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A comparison of two convergent routes for the preparation of metalloporphyrin-core dendrimers: direct condensation *vs.* chemical modification†

Keith W. Pollak,[a] Elizabeth M. Sanford[b] and Jean M. J. Fréchet*[a]

[a]*Department of Chemistry, University of California, Berkeley, CA 94720–1460 USA*
[b]*Hope College, Holland, Michigan 49422-9000, USA*

Porphyrin-core dendrimers consisting of benzyl ether dendrons assembled around a porphyrin core have been prepared by two different convergent syntheses. The first involves the direct condensation of convergent dendrons having 3,5-disubstituted benzaldehyde focal points with an equivalent amount of pyrrole. This route which requires very mild conditions is especially useful for the rapid assembly of small dendrimers but suffers from steric limitations as the size of the dendrons increases above the fourth generation. The second route involves the attachment of pre-formed benzyl bromide dendrons to a functionalized porphyrin through a simple Williamson synthesis. This route is also very practical but it requires careful purification of the final product from the partially functionalized porphyrin dendrimers that are also obtained. MALDI mass spectrometry proved to be a very useful tool both for monitoring the formation of the dendritic porphyrins and for their characterization.

Metalloporphyrins with specific architecture have been developed to model various biological systems; two of the common natural archetypes are chlorophyll, and heme proteins. The light-harvesting and electron-transfer properties of chlorophyll have been modelled by synthetic metalloporphyrins with substituents which modify the photochemical behavior of the porphyrin.[1] Other metalloporphyrins have been synthesized with either one or both faces of the porphyrin sterically obstructed to model proteins like hemoglobin and myoglobin which bind and transport molecular oxygen.[2] But the most common purpose for synthesizing porphyrins with defined architecture is to model natural oxidation catalysts like cytochromes.[3,4]

Some of the latest biological models embed a porphyrin at the core of a dendrimer. The synthesis of such a macromolecule could follow either the divergent[5] or convergent[6] approach to dendrimers, and indeed both routes have been used by different research groups.[7–10] For example Diederich and co-workers[7] have used the divergent approach to grow a polyamide dendrimer from a porphyrin core. Although this method has been successful for the preparation of large porphyrin-core dendrimers, the sensitivity of the porphyrin moiety must be considered in the growth of the dendrimers, a process that typically involves multiple preparative steps and demanding purification procedures. Such potential problems could be avoided by incorporating the porphyrin core into the macromolecule at the last step of the synthesis,[8] as is common practice in the synthesis of dendrimers through the convergent approach.[6]

A convenient route for the synthesis of porphyrin-core dendrimers involves the attachment of convergent dendrons to a pre-formed porphyrin core. Aida and co-workers[8] have used the convergent approach to prepare polyether dendrons and then attached the dendrons to a functionalized tetraaryl porphyrin, tetrakis(3,5-dihydroxyphenyl)porphyrin, through a Williamson ether synthesis. Similarly, Moore *et al.* attached polyester dendrons, prepared through the convergent approach, to a metalloporphyrin core using dicyclohexycarbodiimide (DCC) coupling.[10] A less obvious convergent route to porphyrin-core dendrimers might involve the preparation of dendrons with an aldehyde functionality at their focal point, and their subsequent assembly into a porphyrin by Lindsey[12] condensation with pyrrole. Until now, this *in situ* assembly of porphyrin-core dendrimers had not been reported.

In view of the potential application of site-isolated porphyrin nuclei for electron transfer or other catalytic processes, this study explores and compares the synthesis of metalloporphyrin-core dendrimers of generations 1–4 *via* two routes utilizing the convergent growth approach. Route I, in which dendritic aldehyde and pyrrole are combined in a Lindsey porphyrin synthesis to generate the porphyrin core *in situ* (Scheme 1) and route II, in which zinc tetrakis(3,5-dihydroxyphenyl)porphyrin, a porphyrin core with eight reactive phenolic sites,[8] is alkylated with a dendritic bromide in a Williamson ether synthesis (Scheme 2).

Results and Discussion

Direct formation of the porphyrin core from a dendritic aldehyde and pyrrole

Benzyl ether dendrons were prepared through the iterative bromination and alkylation steps described by Hawker and Fréchet.[6a,11] To prepare the desired generation of dendritic aldehyde, dendritic bromide was used to alkylate 3,5-dihydroxybenzaldehyde (Scheme 3). Classical Lindsey condensation[12] of the dendritic aldehyde and an equivalent amount of pyrrole at a concentration of 10^{-2} M in chloroform was done at room temperature in the presence of a catalytic amount of trifluoroacetic acid, under very mild conditions that can be tolerated by various functionalities which might be present in the dendrons. Monitoring by TLC proved to be effective because the starting materials, desired product, and polypyrrylmethane by-products exhibit very different R_f values. However, analysis by UV–VIS spectroscopy allowed for a more accurate evaluation of the progress of the condensation because the desired product absorbs at sharp, characteristic wavelengths: a strong Soret band at 424 nm and four weak additional bands at 510, 550, 590 and 650 nm while the polypyrrylmethane by-products have a broader absorption (Fig. 1). When the relative intensities of these bands stabilize, the condensation is at equilibrium. As the generation number is increased the reaction became more sluggish and reaction times increased from 1.5 h

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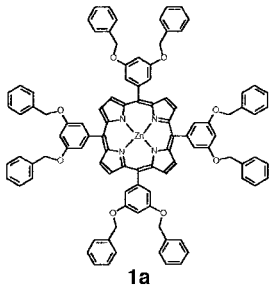
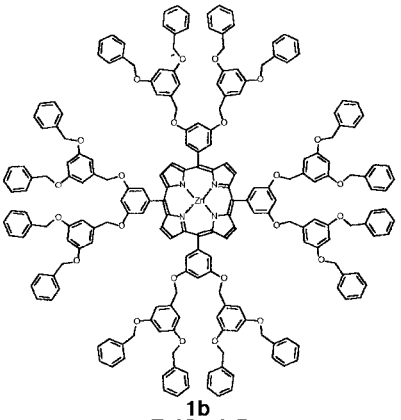
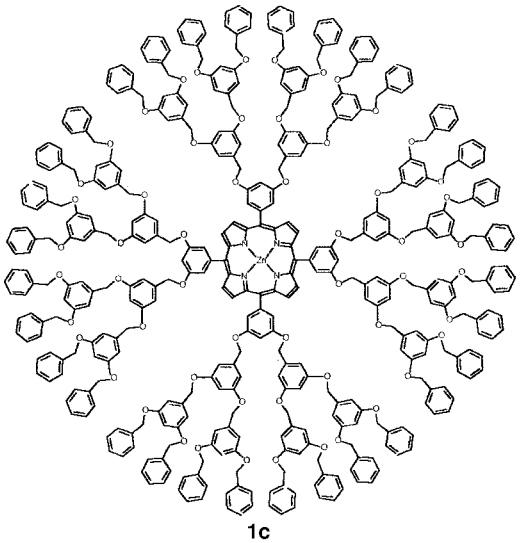
* E-mail: Frechet@cchem.berkeley.edu



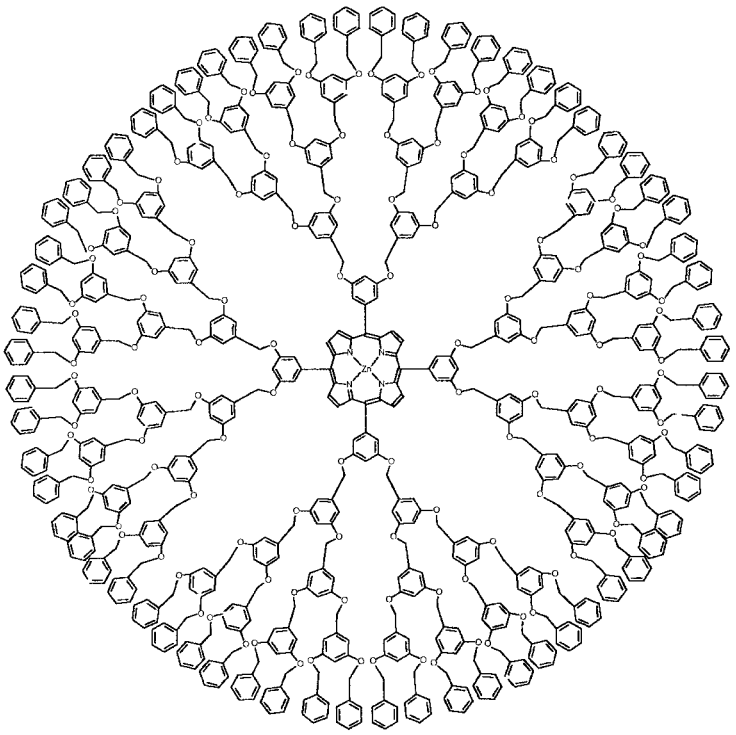
1a
$Zn[G\text{-}1]_4P$



1b
$Zn[G\text{-}2]_4P$



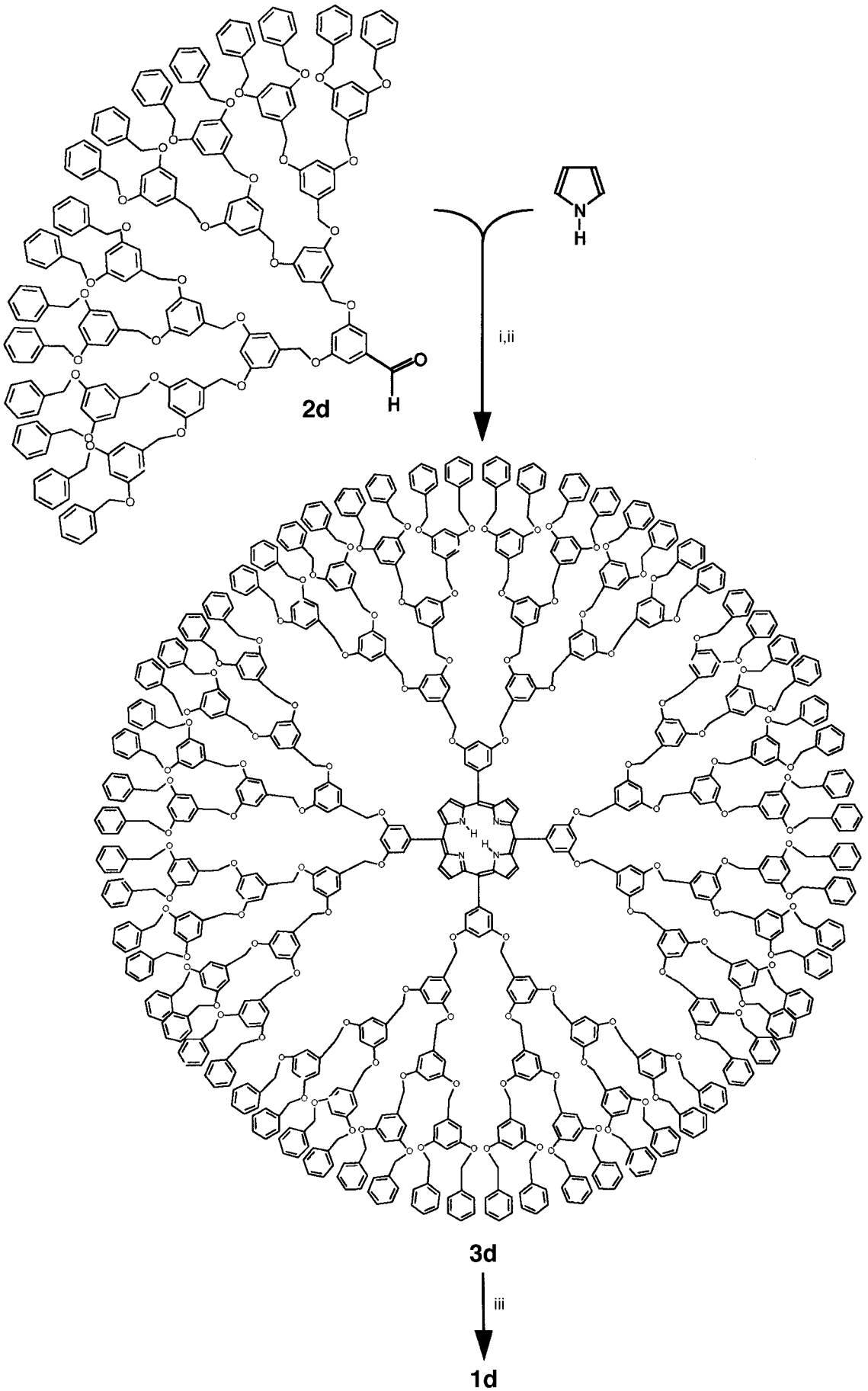
1c
$Zn[G\text{-}3]_4P$



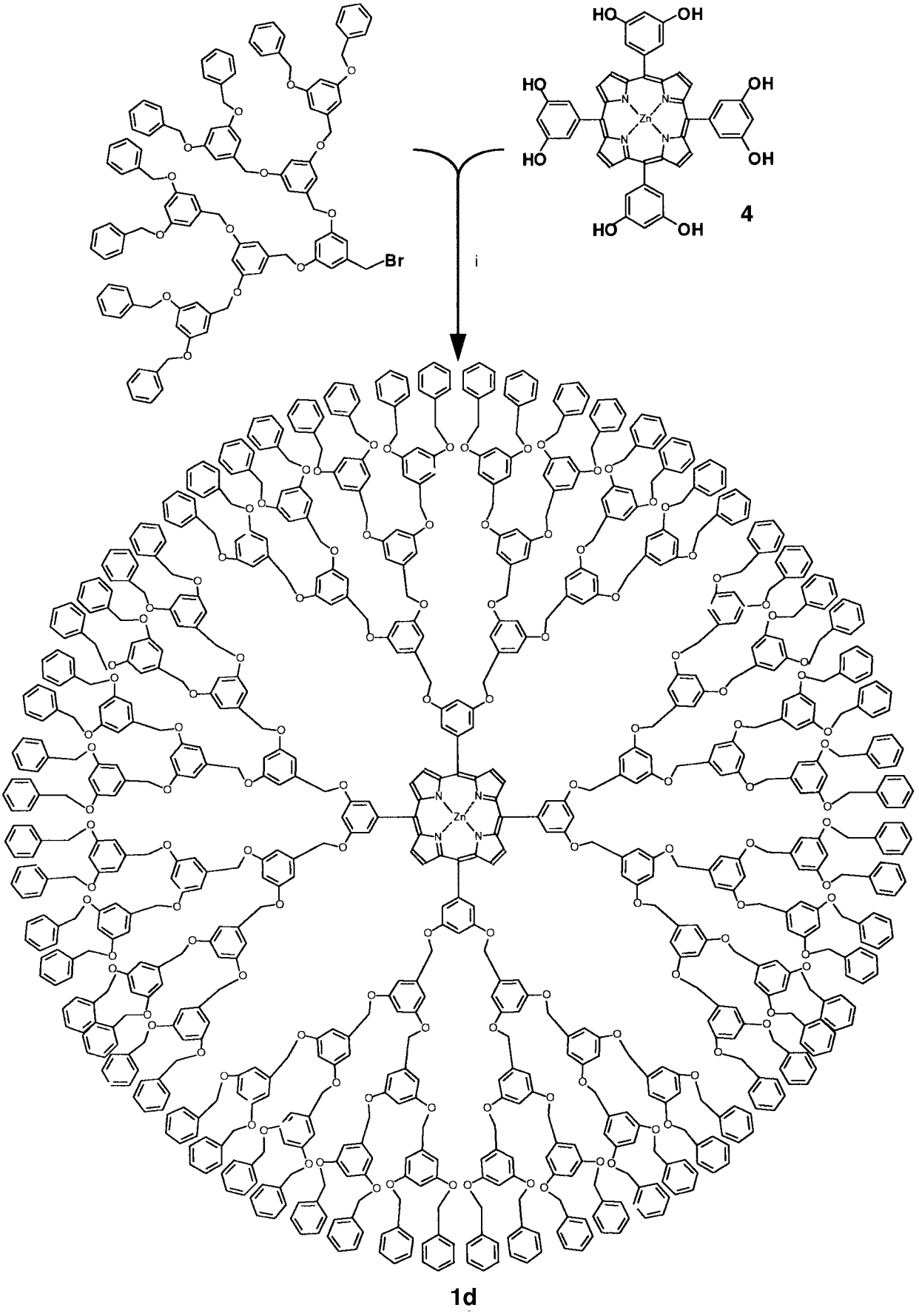
1d
$Zn[G\text{-}4]_4P$

for generations 1 and 2, to 10 and 36 h for generation 3 and 4, respectively, though the latter required different reaction conditions. For the first three generations, the porphyrinogen condensation product was oxidized directly after condensation and in the same reaction flask to the free-base porphyrin-core dendrimers **3a–c** in 25–30% yield by heating it to reflux in the presence of chloranil. Preparation of the fourth generation free-base porphyrin-core dendrimer **3d** was attempted using these reagents and conditions, but it failed. In the condensation step, formation of porphyrin was observed in the reaction samples both by TLC and UV–VIS spectroscopy, yet after the oxidation step, no porphyrin was produced. This was probably due to *in situ* decomposition of the product as a result of the elevated reaction temperature required for the oxidation reaction using chloranil. Using a stronger oxidizing agent, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), the oxidation could be performed at room temperature, thereby preserving the porphyrinogen and producing **3d** in 14% yield. Purification of all of the free-base porphyrin-core dendrimers by column chromatography proved to be very simple because the desired product elutes much faster than the polypyrrylmethane by-products.

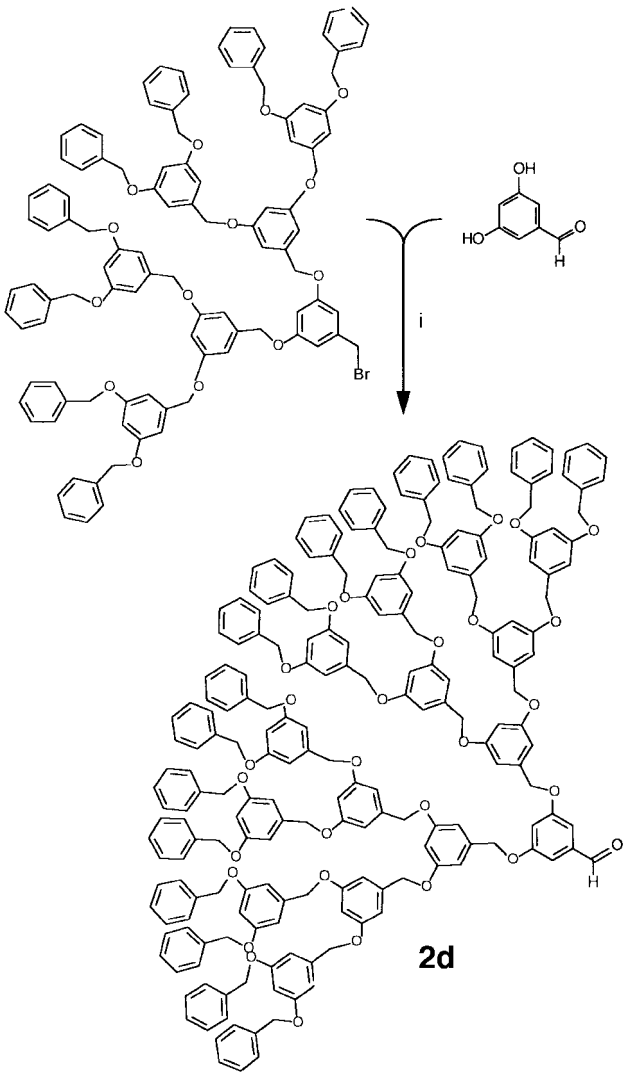
Analysis of the free-base porphyrin core dendrimers by ^1H NMR was facilitated by the high degree of symmetry in the macromolecule. Evidence for the free-base porphyrin core of **3a–d** is provided by the eight β-pyrrole and two free-base protons seen as singlets at 8.9 and -2.9 ppm, respectively. The spectral features of the dendrons, which surround the porphyrin core with generational tiers of benzyl ethers, are also readily attributed. The phenyl protons located on the outermost phenyl rings are seen at 7.2–7.5 ppm, and those on the aromatic ring at the *meso* position of the porphyrin appear as a one-proton triplet at 7.10 ppm and a two-proton doublet at 7.50 ppm. The benzyl protons appear as a series of singlets around 4.6–5.0 ppm, depending on the generation number. Not all of the ^{13}C NMR resonances for the dendrons can be assigned because of the many overlapping signals,[11] and at high generation, the intensities of some of the resonances of the core carbons are too weak to be seen. However when the core carbons are detectable, the porphyrin gives rise to three distinct resonances:[13] C_α at 145.8 ppm, C_β at 130.6 ppm, and C_{meso} at 119.6 ppm. Analysis of the free-base porphyrin-core dendrimers **3a–d** by matrix-assisted laser-desorption ionization (MALDI) mass spectrometry (Fig. 2) shows that well defined macromolecules exhibiting the expected peaks corresponding to $M+H^+$, $M+Na^+$ and/or $M+K^+$ are obtained.



Scheme 1 *Reagents and conditions*: i, CF_3CO_3H; ii, DDQ; iii, $Zn(OAc)_2$



Scheme 2 *Reagents and conditions*: i, K_2CO_3, 18-crown-6



Scheme 3 *Reagents and conditions*: i, K_2CO_3, 18-crown-6

The free-base porphyrin-core dendrimers **3a–d** were quantitatively metallated by dissolving the macromolecule and zinc acetate in methanol–chloroform (1:1) and heating at reflux overnight. Spectroscopic confirmation of the metallation reaction is provided by the UV–VIS absorption spectra since the metallated dendrimers **1a–d** exhibit a strong Soret band at 430 nm and two additional bands at 560 and 600 nm.[14] In addition, the ^{1}H NMR spectra of the products no longer exhibit the characteristic signal for the two protons located inside the porphyrin ring of the free-base starting materials.

Preparation by dendron alkylation of a pre-formed porphyrin core

As will be seen below, a comparison of this approach first reported by Aida and co-workers[8] with the direct Lindsey-type synthesis shows that each route has its own advantages and shortcomings.

Specifically, this route requires that a porphyrin core with multiple reactive functionalities be prepared first then coupled to the appropriate number of benzyl ether dendrons. For example, Scheme 4 shows the preparation of a core with eight protected phenolic functionalities by condensation of pyrrole and 3,5-dimethoxybenzaldehyde. The resulting porphyrinogen is then oxidized to the free base 5,10,15,20-tetrakis(3,5-dimethoxyphenyl)porphyrin **5** in 52% yield. Following removal of the methoxy protecting groups by reaction with boron tribromide, the free base 5,10,15,20-tetrakis(3,5-dihydroxyphenyl)porphyrin **6** is obtained. Metallation of this porphyrin with zinc acetate produced zinc 5,10,15,20-tetrakis(3,5-dihydroxyphenyl)porphyrin **4**, the octafunctional core for the porphyrin-core dendrimers. The dendrons used for the subsequent alkylation are readily obtained through the iterative bromination and alkylation steps described by Hawker and Fréchet.[11] Formation of the porphyrin-core dendrimers requires that all eight phenolic pendant groups of the core be alkylated. This is best done using a 20% excess of the benzylic bromide dendron while monitoring the progress of the reaction. Thin layer chromatography (TLC) is not sufficient for this purpose because some of the partially alkylated cores such as those with six or seven dendrons added to the core exhibit an R_f value similar to that of the fully alkylated product. In the final stages of the reaction, monitoring by MALDI mass spectroscopy is more effective as the partially alkylated cores are readily identified as shown in Fig. 3.

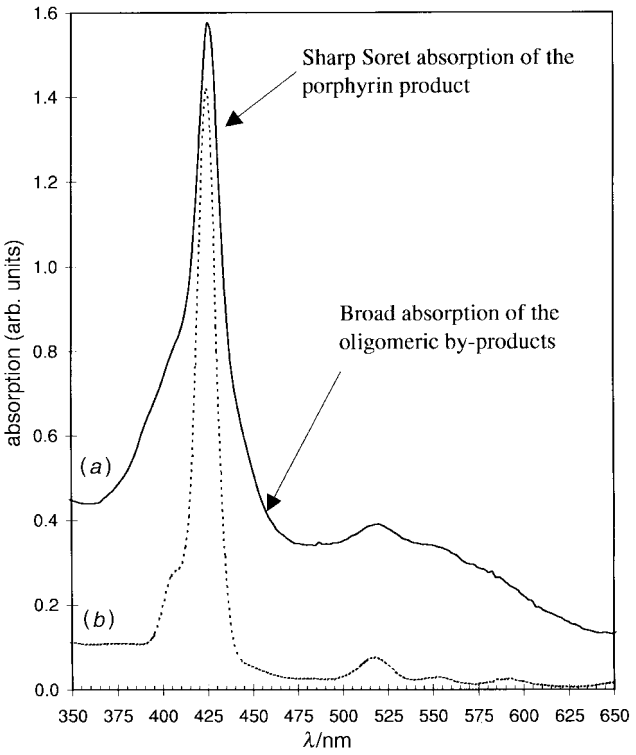


Fig. 1 (*a*) UV–VIS spectrum of the crude reaction mixture obtained in the preparation of a generation 3 porphyrin-core dendrimer **3c** *via* Route I. (*b*) UV–VIS absorption spectrum of pure **3c**.

Careful control of the reaction temperature is required during the alkylation as temperature affects both the rate and the site of alkylation. If the temperature is significantly higher than 60 °C, the reaction rate increases but significant *C*-alkylation involving the 2 position of the phenyl ring of the porphyrin core is observed as evidenced by the presence of two singlets of equal intensity at 7.82 and 8.59 ppm characteristic of the two remaining phenyl protons in the ^{1}H NMR spectrum of the product mixture. Below 60 °C, the extent of *C*-alkylation is insignificant but the reaction times increase considerably. A reaction temperature of 60 °C produced a good compromise affording primarily *O*-alkylated product in a reasonable reaction time. As expected in view of increased steric requirements around the core, the reaction time required for complete alkylation varies as a function of generation: 1, 3 and 5 d for generation 2, 3 and 4, respectively. Regardless of conditions used the final product must be purified by column chromatography to remove by-products or partially alkylated products. Purification is best achieved by chromatography through silica, eluting with a continuous linear gradient from hexane to CH_2Cl_2. Isolation of the desired product by column

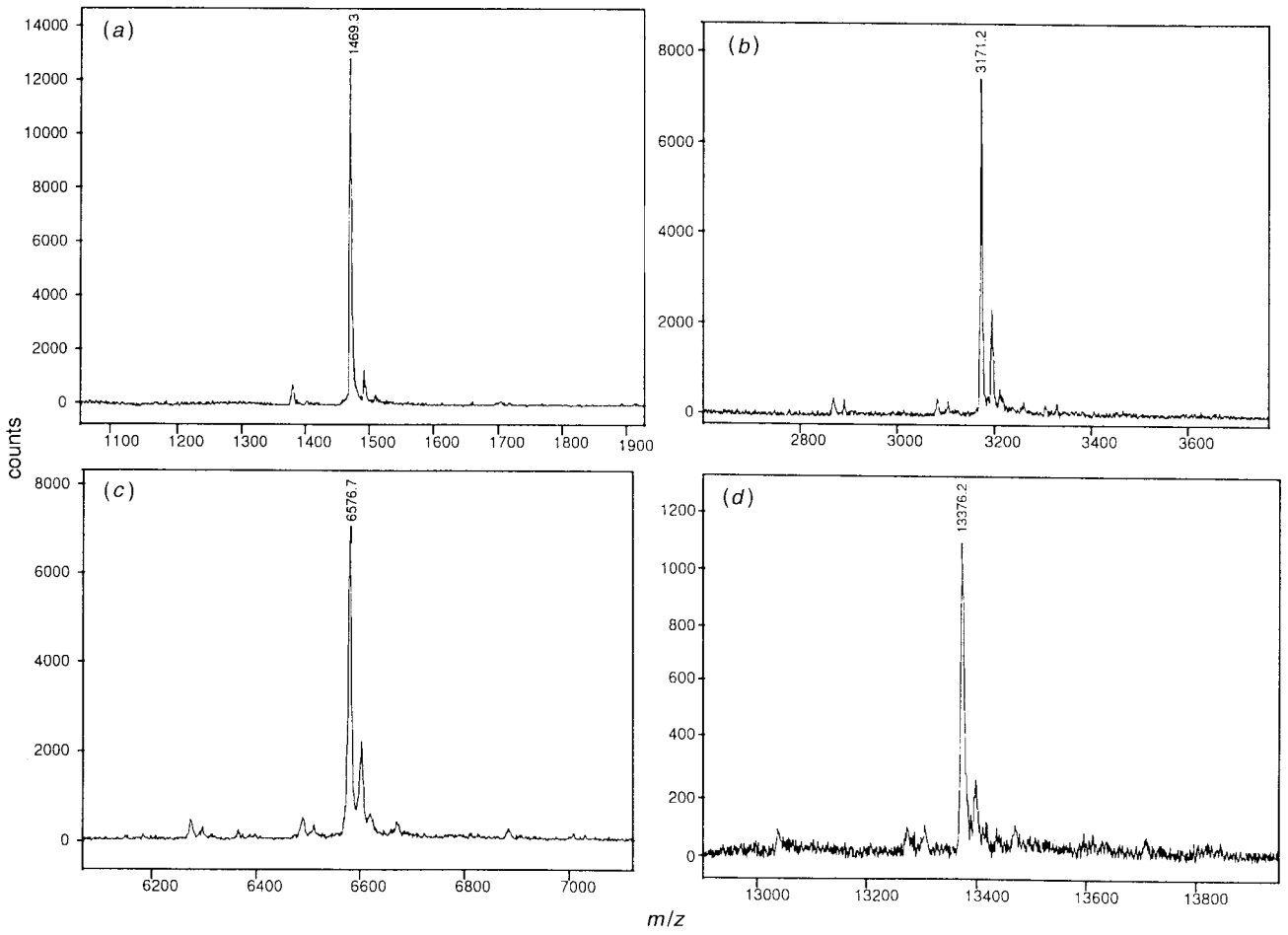
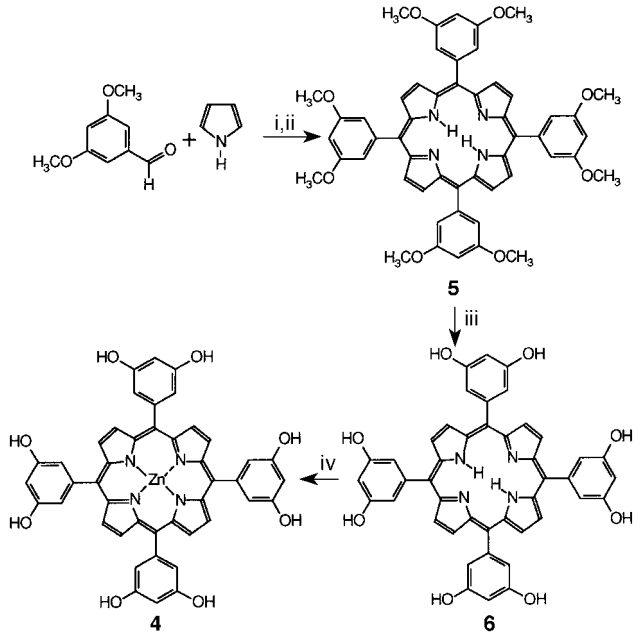


Fig. 2 MALDI mass spectra of the generation 1–4 free-base porphyrin-core dendrimers prepared *via* Route I. Sodium and potassium adducts are clearly seen at the right of the main peaks. (*a*) Generation 1, (*b*) 2, (*c*) 3 and (*d*) 4.



Scheme 4 *Reagents and conditions*: i, $BF_3 \cdot OEt_2$; ii, DDQ; iii, BB_3; iv, $Zn(OAc)_2$

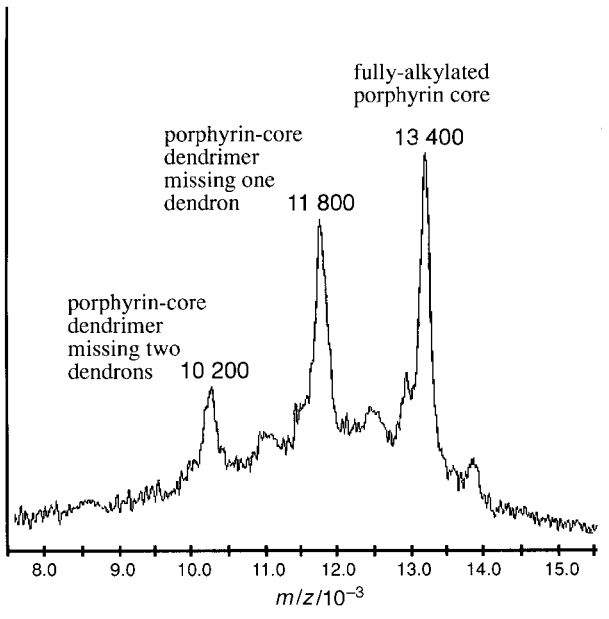


Fig. 3 MALDI mass spectrum of the crude product obtained in the preparation of fourth generation porphyrin-core dendrimer **1d** *via* Route II. Partly alkylated dendrons are clearly seen at *m/z* 10 200 and 11 800.

chromatography is difficult since the excess dendritic bromide, some partially alkylated core, and any by-products (*i.e. C*-alkylated core) behave very similarly to the desired product on a silica gel column. However, with careful chromatography, pure product is isolated, and the excess dendritic bromide can be recovered. Since high generation dendrons require considerable synthetic effort, recovering the unreacted starting material is often desirable. After evaporating the solvent, the product was isolated as a violet glass. Subsequent trituration with methanol allowed the porphyrin-core dendrimer to be handled

as a powder. Dendrimers **1b**, **1c**, and **1d** were prepared by this route in 71, 68 and 20% yields respectively.

Conclusions

This study demonstrates the versatility of the convergent synthesis for the preparation of dendritic porphyrins. A clear advantage of the two convergent approaches described herein is that few steps involving dendrimers are involved; this helps ensure that impurities or unreacted functionalities do not accumulate as might be the case in a divergent synthesis involving multiple steps for the growth of the dendrimer onto the porphyrin core. This may be particularly useful in instances where very accurate structural control is required or where the end-functionalities of the porphyrin ring itself might not survive the reactions used during multistep syntheses.

While both convergent routes benefit from the architectural control afforded by the convergent synthesis, each route offers unique synthetic advantages. The direct Lindsey-type condensation is done in the presence of a catalytic amount of acid, while the alkylation route is done under prolonged basic conditions. As a result, the choice of a specific route may be determined by any sensitive functionality that may be present on the dendrons. A clear advantage of the Lindsey-type route is the ease of both monitoring of product formation and purification of the desired free-base dendritic porphyrins by simple column chromatography. Reaction times for the direct condensation are also consistently shorter than those for route II. However, despite the larger number of steps required for the chemical modification route it affords higher yields than the direct Lindsey-type synthesis, especially in the preparation of low generation porphyrin-core dendrimers. The chemical modification route appears to be more suitable than the Lindsey route for very large dendrimers since it does not appear to be as sensitive to steric constraints. It is anticipated that similar trends would be observed for syntheses using other types of dendrons.

Finally, since the convergent synthesis of the dendritic porphyrin affords precise control of the dendrimer architecture it provides the means for incorporating potential prosthetic functionalities at precise locations within the assembly. Through careful design, functionalizing the dendrons with either specific guest-binding sites or rate-enhancing ligands near the catalytic core could create 'suprabiotic'[4] catalysts.

Experimental

General directions

Silica for flash chromatography was Merck Silica Gel 60 (230–400 mesh). Matrix-assisted laser-desorption ionization time of flight (MALDI-TOF) mass spectroscopy was performed on a Finnigan Lasermat or Perseptive Voyager DE. The energy source was a 337 nm nitrogen laser. Samples were prepared as 10^{-4} M solutions in tetrahydrofuran. The matrix was a solution consisting of 0.2 M indoleacrylic acid and 7×10^{-4} M sodium dodecyl sulfate in tetrahydrofuran. Four microlitres of the sample and 40 microlitres of matrix were combined and analyzed. All NMR spectra were recorded as solutions in $CDCl_3$ on a Bruker WM 300 (300 MHz) spectrometer with the solvent proton signal as standard: 7.24 ppm for ^1H and 77.0 ppm for ^{13}C. The following abbreviations are used: Dendritic aldehydes are referred to as [G-*n*]CHO, where *n* designates the dendrimer generation. Dendritic free-base porphyrins are referred to as H_2[G-*n*]$_4$P, where *n*, again, designates the dendrimer generation. Ar refers to the aromatic repeat units within the dendrimer. Ph refers to the phenyl endgroups, the surface, of the dendrimer. Bn refers to the benzylic positions within the dendrimer. Porph refers to the two protons inside the porphyrin ring, and specific sites of the porphyrin ring are designated by α, β and *meso*.

General procedure for the preparation of dendritic benzyl bromides[11]

To a mixture of the appropriate dendritic benzylic alcohol (1.00 equiv.) and carbon tetrabromide (1.25 equiv.) in the minimum amount of dry THF was added triphenylphosphine (1.25 equiv.), and the reaction mixture was stirred under nitrogen for 20 min. The reaction mixture was then poured onto water and extracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and evaporated to dryness. The crude product was purified by column chromatography. Analyses agreed with those published.[11]

General procedure for preparation of porphyrin-core dendrimers *via* Williamson ether synthesis

The second, third and fourth generation porphyrin-core dendrimers were synthesized by coupling zinc tetrakis(3,5-dihydroxyphenyl)porphyrin **4** to the appropriate dendritic bromide in a Williamson ether synthesis. Under nitrogen, zinc tetrakis(3,5-dihydroxyphenyl)porphyrin (1.00 equiv.) and the dendritic bromide (9.60 equiv) were dissolved in acetone. To this solution, K_2CO_3 (16.0 equiv.) and 18-crown-6 (1.60 equiv) were added, and the mixture was stirred and warmed to 60 °C. The solvent was evaporated, and the residual solids were partitioned between water and CH_2Cl_2. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 ×). The solvent was evaporated, and the residual solids were adsorbed onto silica (20 ml), and the crude product was purified by chromatography through a 40 ml silica column eluting with a linear gradient of solvent from pure hexane to pure CH_2Cl_2. The product fractions were collected, and the solvent was evaporated. The product was dissolved in a minimum amount of $CHCl_3$ then precipitated into methanol. The precipitate was then dissolved in a minimum amount of diethyl acetate and precipitated into diethyl ether. The product was obtained as a dark purple powder.

Zn[G-2]$_4$P 1b. This was prepared as above from zinc tetrakis(3,5-dihydroxyphenyl)porphyrin **4** and [G-1]Br; yield: 71%; UV–VIS λ/nm (ε): 428 (498 000), 560 (20 000), 600 (7000). δ_H 9.18 (s, 8 H, β-H), 7.48 (d, 8 H, Ar-H), 7.33 (m, 80 H, Ph-H), 7.03 (t, 4 H, Ar-H), 6.73 (d, 16 H, Ar-H), 6.56 (t, 8 H, Ar-H), 5.06 (s, 16 H, Bn-H), 4.96 (s, 32 H, Bn-H). δ_C 160.09, 157.71 (Ar *C*-O); 149.92 (α *C*); 144.80 (Ar *C*-porph); 139.15 (Ar *C*-CH_2); 136.63 (Ph *C*-CH_2); 132.10 (β *C*); 128.46, 127.88, 127.43 (Ph *C*-H); 120.67 (*meso C*); 115.02, 106.43, 101.65, 96.66 (Ar *C*-H); 70.00 (Ar/Ph-*C*H_2). Mass spectrum (MALDI-TOF): *m*/*z*, calc. 3225.09; found 3228.3 (Calc. for $C_{212}H_{172}N_4O_{24}Zn$; C 78.95, H 5.38, N 1.74; found C 79.06, H 5.57, N 1.62%).

Zn[G-3]$_4$P 1c. This was prepared as above from zinc tetrakis(3,5-dihydroxyphenyl)porphyrin **4** and [G-2]Br; yield: 68%; UV–VIS, λ/nm (ε): 428 (534 000), 518 (6000), 560 (20 000), 600 (7000). δ_H 8.96 (s, 8 H, β-H), 7.48 (s, 8 H, Ar-H), 7.17 (m, 160 H, Ph-H), 7.03 (s, 4 H, Ar-H), 6.67 (d, 16 H, Ar-H), 6.53 (d, 32 H, Ar-H), 6.43 (t, 8 H, Ar-H), 6.39 (t, 16 H, Ar-H), 5.06 (s, 16 H, Bn-H), 4.83 (s, 32 H, Bn-H), 4.78 (s, 64 H, Bn-H). δ_C 160.08, 160.00, 157.75 (Ar *C*-O); 149.79 (α *C*); 139.25, 139.16 (Ar *C*-CH_2); 136.62 (Ph *C*-CH2); 128.40, 127.81, 127.40 (Ph *C*-H); 120.67, 106.57, 106.25, 101.65, 101.52, 96.67 (Ar *C*-H); 69.89 (Ar/Ph-*C*H_2). Mass spectrum (MALDI-TOF): *m*/*z* calc. 6621; found 6630 (Calc. for $C_{436}H_{364}N_4O_{56}Zn$; C 79.09, H 5.54, N 0.85; found C 78.98, H 5.96, N 0.50%).

Zn[G-4]$_4$P 1d. This was prepared as above from zinc tetrakis(3,5-dihydroxyphenyl)porphyrin **4** and [G-3]Br; yield: 20%; UV–VIS, λ/nm (ε): 430 (463 000), 560 (21 000), 600 (7000). δ_H 9.00 (s, 8 H, β-H), 7.48 (s, 8 H, Ar-H), 7.19 (m, 320

H, Ph-H), 6.67 (s, 4 H, Ar-H), 6.52–6.38 (overlapping resonances, 168 H, Ar-H), 4.91 (s, 16 H, Bn-H), 4.75–4.69 (overlapping resonances, 224 H, Bn-H). δ_C 160.03, 159.90, 159.86, 157.76 (Ar *C*-O); 149.68 (α *C*); 139.16, 139.08 (Ar *C*-CH_2); 136.62 (Ph *C*-CH_2); 132.10 (β *C*); 128.40, 127.78, 127.45 (Ph *C*-H); 106.21, 101.42 (Ar *C*-H); 69.80 (Ar/Ph-*C*H_2). Mass spectrum (MALDI-TOF): *m*/*z* calc. 13 413; found 13 437 (Calc. for $C_{884}H_{748}N_4O_{120}Zn$; C 79.16, H 5.62, N 0.42; found C 79.24, H 5.79, N 0.59%).

General procedure for synthesis of dendritic aldehydes

A mixture of the appropriate dendritic bromide (2.00 equiv.), 3,5-dihydroxybenzaldehyde (1.00 equiv.), potassium carbonate (3.00 equiv.), and 18-crown-6 (0.20 equiv.) was refluxed under nitrogen in dry THF for 48 h. The reaction was allowed to cool then evaporated to dryness under reduced pressure. The residue was partitioned between water and methylene chloride, and the aqueous layer was extracted with methylene chloride. The combined organic layers were then dried ($MgSO_4$) and evaporated to dryness. The product was purified by flash chromatography through a silica column, eluting with methylene chloride to give dendritic aldehyde as a colorless glass.

[G-1]CHO 2a. 3,5-Dibenzyloxybenzaldehyde was purchased from Aldrich and used directly.

[G-2]CHO 2b. This was prepared from [G-1]Br; yield: 83%; ν/cm^{-1} 2873 [Ar(CO)—H st.], 1669 cm^{-1} [Ar(C=O)H st.]; δ_H 9.87 (s, 1 H, ArC*H*O), 7.28–7.41 (m, 20 H, Ph-H), 7.05 (d, 2 H, Ar-H), 6.81 (t, 1 H, Ar-H), 6.67 (d, 4 H, Ar-H), 6.59 (t, 2 H, Ar-H), 5.07 (s, 8 H, Bn-H), 5.03 (s, 4 H, Bn-H); δ_C 70.4, 70.6 (*C*H_2O); 106.6, 107.7, 137.0, 160.6 (Ar*C*); 102.0, 104.7, 136.7, 160.5 (Ar*C*); 128.0, 128.4, 128.9, 139.2 (Ph*C*); 198.6 (Ar*C*HO). Mass spectrum (MALDI): *m*/*z*, calc. 743; found 767.

[G-3]CHO 2c. This was prepared from [G-2]Br; yield: 49%; ν/cm^{-1} 2873 [Ar(CO)—H st.], 1683 cm^{-1} [Ar(C=O)H st.]; δ_H 9.84 (s, 1 H, ArC*H*O), 7.29–7.42 (m, 40 H, Ph-H), 7.08 (d, 2 H, Ar-H), 6.84 (t, 1 H, Ar-H), 6.66 (d, 8 H, Ar-H), 6.65 (d, 4 H, Ar-H), 6.55 (t, 4 H, Ar-H), 6.54 (t, 2 H, Ar-H), 5.00 (s, 16 H, Bn-H), 4.99 (s, 4 H, Bn-H), 4.95 (s, 8 H, Bn-H); δ_C 69.9–70.2 (*C*H_2O); 106.4, 107.5, 136.7, 160.1 (Ar*C*); 101.9, 103.9, 138.8, 160.1 (Ar*C*); 127.7, 128.1, 128.7, 139.0 (Ph*C*); 197.2 (Ar*C*HO). Mass spectrum (MALDI): *m*/*z*, calc. 1592; found 1616.

[G-4]CHO 2d. This was prepared from [G-3]Br; yield: 56%. ν/cm^{-1} 2873 [Ar(CO)—H st.], 1694 cm^{-1} [Ar(C=O)H st.]; δ_H 9.84 (s, 1H, ArC*H*O), 7.26–7.41 (m, 80 H, Ph-H), 7.08 (d, 2 H, Ar-H), 6.84 (t, 1 H, Ar-H), 6.64–6.67 (m, 28 H, Ar-H), 6.54–6.56 (m, 14 H, Ar-H), 4.93, 4.96, 5.01 (s, 60 H, Bn-H); δ_C 69.8–71.1 (*C*H_2O); 101.6, 106.4, 138.9, 160.1–160.3 (Ar*C*); 127.5, 128.0, 128.6, 136.8 (Ph*C*). Mass spectrum (MALDI) *m*/*z*, calc. 3290; found 3313.

General procedure for the preparation of porphyrin-core dendrimers *via* Lindsey synthesis

A solution of the appropriate dendritic aldehyde **2a–d** (1.00 equiv.), freshly distilled pyrrole (1.00 equiv.), and 1 drop of freshly distilled trifluoroacetic acid (TFA) was prepared in dry methylene chloride whose volume was calculated so either starting material had a concentration equal to 10^{-2} M. The reaction was shielded from ambient light and stirred at room temp. for a period of time designated in the following text. Then chloranil (8.00 equiv.) was added, and the reaction mixture was warmed to reflux. This was stirred for a period of time designated in the following text. The solution was allowed to cool then evaporated to dryness under reduced pressure. The residue was taken up in minimal chloroform, and insoluble solids (*i.e.* excess chloranil) were removed. The filtrate was flash chromatographed through a silica column, eluting with chloroform. The product fractions were collected and evaporated to dryness. The residual solid was taken up in minimal chloroform and precipitated into methanol, so the product could be handled as a powder.

H_2[G-1]$_4$P 3a. This was prepared from [G-1]CHO **2a**. The aldehyde and pyrrole were allowed to react for 1.5 h, and the oxidation was carried out for 2 h; yield: 30%; UV–VIS, λ/nm: 280 (dendrimer units); 424 (porphyrin Soret); 516, 550, 590, 648 (porphyrin Q-region); δ_H 8.95 (s, 8H, β-H), 7.39–7.51 (m, 40H, Ph-H), 7.60 (d, 8H, Ar-H), 7.17 (t, 4H, Ar-H), 5.31 (s, 16H, Bn-H), −2.82 (s, 2H, porph-H); δ_C 143.99 (α *C*), 127.63 (β *C*), 119.68 (*meso* C), 70.38 (*C*H_2O), 127.68, 128.07, 128.64, 136.79 (Ph*C*). Mass spectrum (MALDI): *m*/*z*, calc. 1464; found 1469.

H_2[G-2]$_4$P 3b. This was prepared from [G-2]CHO **2b**. The aldehyde and pyrrole were allowed to react for 1.5 h, and the oxidation was caried out for 2 h; yield: 26%; UV–VIS λ/nm: 280 (dendrimer units); 424 (porphyrin Soret); 516, 550, 590, 648 (porphyrin Q-region); δ_H 8.87 (s, 8H, β-H), 7.21–7.39 (m, 80H, Ph-H), 7.49 (d, 8H, Ar-H), 7.05 (t, 4H, Ar-H), 6.76 (d, 16H, Ar-H), 6.59 (t, 8H, Ar-H), 5.15 (s, 16H, Bn-H), 4.98 (s, 32H, Bn-H), −2.89 (s, 2H, porph-H); δ_C 141.45 (α *C*), 128.51 (β *C*), 119.43 (*meso C*), 70.38, 70.18 (*C*H_2O), 99.02, 161.14, 107.08, 139.14 (Ar*C*), 127.44, 127.90, 128.48, 136.68 (Ph*C*). Mass spectrum (MALDI): *m*/*z*, calc. 3162; found 3171.

H_2[G-3]$_4$P 3c. This was prepared from [G-3]CHO **2c**. The aldehyde and pyrrole were allowed to react for 10 h, and the oxidation was run for 5 h; yield: 29%; UV–VIS, λ/nm: 280 (dendrimer units); 424 (porphyrin Soret); 516, 550, 590, 648 (porphyrin Q-region); δ_H 8.91 (s, 8H, β-H), 7.19–7.39 (m, 160H, Ph-H), 7.51 (d, 8H, Ar-H), 7.08 (t, 4H, Ar-H), 6.72 (d, 16H, Ar-H), 6.60 (d, 32H, Ar-H), 6.56 (t, 8H, Ar-H), 6.49 (t, 16H, Ar-H), 5.09 (s, 16H, Bn-H), 4.90 (s, 32H, Bn-H), 4.88 (s, 64H, Bn-H), −2.91 (s, 2H, porph-H); δ_C 143.93 (α *C*), 128.53 (β *C*), 119.69 (*meso C*), 69.89, 69.88, 70.20 (*C*H_2O), 101.51, 101.53, 106.59, 106.23, 139.17, 139.14, 157.89, 160.03 (Ar*C*), 127.49, 128.06, 128.53, 136.67 (Ph*C*). Mass spectrum (MALDI) *m*/*z*, calc. 6557; found 6577.

H_2[G-4]$_4$P 3d. Pyrrole (0.043 ml; 0.626 mmol) and **2d** (2.059 g; 0.626 mmol) were dissolved in dry $CHCl_3$ and condensed in the presence of TFA (0.025 ml; 0.207 mmol). The solution was shielded from ambient light and stirred at room temp. for 36 h. Then DDQ (0.177 g; 0.782 mmol) was added, and the solution was allowed to stir at room temp. for an additional 2 h. After cooling, the solution was evaporated to dryness under reduced pressure and the residue was taken up in a minimum amount of chloroform, then purified by flash chromatography through a silica column eluting with chloroform. The product fractions were collected and evaporated to dryness. The residual solid was taken up in a minimum amount of chloroform and precipitated into methanol, so the product could be handled as a powder; yield: 14%; UV–VIS, λ/nm: 280 (dendrimer units); 424 (porphyrin Soret); 516, 550, 590, 648 (porphyrin Q-region); δ_H 8.88 (s, 8 H, β-H), 7.38 (s, br, Ar-H), 7.19–7.37 (m, Ph-H), 7.02 (s, br, Ar-H), 6.40–6.65 (m, Ar-H), 4.98–4.85 (overlapping resonances, Bn-H), −2.91 (s, 2H, porph-H); δ_C 160.03, 159.90, 159.86, 157.76 (Ar*C*-O); 149.68 (α *C*); 139.16, 139.08 (Ar*C*-CH_2); 136.62 (Ph *C*-CH_2); 132.10 (β *C*); 128.40, 127.78, 127.45 (Ph*C*-H); 106.21, 101.42 (Ar*C*-H); 69.80 (Ar/Ph-*C*H_2). Mass spectrum (MALDI-TOF): *m*/*z*, calc. 13 350 g mol^{-1}; found 13 376.

General procedure for the metallation of free-base porphyrin-core dendrimers

Introduction of zinc into dendrimers **3a–d** was achieved by dissolving the free-base porphyrin-core dendrimer (1.00 equiv.)

and $Zn(OAc)_2 \cdot 2H_2O$ (1.10 equiv.) in chloroform–methanol (1:1) (100 ml) and heating the solution at reflux overnight. The solvent was then evaporated, and the residual solids were partitioned between water and CH_2Cl_2. The organic layer was separated and dried (Na_2SO_4). The solvent was evaporated to afford a violet solid. The solid was redissolved in a minimum amount of chloroform then precipitated into methanol, so the compound could be handled as a powder. (*Nb* the characterization of **1b–d** is given earlier in this section.)

Zn[G-1]$_4$P 1a. This was prepared from H_2[G-1]$_4$P **3a**; yield: 100%; UV–VIS λ/nm (ε) 428 (568 000), 560 (22 000), 600 (7000). δ_H 8.98 (s, 8 H, β-H), 7.48 (d, 8 H, Ar-H), 7.35 (m, 40 H, Ph-H), 7.02 (t, 4 H, Ar-H), 5.18 (s, 16 H, Bn-H). δ_C 157.78 (Ar*C*-O); 149.89 (α *C*); 144.63 (Ar*C*-porph); 136.75 (Ph*C*-CH_2); 131.97 (β *C*); 128.58, 128.01, 127.63 (Ph *C*-H); 120.67 (*meso C*); 115.06, 96.67 (Ar *C*-H). Mass spectrum (MALDI-TOF): *m*/*z* calc. 1527; found 1538 (Calc. for $C_{100}H_{76}N_4O_8Zn$; C 78.65, H 5.02, N 3.67; found C 78.60, H 5.05, N 3.54%).

Zinc tetrakis(3,5-dihydroxyphenyl)porphyrin 4. Tetrakis(3,5-dihydroxyphenyl)porphyrin **6** (700 mg, 0.942 mmol) and $Zn(OAc)_2 \cdot 2H_2O$ (228 mg, 1.043 mmol) were dissolved in methanol (20 ml). The solution was heated to reflux for 4 h, then distilled water (60 ml) was added, and the methanol was evaporated under vacuum. The turbid solution was placed in the refrigerator overnight, and the purple crystalline product was filtered and dried *in vacuo* at 40 °C; yield: 99%; UV–VIS, λ/nm (ε): 428 (523 000), 560 (20 000), 600 (7000). δ_H ([$^2H_6$]DMSO, 2.49 ppm) 9.60 (s, 8 H, Ar-OH), 8.86 (s, 8 H, β-H), 7.01 (d, 8 H, Ar-H), 6.62 (t, 4 H, Ar-H). δ_C ([$^2H_6$DMSO, 39.5 ppm) 156.21 (Ar*C*-OH); 148.93 (α *C*); 144.46 (Ar*C*-porph); 131.33 (β *C*); 120.23 (*meso C*); 114.16, 101.72 (Ar*C*-H). Mass spectrum (MALDI-TOF): *m*/*z*, calc. 806; found 814.

Tetrakis(3,5-dimethoxyphenyl)porphyrin 5. 3,5-dimethoxybenzaldehyde (1.500 g, 9.026 mmol) and freshly distilled pyrrole (626 ml, 9.026 mmol) were dissolved in dry chloroform (903 ml) under nitrogen atmosphere. After adding $BF_3 \cdot OEt_2$ (364 ml, 2.979 mmol) to the mixture, the solution was shielded from ambient light and stirred at room temperature for 90 min. After adding DDQ (1.537 g, 6.770 mmol), the mixture was stirred for an additional 90 min, then triethylamine (415 ml, 2.979 mmol) was added to neutralize the acid. The solvent was evaporated, and the residual solids were adsorbed onto silica (20 ml). The crude product was purified by chromatography through a 40 ml silica column eluting with a linear gradient of solvent from pure hexane to pure CH_2Cl_2. After collecting the product fractions and evaporating the solvent, the product was obtained as purple crystals; yield: 52%; UV–VIS, λ/nm (ε) 424 (280 000), 516 (19 000), 548 (9000), 586 (9000), 648 (5000). δ_H ([$^2H_6$DMSO, 2.49 ppm) 8.95 (s, 8 H, β-H), 7.01 (s, 8 H, Ar-H), 6.65 (s, 4 H, Ar-H), 3.33 (s, 24 H, ArO-CH_3), −3.07 (s, 2 H, N-H); δ_C ([$^2H_6$DMSO, 39.5 ppm) 156.60 (Ar*C*-OCH_3); 142.89 (Ar*C*-porph); 131.12 (β *C*); 119.94 (*meso C*); 114.19, 102.28 (Ar*C*-H); 48.64 (Ar-O*C*H_3) (Calc. for $C_{52}H_{46}N_4O_8$; C 73.05, H 5.42, N 6.55; found C 73.11, H 5.29, N 6.43%).

Tetrakis(3,5-dihydroxyphenyl)porphyrin 6. Tetrakis(3,5-dimethoxyphenyl)porphyrin **5** (740 mg, 0.866 mmol) was dissolved in dry CH_2Cl_2 (20 ml) under nitrogen atmosphere. The solution was cooled to 0 °C, then BBr_3 (7.27 ml, 7.271 mmol, 1 M in CH_2Cl_2) was slowly added to the reaction. After addition, the mixture was allowed to warm to room temp. as it stirred overnight. Enough methanol was then added to deactivate any unreacted BBr_3, distilled water (30 ml) was added, and the mixture was stirred for 2 h. After evaporation of the organic solvents, a green powder was filtered from the water. It was dissolved in diethyl ether, washed twice with saturated $NaHCO_3$, washed once with distilled water, then dried over Na_2SO_4. The solvent was evaporated, and the product was isolated as purple crystals which were dried under vacuum at 40 °C; yield: 100%; UV–VIS λ/nm (ε): 424 (242 000), 516 (14 000), 552 (5000), 592 (4000), 648 (2000); δ_H ([$^2H_6$DMSO, 2.49 ppm) 8.93 (s, 8 H, β-H), 7.05 (s, 8 H, Ar-H), 6.64 (s, 4 H, Ar-H), 3.81 (s, br, Ar-OH). δ_C ([$^2H_6$]DMSO, 39.5 ppm) 156.54 (Ar*C*-OH); 144.97 (Ar*C*-porph); 127.50 (β *C*); 117.81 (*meso C*); 114.15, 102.50 (Ar*C*-H). Mass spectrum (MALDI-TOF): *m*/*z* calc. 743; found 753.

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