Template-directed synthesis of linear and cyclic butadiyne-linked porphyrin oligomers up to a linear octamer

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Efficient syntheses of a cyclic porphyrin dimer, cyclic trimer, cyclic tetramer, linear dimer, linear tetramer, and linear octamer are described. Starting from a zinc porphyrin monomer, simple oligopyridine ligands are used as templates to control oligomerisation by binding to the linear intermediates formed under Glaser–Hay coupling conditions. The oligomeric products have been characterised using FAB, high-resolution electrospray and MALDITOF mass spectrometry.

Introduction

Here we present our most practical preparative routes to cyclic dimer **Zn_2-c-Dim1b**, cyclic trimer[1] **Zn_3-c-Tri1a,b**, cyclic tetramer **Zn_4-c-Tet1b**, linear dimer **Zn_2-l-Dim1b($SiMe_3$)$_2$**, linear tetramer, **Zn_4-l-Tet1b($SiMe_3$)$_2$** and linear octamer, **Zn_8-l-Oct1b($SiMe_3$)$_2$**. The routes are summarised in Scheme 1: all the syntheses except for that of linear dimer are templated using simple oligopyridine ligands. Templates were chosen because they were found to be complementary in shape and size to the cyclic porphyrin hosts[2] designed as potential enzyme mimics. The cyclic oligomers have already demonstrated important catalytic activity,[3,4] while the potential of the linear tetramer and octamer as model enzymes has yet to be explored.

Many of these results have been reported in preliminary form[5,6] and have been the basis for a more general description of templating in synthesis.[7] Two distinct types of templating are described here (Fig. 1): a *positive* template brings together two reactive ends of a single molecule, favouring intramolecular cyclisation. while a *negative* template holds the ends apart, inhibiting intramolecular cyclisation and so encouraging intermolecular reaction. In the course of this work it became clear that *positive* cyclisation templates could also be used to scavenge cyclisable material in a reaction mixture and thus facilitate the formation of linear oligomers. Using the simplest strategy for the synthesis of linear oligomers [Fig. 2(a)], dimerisation of the partially deprotected material can only be carried out efficiently in the absence of fully deprotected molecules because the latter can couple with mono-protected material to generate a new reactive oligomer and ultimately a complex mixture. The problem can be avoided by separation of the doubly-reactive material before coupling, but this becomes more difficult with increasing chain length. *Positive* cyclisation templates can be used as scavengers to overcome the problem by enforcing intramolecular reaction of doubly reactive molecules [Fig. 2(b)]; mono-protected molecules are left with no choice but to couple with each other. When the separation is left until after coupling, it is much easier because the desired linear compound is twice as massive as either the starting material or the cyclic by-product.

Results and discussion

Templated oligomerisation of monomers

Addition of **Py_3T** or **BiPy** as potential templates during pyridine–CuCl Glaser coupling[1] had no effect on the product

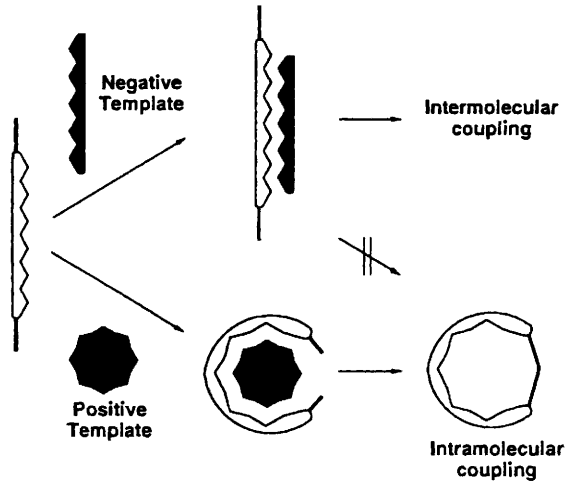

Fig. 1 Schematic illustration of positive and negative templating

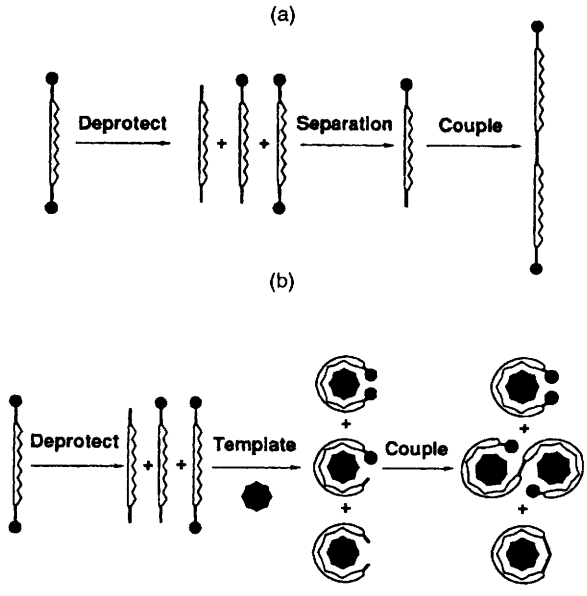

Fig. 2 (*a*) A general strategy for the formation of a linear dimer from a symmetrically protected monomer unit. (*b*) A scavenger template induces molecules with two reactive ends to cyclise, so allowing efficient coupling of mono-protected material. Hatched circles represent protecting groups.

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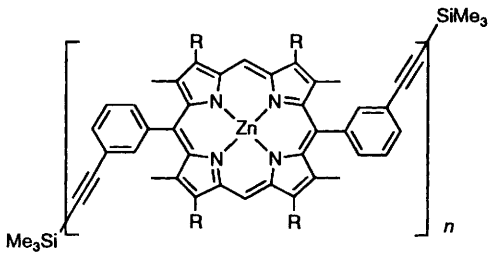
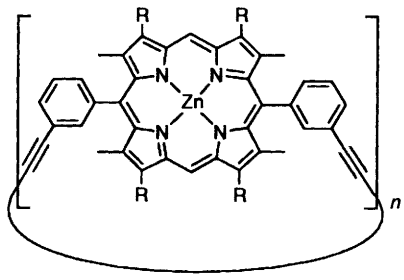




Zn-Mon1a, b(SiMe$_3$)$_2$ $n = 1$

Zn$_2$-l-Dim1b(SiMe$_3$)$_2$ $n = 2$

Zn$_4$-l-Tet1b(SiMe$_3$)$_2$ $n = 4$

Zn$_8$-l-Oct1b(SiMe$_3$)$_2$ $n = 8$

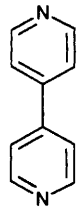
Zn$_2$-c-Dim1b $n = 2$

Zn$_3$-c-Tri1a,b $n = 3$

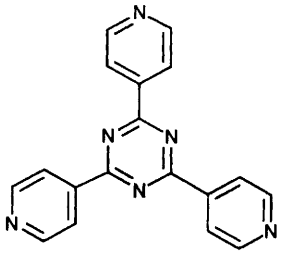
Zn$_4$-c-Tet1b $n = 4$

a R = CH_2CH_3

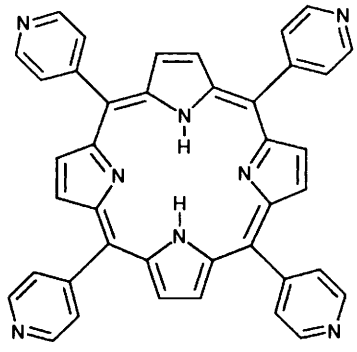
b R = $CH_2CH_2CO_2Me$



Bipy



Py$_3$T



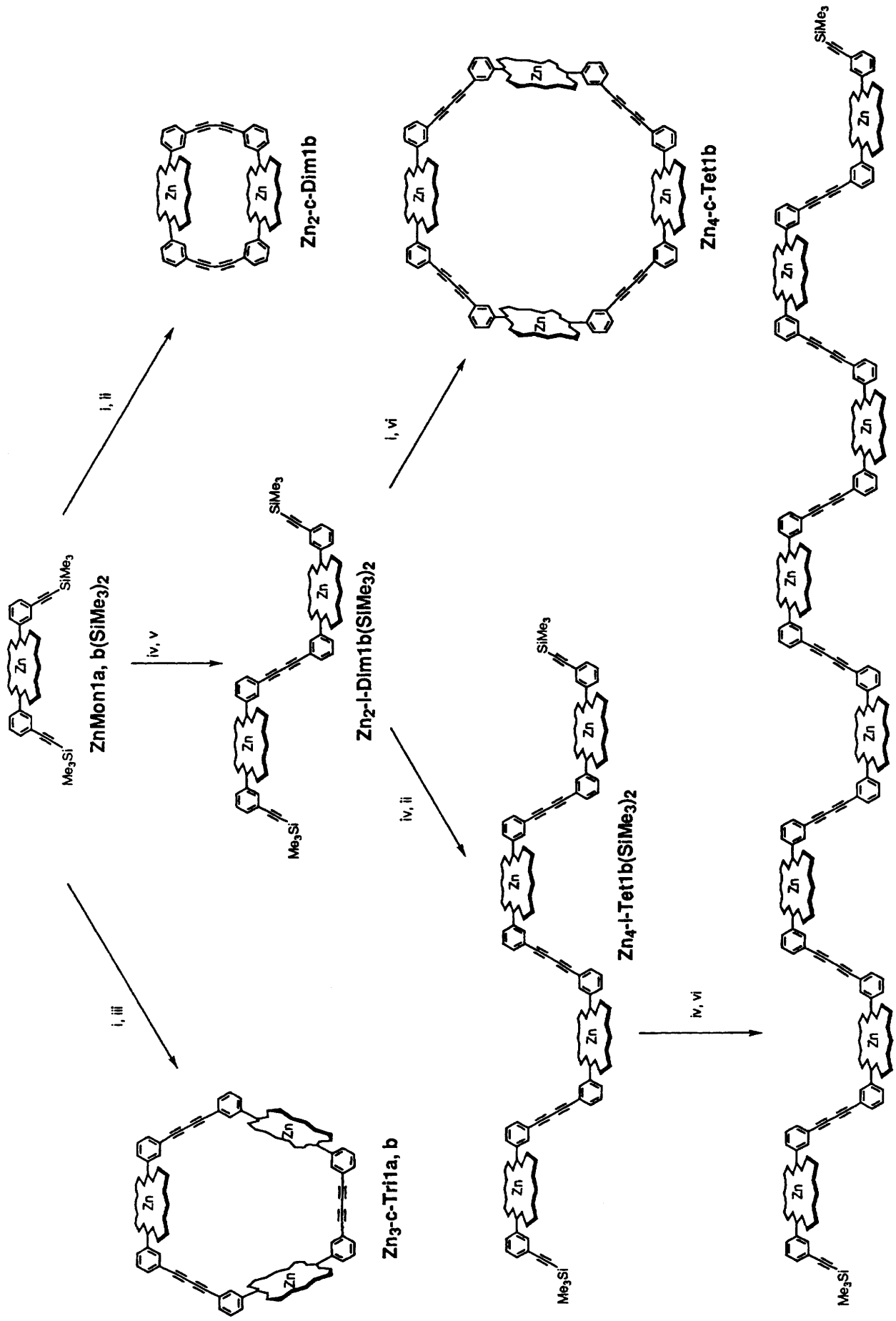
H$_2$-Py$_4$P

distribution: template-binding is too weak in the presence of a large excess of pyridine. We therefore sought new reaction conditions under which efficient coupling and templating could be achieved. Solvent–reagent combinations were screened using the more soluble ester-functionalised starting material **Zn-Mon1b** which facilitated product analysis by making all of the products soluble. Many conditions were rejected because they resulted in copper metallation of the porphyrin; electronic spectra of acid-washed crude reaction mixtures were used to estimate the extent of porphyrin copper metallation, from the Q band-shape, and the extent of coupling, from the intensity of the butadiyne signal. The ratio of **H$_4$-c-Dim1b**:**H$_6$-c-Tri1b**:by-products was estimated from the ^{1}H NMR spectra of the crude reaction mixtures; the *meso*-resonances of **H$_6$-c-Tri1b** and **H$_4$-c-Dim1b** are shifted to progressively lower chemical shift, relative to **H$_2$-Mon1b**, by the trans-cavity porphyrin ring-current so that product distributions can be estimated accurately.

Pyridine, 2-methylpyridine, 2,5-dimethylpyridine, dimethylformamide (DMF), MeCN, acetone, tetrahydrofuran (THF), CH_2Cl_2, $CHCl_3$ and toluene were explored as solvents, using CuCl, CuCl·TMEDA [8] and CuCl·2.2′-BiPy as reagents, in an atmosphere of dry air or oxygen, with **Py$_3$T** or **BiPy** as template. With CuCl as reagent, coupling only occurs in pyridine, 2-methylpyridine, 2,5-dimethylpyridine and DMF. A small template effect was detected in DMF, but not in pyridine, 2-methylpyridine or 2,5-dimethylpyridine; copper-metallation was fastest in DMF. Chelating ligands such as TMEDA and 2,2′-BiPy increase the solubility of the copper(I) chloride and extend the range of solvents which can be used; with CuCl·TMEDA and CuCl·2,2′-BiPy as reagents coupling worked in all the solvents, except $CHCl_3$. Template effects increase as the solvent is made less coordinating and less polar in the order THF < acetone ≈ MeCN < CH_2Cl_2 < toluene. Coupling goes more rapidly and cleanly in CH_2Cl_2 than toluene. Use of TMEDA rather than 2,2′-Bipy generally gave faster coupling; the CuCl·2,2′-Bipy reaction showed slightly larger template effects, but did not always go to completion. In all cases coupling occurs more cleanly under air than oxygen although no coupling occurs under argon.

Coupling with CuCl·TMEDA–CH_2Cl_2 is almost as efficient as with CuCl–pyridine and there is a dramatic template effect. The most useful cyclisation template for the synthesis of cyclic porphyrin dimer was **BiPy**. The addition of a six-fold excess of **BiPy** relative to the monomer porphyrin led to an increase in the yield of cyclic dimer from 23 to 72%, whilst the yield of cyclic trimer was reduced to 4% from 34%. Similarly when **Py$_3$T** was used to template the synthesis of cyclic trimer the yield of trimer increased to 55% from 34% and the yield of dimer was reduced to 6% from 23%. Using this route **H$_4$-c-Dim1b** and **H$_6$-c-Tri1b** can be prepared in 70 and 50% isolated yield, respectively, on the 200 mg scale.

The direct synthesis of cyclic tetramer **Zn$_4$-c-Tet1b** from monomer using **H$_2$-Py$_4$P** as a template was attempted but



Scheme 1 i, CH_2Cl_2, TBAF; ii, TMEDA, CuCl, **BiPy**, dry air; iii, TMEDA, CuCl, **Py_3T**, dry air; iv, $CHCl_3$, 1 equiv. TBAF; v, TMEDA, CuCl, dry air; vi, TMEDA, CuCl, **H_2-Py_4P**, dry air

proved unsuccessful. Although some cyclic tetramer did form, its separation from cyclic pentamer and cyclic trimer was very difficult. **Zn_4-c-Tet1b** was not isolated in this way.

Synthesis of linear porphyrin dimer

Linear porphyrin dimer **Zn_2-l-Dim1b($SiMe_3$)$_2$** was synthesised from the symmetrically protected monomer porphyrin **Zn-Mon1b($SiMe_3$)$_2$** by partial deprotection and coupling (Scheme 1). TMS-protection of the terminal acetylenes was chosen for several reasons: (a) the protecting groups were quantitatively removed by tetrabutylammonium fluoride in refluxing chloroform, (b) the doubly protected porphyrin **Zn-Mon1b($SiMe_3$)$_2$** was synthesised in high yields and was easy to purify by recrystallisation, (c) after removing half of the protecting groups the three components of the mixture were separable by flash column chromatography.

Half of the protecting groups of the TMS-protected porphyrin were removed using 1 equivalent of tetrabutylammonium fluoride in refluxing chloroform to yield a statistical (1:2:1) mixture of porphyrins. (It seemed that the removal of one protecting group had no effect on the rate of removal of the second as judged by TLC.) We used FT IR and ^{1}H NMR to judge the degree of deprotection.

Since the porphyrin with two TMS protecting groups in the mixture is inert to Glaser–Hay coupling there was no need to remove this before coupling. After Glaser–Hay coupling the separation became easier, since dimer was twice as massive as monomer so was much less chromatographically mobile. However, it was imperative that the doubly deprotected material was removed to avoid a complex mixture of linear and cyclic products after coupling.

All the doubly deprotected material was removed by flash column chromatography with only small losses of mono-protected material. After coupling, monomer and dimer were readily separated to yield 34% linear dimer after recrystallisation. This is the overall yield for two steps (partial deprotection and Glaser–Hay coupling) and does not take into account the 19% starting material which was reclaimed and recycled. The maximum theoretical yield for this step is 50% so the effective yield, taking into account reclaimed starting material, was 84%.

Linear porphyrin dimer was characterised using ^{1}H and ^{13}C NMR and mass spectrometry. Positive FAB mass spectrometry gave M^+ and M^{2+} peaks. Electrospray mass spectrometry of the free base porphyrin led to the low and high resolution spectra shown in Fig. 3; in a doubly charged ion the isotopomers are separated by a half mass unit providing a useful method for the determination of the degree of charging. The experimentally observed isotopic pattern fits well with the calculated pattern.

The cyclisation of linear dimer **Zn_2-l-Dim1b** to cyclic dimer **Zn_2-c-Dim1b** can be achieved very efficiently, but it is not preparatively useful, since cyclic dimer can be made directly from monomer **Zn-Mon1b**; the templated cyclisation of linear dimer to cyclic dimer will be discussed in the following paper. The conversion of linear dimer **Zn_2-l-Dim1b** into cyclic tetramer is the most efficient route to this cyclic oligomer; it is described below.

Synthesis of linear porphyrin tetramer and octamer

Having successfully synthesised linear dimer, we then tried to repeat the approach starting with linear dimer to synthesise linear tetramer. Unfortunately, we found that after partial deprotection of **Zn_2-l-Dim1b($SiMe_3$)$_2$**, removal of the unprotected dimer from the mixture was impossible by flash column chromatography. Coupling of the unseparated mixture led to a complex mixture of products. There was some linear tetramer in this mixture but it was difficult to separate it cleanly from the other components. The idea of a scavenger template was devised to overcome this problem as shown in Fig. 2.

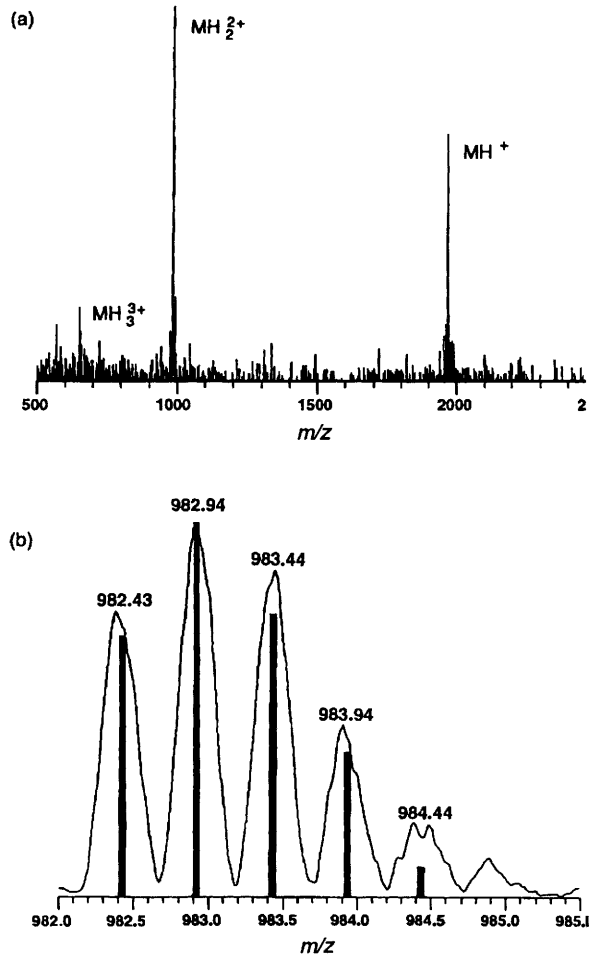


Fig. 3 (*a*) Low resolution ES mass spectrum of linear dimer. (*b*) High resolution mass spectrum of MH_2^{2+} molecular ion. Bold lines represent the calculated isotopic pattern.

BiPy is a good template for the cyclisation of linear dimer **Zn_2-l-Dim1b** to cyclic dimer **Zn_2-c-Dim1b** so it should be an efficient scavenger template in the synthesis of linear tetramer **Zn_4-l-Tet1b($SiMe_3$)$_2$** (Scheme 1). Half of the protecting groups were removed from protected linear dimer to yield a statistical mixture of the unprotected, mono-protected and protected dimers using 1 equivalent of tetrabutylammonium fluoride in refluxing chloroform. No separation was required at this stage; after coupling the reaction mixture consisted of three components, cyclic dimer (24%), linear dimer (25%) and linear tetramer (48%), confirming that **BiPy** had efficiently cyclised the unprotected dimer before it was able to react with any of the valuable mono-protected material. Separation of these products was relatively easy and gave linear tetramer in 29% yield after recrystallisation. This is an overall yield for three steps, and does not take into account the 20% linear dimer which was reclaimed and the 15% cyclic dimer which was also isolated. (See Table 1 for conversions and isolated yields.) The cyclisation properties of linear tetramer will be discussed along with those of linear dimer in the following paper.

The synthesis of linear octamer **H_{16}-l-Oct1b($SiMe_3$)$_2$** was carried out in a similar way. The linear tetramer was deprotected using 1 equivalent of tetrabutylammonium fluoride in refluxing chloroform. FT IR was used to ascertain that half of the protecting groups had been removed; this is particularly useful because the three species in the mixture (doubly protected, mono-protected and unprotected linear tetramer)

Table 1 Product yields (%) in the presence and absence of scavenger templates[a]

Reactant	Template	Linear dimer	Cyclic dimer	Linear tetramer	Cyclic tetramer	Linear Octamer
Linear dimer	**BiPy**	25 (20)	24 (15)	48 (29)	2	0
Linear dimer	None	25	7	30	10	0
Linear tetramer	**H_2-Py_4P**	—	—	25 (16)	25 (13)	50 (15)
Linear tetramer	None	—	—	25	17	36 (0)

[a] Overall product yields for deprotection, coupling in the presence of scavenger templates, and demetallation. Yields are from ^{1}H NMR analysis of crude reaction mixtures except for those in parentheses, which are for recrystallised isolated material.

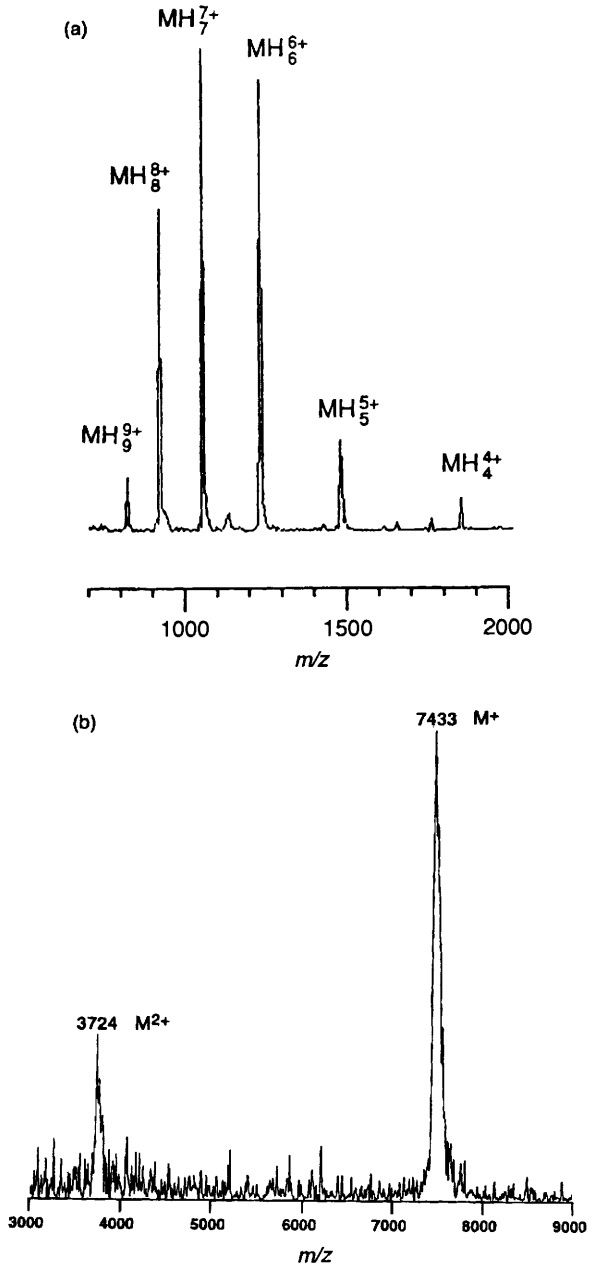


Fig. 4 (*a*) Low resolution ES mass spectrum of linear octamer. (*b*) MALDI mass spectrum of linear octamer.

cannot be resolved by thin layer chromatography. This mixture was coupled in the presence of a six-fold excess of **H_2-Py_4P** to yield a product mixture which contained just three components: linear tetramer, cyclic tetramer and linear octamer (Scheme 1). The crude ^{1}H NMR yields were: linear tetramer 25%, cyclic tetramer 25% and linear octamer 50%. The reaction was effectively quantitative. The chromatographic separation of linear octamer from this mixture was not straightforward, but pure linear octamer was isolated in 15% yield. This yield of recrystallised material is low when compared with the ^{1}H NMR yield obtained from the reaction mixture, but in the absence of template an intractable mixture was obtained from which it was impossible to isolate linear octamer. Both the recrystallised yields and the conversions calculated from ^{1}H NMR are given for the templated and untemplated reactions in Table 1.

Not surprisingly the ^{1}H NMR spectra of the linear oligomers were very similar and since positive FAB mass spectrometry failed to give molecular ions for oligomers larger than free base tetramers it was difficult to establish the purity of linear octamer. Fortunately, both electrospray mass spectrometry and MALDI time of flight MS yielded molecular ions (Fig. 4). MALDI time of flight MS (2,5-dihydroxybenzoic acid as matrix) gave peaks corresponding to M^+ and M^{2+}, whereas in the ES mass spectrum we observed peaks corresponding to MH_9^{9+}, MH_8^{8+}, MH_7^{7+}, MH_6^{6+}, MH_5^{5+} and MH_4^{4+}. The distribution of the ions suggests that the porphyrins are far enough apart that protonation of each unit occurs independently; there is no apparent preference for the species in which alternate porphyrins are protonated. The degree of protonation reflects the acidity of the initial solution.

Synthesis of cyclic porphyrin tetramer

Cyclic tetramer **Zn_4-c-Tet1b** is the major product when linear porphyrin dimer **Zn_2-l-Dim1b** is cyclised in the presence of **H_2-Py_4P** as template; under these conditions the cyclic dimer is a minor product. **Zn_2-l-Dim1b** was synthesised by removal of the TMS protecting groups with TBAF in dry dichloromethane.† The crude ^{1}H NMR yield for cyclic tetramer was 77% using this route and isolated recrystallised yields around 54% were achieved. The template has many roles in this synthesis, as discussed in detail in the following paper.

The low and high resolution electrospray mass spectra for **H_8-c-Tet1b** are shown in Fig. 5. The low resolution spectrum was acquired using a quadrupole detector magnet and showed peaks corresponding to MH_4^{4+}, MH_3^{3+} and MH_2^{2+}. Peaks appeared as broad envelopes encompassing three to four mass units so isotopic patterns, in which peak separations are a fraction of a mass unit were not resolved. Since the isotopic patterns cannot be distinguished there is necessarily some ambiguity as to the origin of the peaks MH_4^{4+} and MH_2^{2+} at 1818 and 909 amu. These peaks could be due to singly and doubly charged cyclic dimer **Zn_2-c-Dim1b**, respectively. From the low resolution mass spectrum of cyclic tetramer it is therefore not possible to be certain that there is no contamination by cyclic dimer. The high resolution mass spectrum using a sector magnet solves this problem since the spacing between isotopic peaks is a direct result of the degree of charging. The peaks in the high resolution spectrum shown in

† Removal of TMS groups with TBAF in chloroform led to quantitative statistical loss of TMS groups, whereas when dry dichloromethane was used as solvent the removal of TMS groups appeared to be catalytic.

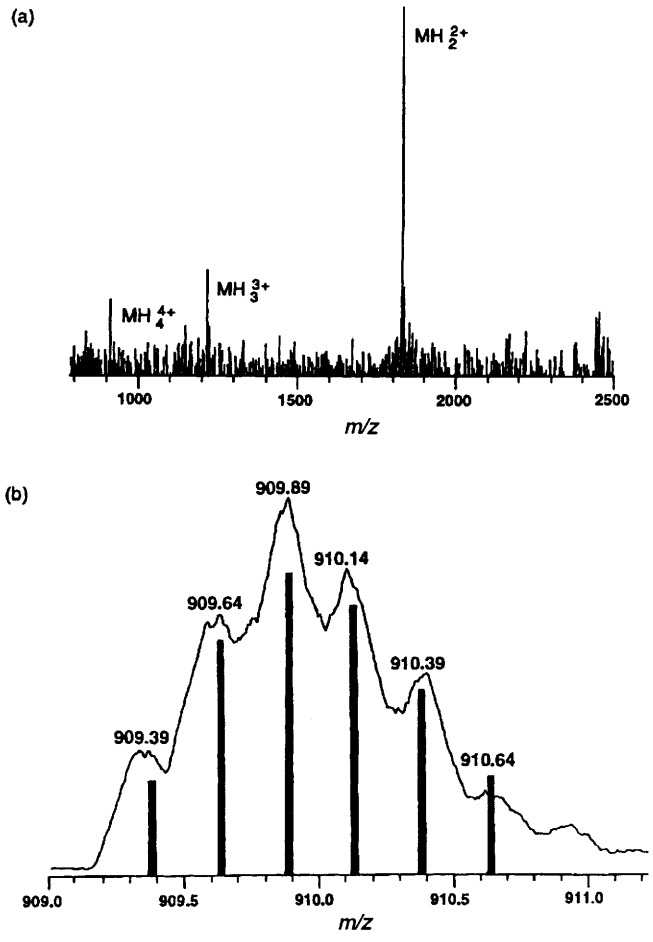


Fig. 5 (*a*) Low resolution ES mass spectrum of cyclic tetramer. (*b*) High resolution spectrum of MH_4^{4+} molecular ion. Bold lines represent the calculated isotopic pattern.

Fig. 5 are separated by quarter mass units indicating that this envelope of peaks must be from a quadruply charged tetramer molecule.

Conclusions

In this paper we have summarised the most efficient preparative syntheses for the porphyrin oligomers whose binding properties were described in the previous paper. In the following paper we consider the templated syntheses of cyclic dimer, trimer and tetramer in greater mechanistic detail and attempt to answer the question of what makes a successful cyclisation template.

The new ideas which emerge from these syntheses are those of negative and scavenger templates. The concept of a negative template which inhibits intramolecular coupling follows as an obvious corollary of the positive template which encourages intramolecular coupling, but we are not aware of any previously recognised examples of this effect recognised as such. There are two advantages gained from using scavenger templates in these type of reactions: firstly the crude yield of coupled product is increased and, just as importantly, the number of by-products which interfere with separation is greatly reduced. The use of scavenger templates can, in principle, be applied to the synthesis of any linear oligomer containing an even number of units, provided an efficient cyclisation template can be found that induces cyclisation of any doubly deprotected starting material. This leaves the mono-protected molecule to couple only with another of its own kind and hence form the required longer oligomer. The length of oligomer accessible by this method is limited only by our ingenuity in devising suitable templates and the ease with which the final products can be separated.‡

Experimental

General directions are given in paper one of the series.[1]

Low resolution electrospray mass spectrometry (ES MS) was carried out on a VG-BIO-Q; the samples were injected as 0.4 mmol dm^{-3} solutions in methanol containing 0.2% trifluoroacetic acid. High resolution spectra were run on a Kratos Concept in the positive ion mode. MALDITOF experiments were carried out by Kratos using 2,5-dihydroxybenzoic acid as a matrix.

Templated synthesis of the cyclic dimer H_4-c-Dim1b

TMEDA (2.11 cm^3, 14 mmol; freshly distilled ex. CaH_2) was added to a solution of **Zn-Mon1b** (200 mg, 0.20 mmol), copper(I) chloride (1.38 g, 14 mmol; freshly prepared), and 4,4′-bipyridyl (187 mg, 1.2 mmol) in dichloromethane (500 cm^3; freshly distilled ex. CaH_2) and stirred under dry air for 1 h. The reaction mixture was washed with water (3 × 500 cm^3), treated with methanolic TFA (10%, 100 cm^3) and then washed again with water (4 × 500 cm^3) and evaporated. The ^1H NMR of crude material was recorded at this stage. The product was purified by flash chromatography (CH_2Cl_2–$CHCl_3$, 1 : 1); yield 120–135 mg (65–75%). See first paper in the series for characterisation data.[1]

Templated synthesis of the trimer H_6-c-Tri1b

A procedure identical with that described above was used except that *s*-tri(4-pyridyl)triazine **Py$_3$T** (375 mg, 1.2 mmol) was used instead of 4,4′-bipyridyl **BiPy**; yield of **H_6-c-Tri1b** 90–100 mg (50–55%). See first paper in the series for characterisation data.[1]

Templated synthesis of the trimer H_6-c-Tri1a

A procedure identical with that described above was used except that **Zn-Mon1a** (200 mg, 0.27 mmol) was used instead of **Zn-Mon1b**. Chloroform (300 cm^3) was also added to the reaction mixture before work-up (to keep the product in solution) and chromatography was carried out as described previously for the untemplated synthesis of **H_6-c-Tri1a**; yield 85 mg (48%). See first paper in the series for characterisation data.

5,15-Bis(3-trimethylsilylethynylphenyl)-2,8,12,18-tetra(2-methoxycarbonylethyl)-3,7,13,17-tetramethylporphyrin H_2-Mon1b(SiMe$_3$)$_2$

Palladium-on-carbon (10%; 350 mg) was added to a solution of 5,5′-dibenzylcarbonyl-3,3′-di(2-methoxycarbonylethyl)-4,4′-dimethyl-2,2′-hydrodipyrrin (6.15 g, 10 mmol) in THF (200 cm^3) containing 1% triethylamine and the mixture was stirred under hydrogen for 1 h, by which time *ca.* 500 cm^3 (20 mmol) of gas had been consumed. The catalyst was filtered off and the filtrate evaporated. TFA (50 cm^3; argon saturated) was added to the residue under argon at 0 °C and the solution stirred for 20 min at 0 °C followed by 20 min at room temperature (periodically the reaction was put under vacuum and then saturated with argon to prevent carbon dioxide build up). At this stage the solution of 3,3′-di(2-methoxycarbonylethyl)-4,4′-dimethyldihydrodipyrrin was orange–brown. The solution was cooled to −30 °C (solid CO_2–ethanol) and 3-

‡ Since completion of this work, it has become clear that templated synthesis of this type of system can be improved dramatically by increasing the zinc–pyridine binding constants. Thus, one-step, virtually quantitative preparation of cyclic dimer, trimer and even tetramer becomes straightforward if conventional porphyrins are replaced by dioxoporphyrins.[9]

trimethylsilylethynylbenzaldehyde (2.02 g, 10 mmol) in methanol (50 cm^3, argon saturated) was added to it by cannula. The mixture was stirred for 2 h, over which time the temperature was allowed to rise from −30 to −20 °C. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (2.35 g, 10 mmol) in $CHCl_3$ (50 cm^3) was added to the mixture which was then stirred for 30 min, before the addition of triethylamine (50 cm^3). The resulting mixture was washed with water and evaporated and the product purified by three recrystallisations from $CHCl_3$–MeOH. The resulting red solid was filtered off and dried *in vacuo* to yield **H_2-Mon1b(SiMe$_3$)$_2$** (3.52 g, 67%); R_F 0.14 in $CHCl_3$; $\lambda_{max}(CH_2Cl_2)$/nm 409, 506, 539, 570 and 655; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3303 (C–H) and 1732 (C=O); δ_H(250 MHz; $CDCl_3$) −2.47 (2 H, s), 0.27 (18 H, s), 2.54 (12 H, s), 3.17 (8 H, t), 3.67 (12 H, s), 4.37 (8 H, t), 7.71 (2 H, t), 7.93 (2 H, t), 8.02 (2 H, br. s), 8.16 (1 H, s), 8.18 (1 H, s) and 10.28 (2 H, s) [Found: *m/z* (+ve FAB, NOBA) 1055.7 (M^+). $C_{62}H_{70}N_4O_8Si_2$ requires 1055.54].

Zn-Mon1b(SiMe$_3$)$_2$. Zinc was added to the free base porphyrin (**H_2-Mon1b(SiMe$_3$)$_2$**) (3.52 g, 3.33 mmol) using the standard procedure.[1] Recrystallisation was carried out from a minimum volume of CH_2Cl_2 layering in MeOH to yield a pinkish solid **Zn-Mon1b(SiMe$_3$)$_2$** (3.4 g, 91%); (Found: C, 66.6; H, 6.1; N, 5.0. $C_{62}H_{68}N_4O_8Si_2Zn$ requires C, 66.6; H, 6.0; N, 4.8%); $\lambda_{max}(CH_2Cl_2)$/nm 412 ($\log_{10}\varepsilon$ 5.82), 540 (4.48), 575 (4.24); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3303 (CH), 1732 (C=O); δ_H(250 MHz; $CDCl_3$) 0.25 (18 H, s), 2.48 (12 H, s), 3.14 (8 H, t), 3.68 (12 H, s), 4.32 (8 H, t), 7.69 (2 H, t), 7.91 (2 H, d), 8.01 (2 H, br, d), 8.14 (1 H, s), 8.15 (1 H, s) and 10.18 (2 H, s); δ_C(400 MHz; $CDCl_3$) 0.2, 15.6, 22.0, 37.2, 51.6, 94.3, 96.8, 105.3, 118.1, 122.4, 127.4, 131.6, 133.25, 133.3, 136.3, 136.4, 138.4, 141.0, 144.1, 145.9, 147.4 and 173.6; [Found: *m/z* (+ve FAB, NOBA) 1119.2 (M^+), 2237.7 ($2M^+$) $C_{62}H_{68}N_4O_8Si_2Zn$ requires 1118.9].

Zn_2-l-Dim1b(SiMe$_3$)$_2$

Half of the protecting groups were removed from protected monomer, **Zn-Mon1b(SiMe$_3$)$_2$** (3.0 g, 2.7 mmol) using TBAF (1 mol dm^{-3} solution in THF; Aldrich; 1.79 cm^3). The fluoride was titrated into a solution of **Zn-Mon1b(SiMe$_3$)$_2$** in $CHCl_3$ until about 50% of the TMS groups had been removed, which generally required 1 equivalent. The reaction was followed by monitoring the ratio of the intensities of the acetylene CH (ν 3303 cm^{-1}) and C=O (ν 1732 cm^{-1}) absorptions using FT IR. The solution was then stirred with $CaCl_2$ for 10 min to remove any excess of fluoride and washed with water. The solvent was evaporated and the porphyrin dried. Flash column chromatography was carried out on silica eluting with $CHCl_3$–CH_2Cl_2 (1:5.7, v/v). The first and second bands were not separated since **Zn-Mon1b(SiMe$_3$)$_2$** is inert to Glaser–Hay coupling. However, any fraction containing **Zn-Mon1b** was kept separate for further chromatography. Three columns were performed under identical conditions yielding almost complete separation of **Zn-Mon1b** from **Zn-Mon1bSiMe$_3$**. The solvent was removed from the mixture of **Zn-Mon1bSiMe$_3$** and **Zn-Mon1b(SiMe$_3$)$_2$** and Glaser–Hay coupling carried out. TMEDA (420 mm^3, 2.8 mmol) was added to a solution of the porphyrin and CuCl (280 mg, 2.8 mmol) in CH_2Cl_2 (100 cm^3). Coupling was complete within 30 min. The reaction mixture was washed with water (4 × 100 cm^3) and evaporated. Flash column chromatography of the residue on silica eluting with $CHCl_3$–CH_2Cl_2 (1:4) for **Zn-Mon1b(SiMe$_3$)$_2$** and $CHCl_3$–CH_2Cl_2 (1:2.3) for **Zn_2-l-Dim1b(SiMe$_3$)$_2$** yielded excellent separation: yield, **Zn_2-l-Dim1b-(SiMe$_3$)$_2$** (838 mg, 30%); R_F 0.08 in $CHCl_3$ (Found: C, 67.6; H, 5.5; N, 5.2. $C_{118}H_{118}N_8O_{16}Si_2Zn_2$ requires C, 67.8; H, 5.7; N, 5.4%); $\lambda_{max}(CH_2Cl_2)$/nm 412 ($\log_{10}\varepsilon$ 5.90), 540 (4.63) and 575 (4.38); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3303 (CH) and 1732 (C=O); δ_H(250 MHz; $CDCl_3$) 0.24 (18 H, s), 2.47 (24 H, s), 3.12 (16 H, t), 3.65 (12 H, s), 3.66 (12 H, s), 4.30 (16 H, t), 7.72–8.25 (16 H, m) and 10.19 (4 H, s); δ_C(100 MHz; $CDCl_3$) −0.1, 15.6, 30.8, 37.1, 51.5, 74.2, 81.9, 94.3, 96.9, 105.2, 117.5, 118.1, 120.8, 122.3, 127.3, 127.6, 131.6, 133.2, 134.0, 136.3, 136.8, 138.2, 138.4, 140.9, 141.0, 144.0, 144.4, 145.8, 147.1, 147.4 and 173.6; [Found: *m/z* (+ve FAB) 2091 (M^+). $C_{118}H_{118}O_{16}N_8Si_2Zn_2$ requires 2091.38]. Yield of reclaimed starting material **Zn-Mon1b(SiMe$_3$)$_2$** (556 mg, 19%).

Zn_2-l-Dim1b

Zn_2-l-Dim1b(SiMe$_3$)$_2$ (109 mg, 52 μmol) was dissolved in CH_2Cl_2 (25 cm^3, freshly distilled ex. CaH_2), thoroughly degassed and saturated with argon and a solution of TBAF (1 mol dm^{-3} solution in THF; Aldrich; 168 mm^3) was added to it. The reaction, the course of which was followed by TLC, was complete after 20 min. The porphyrin was passed through a short silica column and then recrystallised from $CHCl_3$–MeOH to yield **Zn_2-l-Dim1b** (85 mg, 84%); R_F 0.07 in $CHCl_3$; δ_H(250 MHz; $CDCl_3$) 2.46 (24 H, s), 3.12 (16 H, t), 3.15 (2 H, s), 3.65 (12 H, s), 3.66 (12 H, s), 4.30 (16 H, t), 7.67–8.24 (16 H, m) and 10.18 (4 H, s); $\lambda_{max}(CH_2Cl_2)$/nm 334, 411, 538 and 574; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3303 (CH) and 1732 (C=O); [Found: *m/z* (+ve FAB) 1946.0 (M^+) 972.9 (M^{2+}) $C_{112}H_{102}N_8O_{16}Zn_2$ requires 1946.98].

H_8-l-Tet1b(SiMe$_3$)$_2$

Half of the protecting groups were removed from **Zn_2-l-Dim1b(SiMe$_3$)$_2$** (250 mg, 127 μmol) using TBAF (1 mol dm^{-3} in THF; Aldrich). The fluoride was titrated into a solution of **Zn_2-l-Dim1b(SiMe$_3$)$_2$** in $CHCl_3$ (85 cm^3, 1.4 × 10^{-3} mol dm^{-3} in porphyrin units) until about half of the TMS groups had been removed, which generally required about 1 equivalent of TBAF. The reaction was followed monitoring the ratio of the absorbances of the acetylene C–H (ν = 3303 cm^{-1}) and C=O (ν = 1732 cm^{-1}) using FT IR. The mixture was passed through a short silica column. For Glaser–Hay coupling, a solution of the zinc porphyrins in CH_2Cl_2 (500 cm^3, 0.4 × 10^{-3}mol dm^{-3} per porphyrin unit) was treated with CuCl (1.5 g, 15 mmol), TMEDA (2.3 cm^3, 15 mmol), in the presence of **BiPy** (119 mg, 760 μmol) and stirred in dry air until coupling was complete by TLC (15–30 min). The mixture was washed with water, demetallated by treatment with methanolic TFA (10%), washed with water again and evaporated. The three components to the mixture were separated by flash column chromatography $CHCl_3$–CH_2Cl_2 (1:1.5) for **H_4-l-Dim1b(SiMe$_3$)$_2$** and **H_4-c-Dim1b** and $CHCl_3$–CH_2Cl_2 (1:1) for **H_8-l-Tet1b(SiMe$_3$)$_2$**. **H_8-l-Tet1b(SiMe$_3$)$_2$** was recrystallised from $CHCl_3$–MeOH (70 mg, 29%); R_F 0.06 in $CHCl_3$; $\lambda_{max}(CH_2Cl_2)$/nm 332, 410, 507, 540, 574 and 625; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3303 (CH), 1732 (C=O); δ_H(400 MHz; $CDCl_3$) −2.50 (8 H, s), 0.26 (18 H, s), 2.53 (48 H, s), 3.10 (32 H, br t), 3.63 (48 H, set of very close singlets), 4.33 (32 H, br t), 7.60–8.30 (32 H, m) and 10.26 (8 H, s) [Found: *m/z* 3782 (M^+) and 1893 (M^{2+}) $C_{230}H_{226}N_{16}O_{32}Si_2$ requires 3782.9]. Yields of by-products **H_4-l-Dim1b(SiMe$_3$)$_2$** (36 mg, 15%) and **H_4-c-Dim1b** (51 mg, 20%).

Zn_4-l-Tet1b(SiMe$_3$)$_2$

H_8-l-Tet1b(SiMe$_3$)$_2$ (60 mg, 16 mmol) was metallated with zinc using the standard procedure. Yield of **Zn_4-l-Tet1b(SiMe$_3$)$_2$** (61 mg 95%) (Found: C, 68.3; H, 5.4; N, 5.4. $C_{230}H_{218}N_{16}O_{32}Si_2Zn_4$ requires C, 68.4; H, 5.4; N, 5.5%); $\lambda_{max}(CH_2Cl_2)$/nm 333, 411, 538 and 574; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3303 (CH) and 1732 (C=O); δ_H(400 MHz; $CDCl_3$) 0.29 (9 H, s), 0.23 (9 H, s), 2.42 (48 H, set of four overlapping singlets), 3.08 (32 H, br t), 3.58 (48 H, set of four overlapping singlets), 4.27 (32 H, br t), 8.22–7.63 (32 H, m) and 10.02 (8 H, s); δ_C(100 MHz; $CDCl_3$/[$^2H_5$]pyridine) −0.1, 15.6, 22.0, 37.1, 51.5, 74.2, 81.9, 94.3, 96.8, 96.9, 105.2, 117.5, 117.6, 118.6, 120.9, 122.4, 127.4, 127.6, 131.5, 132.1, 133.4, 134.0, 136.0, 136.9, 138.17, 138.22, 140.99, 141.1, 144.4,

145.9, 147.3, 147.4 and 173.5 (C=O) [Found: *m/z* 4036 (M^+) and 2018 (M^{2+}). $C_{230}H_{218}N_{16}O_{32}Si_2Zn_4$ requires 4036.34].

H_{16}-l-Oct1b(SiMe$_3$)$_2$

Zn_4-l-Tet1b(SiMe$_3$)$_2$ (170 mg, 45 μmol) was partially deprotected. The TBAF was titrated into a solution of **Zn_4-l-Tet1b(SiMe$_3$)$_2$** in $CHCl_3$ until about half of the TMS groups had been removed, which generally required about 1 equivalent of TBAF. The reaction was followed monitoring the ratio of the absorbances of the alkyne CH (ν 3303 cm^{-1}) and C=O (ν 1732 cm^{-1}) using FT IR. For Glaser–Hay coupling, a solution of the zinc porphyrins in CH_2Cl_2 (400 cm^3, 0.5 × 10^{-3} mol dm^{-3} per porphyrin unit) was treated with CuCl (1.3 g, 13 mmol), TMEDA (2.0 cm^3, 13 mmol), in the presence of **H_2-Py$_4$P** (177 mg, 286 μmol) and stirred in dry air until coupling was complete by TLC (15–30 min). The mixture was washed with water, demetallated by treatment with methanolic TFA (10%), washed with water and evaporated. The three components of the mixture were separated by flash column chromatography. **H_8-l-Tet1b(SiMe$_3$)$_2$** and **H_8-c-Tet1b** were collected as separate fractions using CH_2Cl_2–$CHCl_3$ (1:1.9) and recrystallised from $CHCl_3$–MeOH. The solvent was changed to CH_2Cl_2–$CHCl_3$ (1:9) to remove the **H_{16}-l-Oct1b(SiMe$_3$)$_2$** from the column. Yield **H_{16}-l-Oct1b(SiMe$_3$)$_2$** (25 mg, 15%); R_F 0.02 in $CHCl_3$; λ_{max}(CH_2Cl_2)/nm 332, 411, 506, 539, 574 and 625; ν_{max}(CH_2Cl_2)/cm^{-1} 1732 (C=O); δ_H(250 MHz; $CDCl_3$) −2.50 (16 H, s), 0.25 (18 H, s), 2.49 (96 H, s), 3.12 (64 H, br s), 3.61 (96 H, m), 4.32 (64 H, br s), 7.68–8.23 (64 H, m) and 10.25 (16 H, s); *m/z* (ES MS) 825 (MH_9^{9+}), 928 (MH_8^{8+}), 1061 (MH_7^{7+}), 1237 (MH_6^{6+}), 1485 (MH_5^{5+}) and 1856 (MH_4^{4+})-($C_{454}H_{434}N_{32}O_{64}Si_2$ requires 7419.38). Yields of by-products **H_8-c-Tet1b** (22 mg, 13%) and **H_8-l-Tet1b(SiMe$_3$)$_2$** (28 mg, 16%).

H_8-c-Tet1b

TMEDA (0.5 cm^3, 3.4 mmol) was added to a solution of **Zn_2-l-Dim1b** (100 mg, 51 μmol), **H_2-Py$_4$P** (191 mg, 309 μmol) and CuCl (336 mg, 3.4 mmol) in CH_2Cl_2 (120 cm^3; freshly distilled ex. CaH_2). Coupling was complete within 30 min. The reaction mixture was washed with water (5 × 100 cm^3), treated with TFA (10% in MeOH; 100 cm^3) washed again with water and evaporated. Flash column chromatography was used to purify the product. $CHCl_3$–CH_2Cl_2 (1:1) removed any **H_4-c-Dim1b** and $CHCl_3$–CH_2Cl_2 (1.5:1) the **H_8-c-Tet1b**; yield of **H_8-c-Tet1b** after recrystallisation from $CHCl_3$–MeOH was 50 mg (54%); δ_H(250 MHz; $CDCl_3$) −2.53 (8 H, br s), 2.38, 2.42, 2.49, 2.53 (48 H, m), 3.10 (m, 32 H), 3.46, 3.54, 3.59, 3.60, 3.62 (48 H, m), 4.30 (32 H, m), 7.68–8.47 (32 H, m), 10.07, 10.15 and 10.24 (8 H, s); *m/z* (ES MS) 910 (MH_4^{4+}), 1213 (MH_3^{3+}) and 1819 (MH_2^{2+}) ($C_{224}H_{208}N_{16}O_{32}$ requires 3636.48).

Zn_4-c-Tet1b

H_8-c-Tet1b (50 mg, 14 μmol) was metallated with zinc using the standard procedure; yield of **Zn_4-c-Tet1b** 50 mg (93%) (Found: C, 69.3; H, 5.2; N, 5.7. $C_{224}H_{200}N_{16}O_{32}Zn_4$ requires C, 69.2; H, 5.2; N, 5.8%); λ_{max}(CH_2Cl_2)/nm 333, 414($\log_{10}\varepsilon$ 6.3), 538 and 574; δ_H(400 MHz; $CDCl_3$) 2.34, 2.38, 2.43, 2.45, 2.49 (48 H, s), 3.08 (32 H, br.t), 3.46, 3.54, 3.58, 3.59, 3.60 (48 H, s), 4.28 (32 H, br t), 7.64–8.55 (32 H, m), 9.90, 9.97 and 10.04 (8 H, m); δ_C(100 MHz; $CDCl_3$–[$^2H_5$]pyridine) 15.5, 15.6, 22.0, 36.9, 37.0, 37.1, 51.4, 51.6, 74.1, 74.1, 74.3, 81.8, 82.1, 96.9, 117.5, 117.6, 120.8, 127.5, 127.7, 131.1, 132.3, 134.0, 134.1, 136.7, 136.9, 138.0, 138.1, 138.2, 140.9, 141.0, 141.1, 144.2, 144.4, 145.8, 145.9, 147.3, 173.47, 173.52 and 173.6; *m/z* (+ve FAB) 3887 (M^+) and 1945 (M^{2+}) (very weak signals) ($C_{224}H_{200}N_{16}O_{32}Zn_4$ requires 3889.9).

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