 7.8 Hz, 1H, H-1′), 5.28 (d, *J* = 7.8 Hz, 1H, H-2′), 4.57 (dd, *J* = 5.8, 5.1 Hz, H-3′), 3.98 (dd, *J* = 5.8, 8.7 Hz, H-4′A), 3.74 (dd, *J* = 5.1, 8.7 Hz, H-4′B), 2.16 (s, 24H, CH_3), 1.98 (s, 24H, CH_3), −2.65 (s, 2H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) CH_3 δ 30.0 (4), 29.6 (4), 26.3 (4), 25.4 (4), CH_2 67.2 (4), CH 130.1 (8), 99.5 (4), 87.9 (4), 82.0 (4), quaternary carbons 147.2 (8), 113.0 (4), 110.0 (8); HRMS (CI, CH_4) exact mass calcd for $C_{60}H_{79}N_4O_{16}$ 1111.5494 (MH^+), found 1110.5514. Anal. Calcd for $C_{60}H_{78}N_4O_{16}$: C, 64.85; H, 7.08; N, 5.04. Found: C, 64.91; H, 7.25, N, 4.91. Compound 8: brown-red powder; R_f 0.28 (50:50 CH_2Cl_2/ethyl acetate); $[\alpha]^{23}_{546}$ −350.0° (*c* 0.009, $CHCl_3$); UV-vis ($CHCl_3$) λ_{max} 417 nm (ϵ = 49496 cm^{-1} M^{-1}), 517 (ϵ = 3820), 549 (ϵ = 1032), 595 (ϵ = 1373), 649 (ϵ = 250); CD ($CHCl_3$) $[\theta]_{413}$ = −40968; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 4H, H-β), 9.78 (s, 4H, H-β), 7.63 (d, *J* = 8.3 Hz, 1H, H-1′), 7.54 (d, *J* = 8.1 Hz, 1H, H-1′), 7.53 (d, *J* = 8.3 Hz, 2H, H-1′), 5.29 (m, 3H, H-2′), 5.20 (dd, *J* = 8.3, 5.0 Hz, 1H, H-2′), 4.57 (dd, *J* = 5.0, 12.5 Hz, 3H, H-3′), 4.22 (m, 1H, H-3′), 3.97 (m, 3H, H-4′A), 3.75 (m, 3H, H-4′B), 3.24 (m, 2H, H-4′A and H-4′B), 2.14 (m, 12H, CH_3), 1.97 (m, 12H, CH_3), 1.60 (bs, 2H, OH), 1.25 (s, 6H, CH_3), 1.00 (s, 12H, CH_3), −2.67 (bs, 2H, NH); ^{13}C (100 MHz, $CDCl_3$) CH_3 δ 30.3 (4), 28.7 (4), 27.8 (3), 26.5 (2), 25.7, CH_2 67.6, 66.3 (3), CH 137.0 (4), 130.0 (4), 100.0, 98.8, 98.0, 96.0, 89.8, 88.3 (3), 83.1–80.0 (4), quaternary carbons 149.0–144.0 (8), 114.0–110.3 (4), 109.7 (7); HRMS (CI, CH_4) exact mass calcd for $C_{57}H_{75}N_4O_{16}$ 1071.5181 (MH^+), found 1071.5200. Compound 9: brown-red powder; R_f 0.03 (50:50 CH_2Cl_2/ethyl acetate); $[\alpha]^{23}_{546}$ −175.0° (*c* 0.02, $CHCl_3$); UV-vis ($CHCl_3$) λ_{max} 417 nm (ϵ = 21746 cm^{-1} M^{-1}), 518 (ϵ = 1530), 556 (ϵ = 567), 595 (ϵ = 633), 650 (ϵ = 160); CD ($CHCl_3$) $[\theta]_{415}$ −6613; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (bs, 8H, H-β), 7.52 (m, 4H, H-1′), 5.16 (m, 2H, H-2′), 4.62 (m, 2H, H-2′), 4.03 (m, 6H, H-3′ and H-4′), 3.85–3.55 (m, 2H, H-4′), 3.20 (m, 4H, H-4′), 2.14 and 1.97 (2s, each 6H, CH_3), 1.60 (bs, 4H, OH), 1.27 (m, 24H, CH_3), 0.22 (bs, 2H, NH); ^{13}C (100 MHz, $CDCl_3$) CH_3 δ 29.5 (4), 28.0, 26.9 (3), 26.3, 26.0, 25.2 (2), CH_2 70.7 (2), 63.9 (2), CH 130.0 (2), 130.0 (2), 129.4 (2), 128.6 (2), 107.0 (2), 104.8 (2), 87.6 (4), 82.5 (2), 81.3 (2), quaternary carbons 149.8 (4), 145.0 (4), 113.8 (2), 112.0 (2), 110.3 (6); HRMS (CI, CH_4) exact mass calcd for $C_{54}H_{71}N_4O_{16}$ 1031.4867 (MH^+), found 1031.4890.

5α,10β,15α,20β-Tetrakis(D-*arabino*-tetritol-1-yl)porphyrin (10). To a solution of porphyrin 7 (3.0 mg, 2.7 μmol) in CH_2Cl_2 (1 mL) a 50% aqueous trifluoroacetic acid solution (1 mL) was added under stirring at room temperature. The biphasic mixture was sonicated until the organic phase discolored completely, while the aqueous phase assumed the green color of the porphyrin dication (ca. 2 h). The aqueous phase was separated, neutralized with a 2 N aqueous ammonia solution, and evaporated under vacuum to give free-base 10 as a brown-red solid (2.7 mg, 90%): R_f 0.26 [70:20:10, $CHCl_3$/CH_3OH/NH_4OH (2 N)]; $[\alpha]^{23}_{546}$ −122.0°, $[\alpha]^{23}_{589}$ −118.0° (*c* 0.0005, H_2O); UV-vis (H_2O) λ_{max} 418 nm (ϵ = 28200 cm^{-1} M^{-1}), 514 (ϵ = 1700), 556 (ϵ = 1700); CD (H_2O) $[\theta]_{417}$ = −3366; ^{1}H NMR δ 9.75 (bs, 8H, H-β), 7.28 (bs, 4H, H-1′), 5.35 (m, 4H, H-2′), 4.14 (m, 4H, H-3′), 3.90–2.90 (m, 8H, H-4′); HRMS (FAB, 3-nitrobenzyl alcohol) exact mass calcd for $C_{36}H_{47}N_4O_{16}$ 791.2988 (MH^+), found 791.3001. Anal. Calcd for $C_{36}H_{46}C_4O_{16}$: C, 54.68; H, 5.86; N, 7.09. Found: C, 54.50; H, 5.93; N, 7.01.

5α,10β,15α,20β-Tetrakis(1,2:3,4-di-*O*-isopropylidene-L-*arabino*-tetritol-1-yl)porphyrin (*ent*-7). From *ent*-3 and pyrrole in 2% yield: red-brown powder; $[\alpha]^{23}_{589}$ +10.5° (*c* 0.019, $CHCl_3$); CD ($CHCl_3$) $[\theta]_{413}$ = +13783; HRMS (CI, CH_4) exact mass calcd for $C_{60}H_{79}N_4O_{16}$ 1111.5494 (MH^+), found 1111.5503. Anal. Calcd for $C_{60}H_{78}N_4O_{16}$: C, 64.85; H, 7.08; N, 5.04. Found: C, 64.94; H, 6.94; N, 4.90. R_f value and UV-vis and ^{1}H NMR spectral characteristics identical to those reported for its enantiomer 7.

5α,10β,15α,20β-Tetrakis(L-*arabino*-tetritol-1-yl)porphyrin (*ent*-10). This compound was prepared from *ent*-7 by following the same protocol as used for 10: yield 90%; red-brown

powder; $[\alpha]^{23}_{546}$ +120.0°, $[\alpha]^{23}_{589}$ +108.0° (c 0.008, H_2O); CD (H_2O) $[\theta]_{413}$ = +3640; HRMS (FAB, 3-nitrobenzyl alcohol) exact mass calcd for $C_{36}H_{47}N_4O_{16}$ 791.2988 (MH^+), found 791.2998. R_f value and UV-vis and ^1H NMR spectral characteristics identical to those reported for its enantiomer **10**.

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Supplementary Material Available: ^1H NMR, UV-vis, CD, and mass spectra for compounds **4–7**, CD spectra for compounds *ent*-**7** and *ent*-**10**, and UV-vis and CD spectra for compound **10** (20 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Additions and Corrections

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Andrew D. Abell,* Deborah A. Hoult, Kathryn B. Morris, Jane M. Taylor, and John O. Trent. Halogenation of Keto Acid Phosphoranes: Synthesis of Halo Enol Lactones and Haloallenes.

Page 1531. Kathy M. Morris should read Kathryn B. Morris.