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The synthesis and studies towards the self-replication of bis(capped porphyrins)

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Connecting two facially-protected porphyrins was expected to lead to an equal mixture of laterally-bridged doubly-protected bis-porphyrins; one in which the two porphyrin units were protected on the same face (*syn*) and one with the two porphyrin units protected on opposite faces (*anti*). Addition of a co-factor (bidentate ligand) was expected to lead predominantly to the *syn*-bis-porphyrin by a templated self-replication process. This concept was explored using Baldwin's capped porphyrin. Bis(capped porphyrins) were synthesised in several steps starting from zinc(II) capped porphyrin **2**. Nitration of **2** followed by reduction and photo-oxidation yields a mixture of zinc(II) porphyrin-diones **7** and **8** that can be separated by HPLC. The condensation of 2 molar eq. of zinc(II) porphyrin-7,8-dione **8** with 1,2,4,5-benzenetetramine leads to the formation of a 1 : 1 mixture of *syn*- and *anti*-dizinc(II) bis(7,8-capped porphyrins), **11** and **12**, respectively, that have almost identical spectroscopic properties. These two geometric isomers were distinguished by significant differences in their molecular recognition properties. Likewise the *syn*- and *anti*-dizinc(II) bis(2,3-capped porphyrins), **9** and **10**, respectively, are synthesised from the related zinc(II) capped porphyrin-2,3-dione **7**, and were also identified using molecular recognition studies. The molecular recognition properties of these bis(capped porphyrins) were utilised in studies of self-replicating porphyrin systems. The results show that tetraazaanthraceno-bis-porphyrins **9**–**12** can catalyse their own formation but self-replication was not observed. These results highlight the potential that these interesting hosts could have as templates in supramolecular chemistry, synthesis and catalysis.

Introduction

The questions surrounding the origins of life remain among the most challenging questions within Science. Although there are a number of conflicting theories a common point of most of the credible ideas[1] is that an important transition point between live and inanimate matter was when the first self-replicating molecule arose from the pre-biotic soup. For this reason, it is not surprising there have been a number of studies of artificial self-replication in the laboratory to shed more light on this important phenomenon. The first artificial self-replicating system was reported in 1986 by von Kiedrowski,[2] soon to be followed by other groups.[3–13] Central to the design of any self-replicating system is complementarity between the product (template) and the reagent from which the template is formed. It is this complementarity that distinguishes self-replication from other forms of autocatalysis or as Wintner and Rebek pointed out: "self-replication is a special subset of autocatalytic reactions in which molecular recognition plays a role".[14]

Designing a system with molecular recognition properties for applications such as self-replication, depends heavily on the ability to synthesise well-defined host molecules. As any potential self-replicating molecule is made up of two or more smaller sub-units, multi-site hosts (*e.g.*, ditopic) are particularly interesting in this respect. Additionally, multi-site hosts are of great interest to researchers in supramolecular chemistry as they can be utilised for such diverse applications as signal magnification by allosteric interactions[15] and templated synthesis.[16,17] Some of the desirable features of a successful multi-site host are a certain rigidity (to keep the binding sites at a fixed distance) and steric restrictions (*e.g.* a protecting group) around the binding sites. Considering these features, we have designed and synthesised four different isomers of a rigid bis(capped porphyrin) host. These host molecules were designed for use in studies of molecular recognition,[18,19] self- and complementary-recognition and self-replication.

Our concept for a porphyrin-based self-replicating system is based on the idea that a *syn* bis(capped porphyrin) could act as a template for its own formation in the presence of a co-factor while in the "background" reaction, in the absence of co-factor, both the *syn*-isomer and the *anti* bis(capped porphyrin) would be formed in a 1 : 1 ratio (Fig. 1). Therefore, by looking at the final product distribution the extent of self-replication should be easily determined. This design should be valid for any potentially self-replicating system based on a rigid host and/or guest ligand-mediated recognition of the reactants to the template (product) to give one geometric isomer instead of two or more isomers in the absence of the ligand interaction.

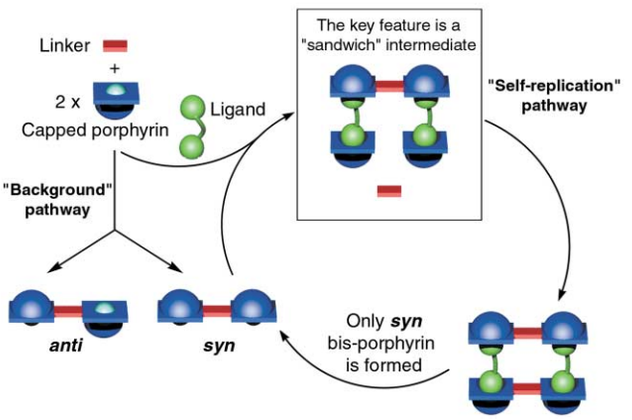

Fig. 1 Schematic representation of a self-replicating porphyrin system.

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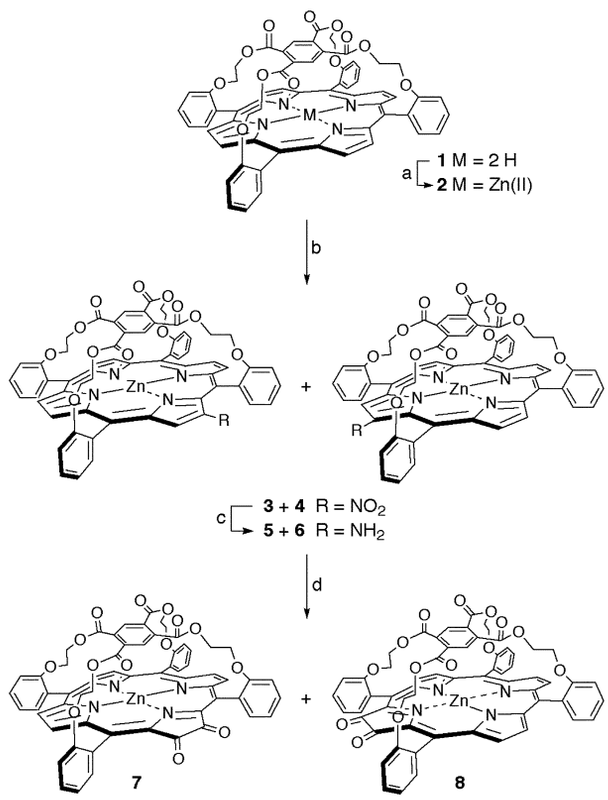
The compounds developed in this study are derived from the C_2-capped porphyrin **1** which is encumbered on one face. This compound, and related capped porphyrins, was developed by Baldwin and co-workers in their studies of reversible oxygen carriers.[20,21] They showed that compounds like the C_2-capped porphyrin **1** could reversibly bind dioxygen and other small molecules within the cavity when the porphyrin was chelated with iron and the co-ordination site on the unencumbered face is ligated.[21–23]

In studies by Baldwin and co-workers it was also shown that capped porphyrins can easily be functionalised like ordinary porphyrins, for instance to introduce a β-pyrrolic nitro or amino functionality.[24,25] In previous work by Crossley and co-workers porphyrin-2,3-diones, obtained by the photo-oxidation of 2-aminoporphyrins, have served as the main building block for more elaborated porphyrin systems such as rigid, laterally-bridged oligoporphyrins.[26–28] Therefore the methodology to synthesise a capped porphyrin-2,3-dione as the building block for a bis(capped porphyrin) system was applied. Compared to previous syntheses of bis- and oligomeric-porphyrins, capped porphyrins provided two additional challenges. One related to the sensitivity of the ester-functionality in the capping superstructure to some reaction conditions that the simpler porphyrin system can easily tolerate. The other was the presence of two regioisomers of the substituted capped porphyrin due to the presence of the capping aryl protons, requiring separation of these at some stage in the synthetic scheme. In addition, once the capped porphyrin-diones were reacted to form bis(capped-porphyrins), two isomers, the *syn*- and *anti*-isomers were formed and had to be separated. After overcoming these problems, a total of four different bis(capped porphyrins), two pairs of *syn*- and *anti*-isomers, were obtained. Some of their interesting molecular recognition properties have been reported previously,[18] here their synthesis and the studies towards the possible self-replication of these bis(capped porphyrins) will be discussed.

Results and discussion

Synthesis

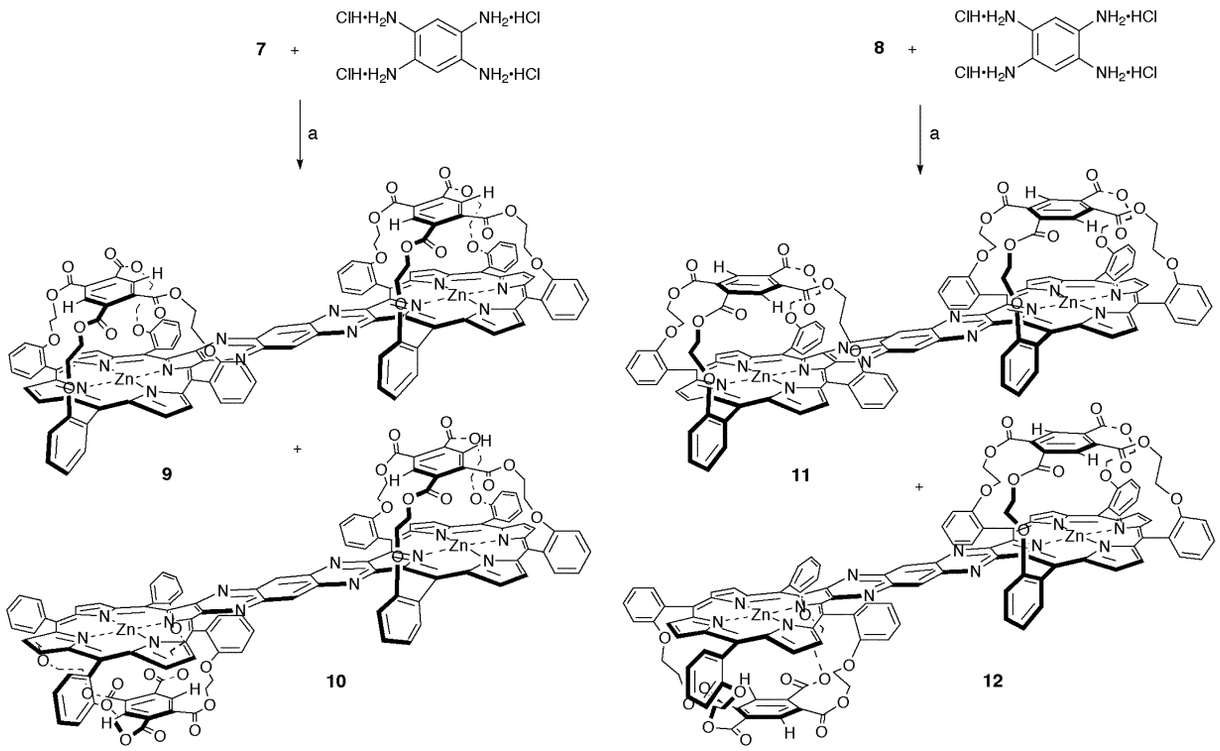
The nitration of **2** following Baldwin's method,[24,25] gave as expected two zinc(II) nitro-capped porphyrin regioisomers, **3** and **4**. These were reduced[24,25] to yield the unstable zinc(II) amino-capped porphyrins, **5** and **6**, which were photo-oxidised to give the desired zinc(II) capped porphyrin-diones, **7** and **8** (Scheme 1). Two different approaches were explored for this synthesis. In the first, the mixture of **3** and **4** was separated[25] and the individual fractions of **3** and **4** were reduced and photo-oxidised[29] to the corresponding porphyrin-diones, **7** from **2** in 17% overall yield and **8** from **2** in 13% yield. Alternatively, the mixture of **3** and **4** could be reduced and photo-oxidised to give a 1 : 1 mixture of **7** and **8** which was then separated by preparative HPLC. The overall yield by this method of **7** from **2** was 26% and that of **8** from **2** was 22%. The latter method therefore became the method of choice. The difference in yields between the two methods is due to the reduction and photo-oxidation steps of **3** and **4** that always leads to some formation of side-products that need to be removed. It is desirable therefore to couple the purification of the porphyrin-diones **7** and **8** with the necessary separation of the two regioisomers formed. It should also be noted here that the synthesis of **7** and **8** from **3** and **4**, respectively, confirmed the assignments of **3** and **4** by Baldwin and co-workers.[29] The two porphyrin-diones **7** and **8** differ in the ^{1}H NMR spectrum as **7** has two chemically unequivalent capping protons whilst these protons are chemically equivalent in **8**. Related compounds obtained by Baldwin and DeBernardis and reported as 2,13-dioxoporphyrins were clearly incorrectly assigned by them.[24]



Scheme 1 *Reagents and conditions*: a, $Zn(OAc)_2{\cdot}2H_2O$ in CH_2Cl_2–MeOH, heat, 1 h; b, I_2–$AgNO_2$ in CH_2Cl_2–MeCN; c, $NaBH_4$–Pd–C in CH_2Cl_2–MeOH; d, Rose Bengal, O_2, *hv* in CH_2Cl_2, chromatography over silica.

The zinc(II) capped porphyrin-diones **7** and **8** were then condensed with 1,2,4,5-benzenetetramine[26] to give the desired bis(capped porphyrins). The porphyrin-dione **7** gave a 1 : 1 mixture of *syn*- and *anti*-dizinc(II) bis(2,3-capped porphyrins), **9** and **10**, respectively and the porphyrin-dione **8** gave a 1 : 1 mixture of *syn*- and *anti*-dizinc(II) bis(7,8-capped porphyrins), **11** and **12**, respectively (Scheme 2). Both reactions were concentration dependent and that some demetallation occurred during the course of the reaction. As these compounds were required as the dizinc(II) derivatives, the reaction mixture was treated with zinc(II) acetate dihydrate after the initial workup. The separation and characterisation of these two pairs of *syn*- and *anti*-isomers [bis(2,3- and 7,8-capped porphyrins)] will now be discussed separately.

Before the two isomers **11** and **12** were separated it was found beneficial to run the mixture through a size-exclusion column. This removed all the unreacted starting material resulting in the isolation of a mixture of **11** and **12**. The separation of **11** and **12** was achieved on either a silica column or by preparative HPLC, the latter method being preferred. The spectroscopic properties of the two fractions collected were so similar (albeit not identical) that initially they could not be unambiguously assigned to the structures of **11** and **12**. Assignment of the more polar and the less polar fractions as **11** and **12**, respectively, was achieved by their molecular recognition properties towards a "molecular ruler" ligand 1,12-diaminododecane.[18] These findings were reinforced by studies using several different ditopic ligands.[19] It should also be pointed out that the polarity difference and order of elution of **11** and **12** on a silica column was not unexpected. Previous work has shown that zinc(II) porphyrins are generally more polar on silica than their free-base counterparts.[28] This implies higher specificity for zinc(II) porphyrin interactions towards silica. Based on this, a difference in polarity on silica of **11** and **12** would be expected and could be used for their tentative assignment as the geometry of the *syn*-isomer **11** leaves two zinc(II) molecules (binding sites) exposed to the



Scheme 2 *Reagents and conditions*: a, pyridine, N_2, heat.

same silica particle unlike the *anti*-isomer, hence making it more tightly bound to the silica support.

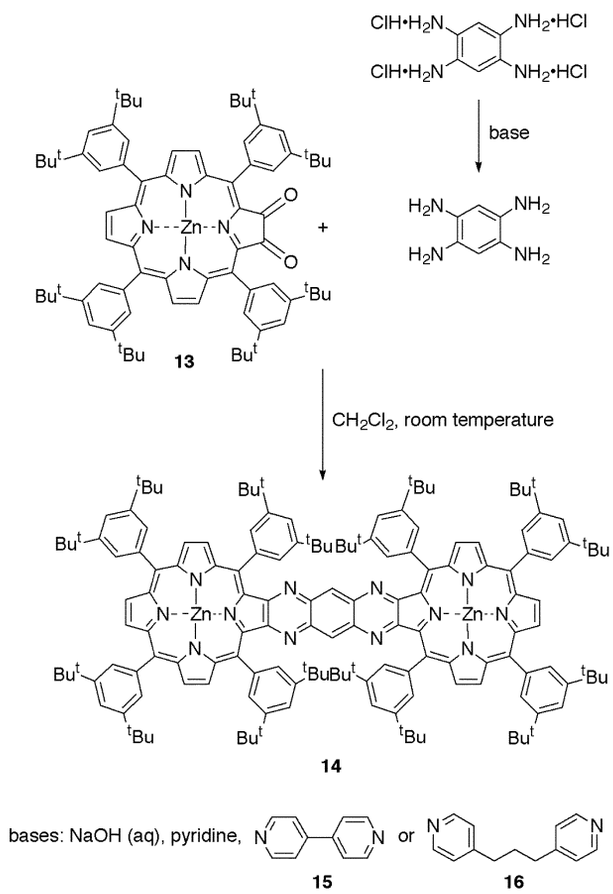
The other pair of bis(capped porphyrins), **9** and **10**, which differ from **11** and **12** by being connected *via* the 2,3-position (relative to the capping protons) while **11** and **12** are connected by the 7,8-position, have some different properties to the previous pair. The bis(capped porphyrins) **9** and **10** were first purified by size-exclusion chromatography. Membrane filtration through a cellulose membrane (0.5 μm), originally designed to remove foreign particles from the solution prior to injection on the preparative HPLC column, achieved partial separation of the two isomers. A precipitate collected on the membrane of the syringe was washed off with excess chloroform. Analytical TLC analysis showed the collected precipitate to be an almost pure fraction of the less polar isomer. By repeating the filtration process on this fraction, a pure sample of the less polar isomer was obtained, identical by ^{1}H NMR spectroscopy to samples of less polar fractions obtained later by preparative HPLC. The filtrate obtained from the membrane filtration was, however, always a mixture of the two isomers **9** and **10**, with the more polar isomer in large excess. The membrane filtration technique, therefore, relies on the low solubility of the less polar isomer in chloroform. The filtrate was then separated by preparative HPLC and two fractions were collected. The spectroscopic properties of the two fractions were almost identical with the result that they could not be assigned to the structures of **9** and **10**. As detailed elsewhere,[19] molecular recognition studies did later allow the unambiguous assignment of the more polar and less polar fractions as **9** and **10**, respectively, again in agreement with their expected difference in polarity on silica. The two compounds **9** and **10** showed some interesting differences. The less polar fraction (later assigned as **10**) did not only have much lower solubility in common organic solvents than the more polar fraction but, for reasons not understood, repetitively failed to give satisfactory results from microanalysis. Despite this all the other spectroscopic data were in agreement with the expected structure of **10** (or **9**). The more polar fraction (later assigned as **9**) showed only one singlet for the capping protons at 300 K, not two as expected and shown for the other isomer. Variable temperature studies showed this to be a coincidence, at temperatures above and below 300 K, two singlets were observed in the capping proton region for the more polar fraction as expected.

Development of self-replication methodology

To be able to study a self-replicating system as described above (Fig. 1) several issues had first to be addressed. One was the choice of ligand to template the formation of the *syn* bis-(capped porphyrins). The molecular recognition studies carried out on the bis(capped porphyrins) indicated that if a relatively short bidentate ligand was chosen, a sandwich structure (the key intermediate in Fig. 1) would result.[18,19] Although their complexation with dizinc(II) bis-porphyrins does generate "sandwich" structures, the α,ω-diaminoalkane ligands were ruled out from the self-replication studies as the primary amines might well react with the porphyrin-diones. The promising results obtained from binding studies on the 4,4′-bipyridine ligand **15** with the simpler bis-porphyrin **14** made it a good candidate.[19] The pyridine functionality was known not to cause problems in reactions with a porphyrin-2,3-dione although the rigidity of **15** might cause problems as some flexibility in the proposed "sandwich" complex could be necessary. Therefore, 1,3-bis(4-pyridyl)propane **16** was also chosen as it contains a flexible linker between the two pyridine functionalities.

It was also necessary to determine how to carry out these reactions without using pyridine (that would otherwise block all the binding sites). To do this, preliminary studies were carried out on the simpler zinc(II) porphyrin-dione **13** and dizinc(II) bis-porphyrin[26] **14**. Pyridine had served the dual roles of solvent and base to liberate 1,2,4,5-benzenetetramine from its tetrahydrochloride salt form *in situ*. The obvious approach was to liberate and isolate the 1,2,4,5-benzenetetramine§ first and to carry the condensation reaction out in a different solvent. Liberated 1,2,4,5-benzenetetramine was immediately added to a solution of the zinc(II) porphyrin-dione **13** in dichloromethane in the presence of molecular sieves. The solution was stirred at room temperature for 7 days to give the dizinc(II)

§ Sensitive to moisture and oxygen.



Scheme 3

bis-porphyrin **14** in 11% yield (Scheme 3). These results were not encouraging, so a different approach was desirable.

Using lithium hydroxide was also ruled out as a trial reaction on the zinc(II) C_2-capped porphyrin-7,8-dione **8** in chloroform at room temperature failed to give the desired product and showed that the ester groups of the starting material had been completely hydrolysed by the base. This meant that a milder method would be necessary to liberate the 1,2,4,5-benzenetetramine *in situ*. One option here would be to see if the ligands **15** and **16** themselves could be efficient as bases in liberating the 1,2,4,5-benzenetetramine tetrahydrochloride. To test this, the reaction between zinc(II) porphyrin-dione **13** and 1,2,4,5-benzenetetramine tetrahydrochloride in chloroform was performed in the presence of the ligand **16**. The results were compared to those obtained in the absence of the ligands **15** and **16**, and also in the presence of the ligand with triethylamine (Et_3N) base (Table 1).

These results showed that the ligand **16** would act as the base in the reaction to give **14** in considerably higher yields than in the absence of a ligand (35% *vs.* 11%) that in turn were higher than in the presence of Et_3N and the ligand **16**. No explanation could be found for the latter observation. Interestingly, addition of the template (product), dizinc(II) bis-porphyrin **14**, seemed to significantly increase the yield of **14**. It appeared to either act as a base, or to catalyse the reaction. These results hint that the tetraazaanthracene-bridge in the structure of **14** could act as a base to liberate 1,2,4,5-benzenetetramine *in situ*.

These preliminary studies on the simple zinc(II) porphyrin-dione **13** gave an indication of what could be expected in self-replication studies on bis(C_2-capped porphyrins). Particularly, these studies highlighted the difficulties associated with the liberation of the 1,2,4,5-benzenetetramine tetrahydrochloride. These results also showed that secondary unexpected effects, such as the product acting as a base, might create ambiguity in these studies.

Table 1 Yields of bis-porphyrin **14** after 3 days from the reaction of 1,2,4,5-benzenetetramine tetrahydrochloride and porphyrin-dione **13** in the presence of different bases (ligands)

Entry	Template	Base 1	Base 2	Yield (%)
1	No	**16**		35
2	Yes[a]	**16**		49
3	No	**16**	Et_3N	<5
4	Yes[a]	None		19
5	No	None		11

[a] 0.5 Eq. of bis-porphyrin **14** was added (yields are then net yields).

Self-replication studies on bis(capped porphyrins)

Because of the solubility problems encountered with the *anti*-dizinc(II) bis(2,3-C_2-capped porphyrin) **10**, as detailed above, the focus in this work was on the *syn*- and *anti*-dizinc(II) bis-(7,8-C_2-capped porphyrins), **11** and **12**.

Continuing from the preliminary studies outlined above, the zinc(II) C_2-capped porphyrin-7,8-dione **8** and 1,2,4,5-benzenetetramine tetrahydrochloride were reacted together in chloroform in the presence of the 1,3-bis(4-pyridyl)propane **16** ligand. Dizinc(II) bis(7,8-C_2-capped porphyrins) were not observed in the reaction mixture after 16 days.

In light of this result and the problems encountered earlier with the liberation of 1,2,4,5-benzenetetramine tetrahydrochloride, the approach was modified. Instead of trying to use the 1,2,4,5-benzenetetramine tetrahydrochloride together with zinc(II) C_2-capped porphyrin-7,8-dione **8**, in the presence of the ligand and an appropriate solvent, the process was separated into two steps. First the zinc(II) C_2-capped 6′,7′-diamino-quinoxalino-porphyrin **17** was formed and then it was added to a solution of **8** (in a 1 : 1 ratio) in the presence of the desired ligands and templates.

The zinc(II) C_2-capped 6′,7′-diaminoquinoxalino-porphyrin **17** was synthesised by treating the zinc(II) C_2-capped porphyrin-7,8-dione **8** with excess 1,2,4,5-benzenetetramine tetrahydrochloride in refluxing pyridine for 20 h. As some demetallation had occurred in removing the pyridine in the workup, the mixture was remetallated with zinc(II) acetate dihydrate in refluxing dichloromethane–methanol. The polar product was then purified quickly by flash silica chromatography to give the crude **17** product in 66% yield (Scheme 4).

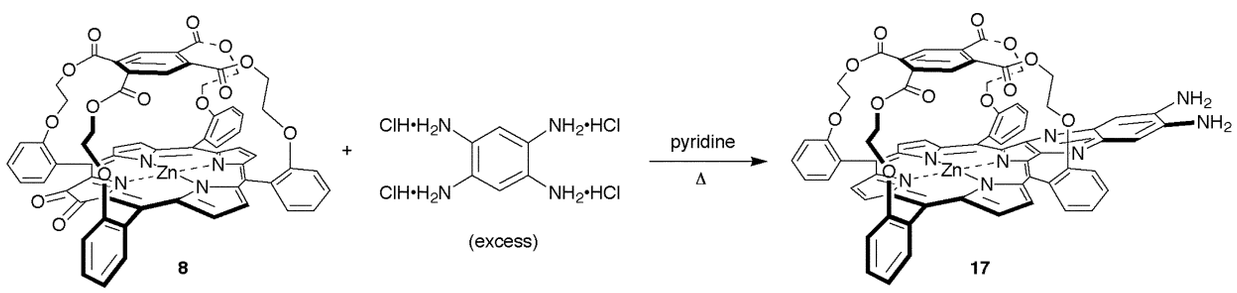
The product **17** was unstable and therefore used quickly without extensive purification. Characterisation by techniques other than ^{1}H NMR spectroscopy was not attempted. Its ^{1}H NMR spectrum showed the expected amine protons as a broad peak around 2.8 ppm and the β-pyrrolic protons in the 8.7–8.9 ppm region with the expected pattern of a ABq system and a singlet.

Once zinc(II) C_2-capped 6′,7′-diaminoquinoxalino-porphyrin **17** was obtained, self-replication studies were performed. These studies were conducted in a manner allowing comparison for experiments under different conditions to be made with some confidence using stock solutions of the main reagents in dry, deacidified chloroform. The ligands used were 4,4′-bipyridine **15**, 1,3-bis(4-pyridyl)propane **16** and pyridine. The appropriate ligands and templates were mixed and diluted to a constant volume and then stirred for several days while monitored by analytical HPLC and ^{1}H NMR spectroscopy. After 7 days, the products were purified by size-exclusion chromatography and analysed by ^{1}H NMR spectroscopy. The products obtained from the size-exclusion chromatography were not further purified and the yields reported therefore only indicative. Furthermore, it was noted that some of the *anti*-isomer **12** was lost in the workup in preference to the *syn*-isomer **11**. Based on this observation, only the product distributions obtained from analysing the reaction product (before size-exclusion chromatography) are reported here. The templates used in these

Table 2 Product distribution and crude yields (upper limit) for the reaction between **8** and **17** in the presence of various ligands and templates

			Product after 7 days[a]							
			HPLC		NMR		Ratio of **12/11** (*anti*/*syn*)			
Entry	Ligand	Template	*anti* (%)	*syn* (%)	*anti* (%)	*syn* (%)	3 days [b]	7 days [b]	7 days[c]	Yield (%)
1	None	None	75	25	78	22	3.3	3.0		38
2	None	**14**	73	27	72	28	3.3	2.7		28
3	Pyridine	None			60	40		1.5[d]		47
4	Pyridine	None	82	18	74	26	4.6	4.6		31
5	**15**	None			86	14		4.9[d]		36
6	**16**	None			68	32		2.1[d]		38
7	**16**	None			94	6		11.5[d]		53
8	**16**	**14**	84	16	82	18	10.1	5.3		15
9	**16**	**12** (*anti* 7,8)	92	8	85	15	32.3[e]	11.5[e]	4.3	71
10	**16**	**9** (*syn* 2,3)	84	16	83	17	13.3	5.3		36
11	**16**	**11** (*syn* 7,8)	73	27	70	30	2.7[e]	2.7[e]	8.1	54

[a] The values for *anti* and *syn* refer to *anti*- and *syn*-bis(capped porphyrins), **12** and **11**, respectively, as measured by HPLC or ^{1}H NMR spectroscopy. [b] Ratio of *anti*-/*syn*-bis(capped porphyrins), **12** : **11**, formed measured by analytical HPLC. Data not corrected for amounts of template present. [c] Ratio of *anti*-/*syn*-bis(capped porphyrins), **12** : **11**, formed measured by ^{1}H NMR and corrected for the amount of template present. [d] Ratio of *anti*-/*syn*-bis(capped porphyrins), **12** : **11**, formed measured by ^{1}H NMR. [e] Note that the template is the same as one of the products.



Scheme 4

reactions were the *anti*- and *syn*-dizinc(II) bis(7,8-C_2-capped porphyrins), **12** and **11** as well as the *syn* dizinc(II) bis(2,3-C_2-capped porphyrin) **9** and dizinc(II) bis-porphyrin **14**. The results from these experiments are summarised in Table 2.

These results indicate that self-replication did not occur, at least not according to the scenario outlined in Fig. 1. In every reaction more of the *anti* dizinc(II) bis(7,8-C_2-capped porphyrin) **12** was formed than the corresponding *syn*-isomer **11**. Even in reactions when no ligand was present (entries 1–2 in Table 2) or when pyridine was the ligand (entries 3–4 in Table 2), the *anti*-isomer **12** was formed in 2 : 1 up to 5 : 1 ratio to the *syn*-isomer **11**. This indicates that under these conditions, the assumption that the "background" reaction (Fig. 1) gives a 1 : 1 mixture of **12** and **11** is no longer valid. One trend observed in these results (Table 2) is that the **12** : **11** ratio seems slightly higher (*i.e.* more **12**) in cases when a ligand or template is present.

These results also indicate that the ratio of the *anti*-isomer **12** to the *syn*-isomer **11** is higher after 3 days than after 7 days when a template and a ligand is present. Note that this also suggests that the *anti*-isomer **12** is acting as the template but according to the initial self-replication model (Fig. 1) the *anti*-isomer **12** should not catalyse its own formation. Changing the solvent from chloroform to toluene did not change the product distribution greatly; the *anti*-isomer **12** was always formed in preference to the *syn*-isomer **11** (results not shown).

The conclusion from these studies is that changing the solvent and temperature from refluxing pyridine changes the product distribution so that the *syn*- and *anti*-isomers **11** and **12** are no longer formed in a 1 : 1 ratio. These results are difficult to explain but kinetic effects offer an explanation. Thermodynamic effect cannot be ruled out either, as the products **11** and **12** are not necessarily equal in energy ($\Delta G_{formation}$) even though they are structural isomers (force field calculations[30] indicate that the heat of formation is 15 kJ mol^{-1} lower for the *anti*-isomer **12** than for the *syn*-isomer **11**). Of the two options, kinetic factors are more likely, as there are different product distributions at different temperatures. To try to determine the effect of temperature on the reactions, the reaction to form **11** and **12** was tested in pyridine at room temperature. Unfortunately, no product was obtained so no direct comparison in pyridine was possible.

The reason the *anti*-isomer **12** might form faster (kinetically) than the *syn*-isomer **11** at room temperature is likely to be some steric hindrance between the two caps in the initial steps in one of the pathways to the formation of the *syn*-isomer, which is absent in the formation of the *anti*-isomer (Fig. 2).

At elevated temperatures, the thermal energy is enough to overcome this kinetic barrier for the formation of the *syn*-isomer **11**, leading to the observed 1 : 1 product ratio. The relatively small effects of the templates leading to an increase in the relative amounts of *anti*-isomer **12** remain unexplained. Studies towards self-replication at elevated temperatures are currently in progress.

Conclusions

The synthesis of the four facially protected bis(capped porphyrins) **9**–**12** based on our earlier methodology for the synthesis of rigid, laterally-bridged bis-porphyrins has been shown to proceed in a similar fashion to the simpler bis-porphyrins (such as **14**) if challenges with separation of all the possible different stereoisomers are excluded. This demonstrates the usefulness of this approach to multi-porphyrin arrays. The bis(capped porphyrins) described here have already been shown to have interesting molecular recognition properties.[18,19] Studies described here to utilise these compounds as the basis for a self-replicating porphyrin system were inconclusive. These studies did indicate that these bis(capped porphyrins) could act as catalysts for their own formation; however, whether

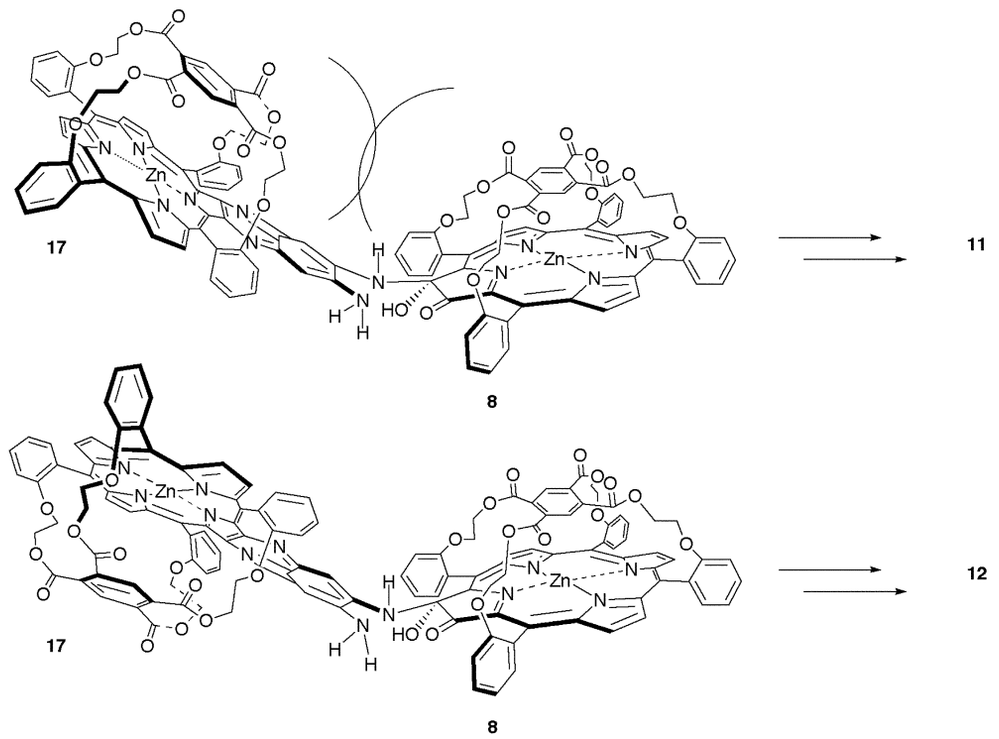


Fig. 2 The proposed key intermediate in the mechanism for the formation of *anti*- and *syn*-bis(capped porphyrins), **12** and **11**, from **17** and **8** indicating the steric hindrance in the formation of **11**. Note that the last step, aromatisation of the tetraazaanthracene-bridge (not shown), is the only irreversible step and the two units can rotate freely around the hemiaminal-linkage.

they can truly act as templates or are capable of unequivocal self-replication remains to be determined. While these systems do not show signs of self-replication, other uses of the bis(capped porphyrins) can be envisaged such as acting as co-factors for other types of templated synthesis and templated catalyses and as substrates for self- and complementary recognition studies.

Experimental

General remarks

Melting points were recorded on a Reichert melting point stage microscope and are uncorrected. Microanalyses were performed by the Campbell Microanalytical Laboratory, The University of Otago, New Zealand. Infrared spectra were recorded on chloroform solutions with a Perkin-Elmer Model 1600 FT-IR spectrophotometer. Electronic absorption spectra were recorded on a Cary 5E UV–vis spectrophotometer at 25 °C. ^{1}H NMR spectra were recorded on a Bruker AC-200F (200 MHz), a Bruker DRX-400 (400 MHz) or a Bruker DPX-400 (400 MHz) spectrometer and signals are quoted in ppm relative to tetramethylsilane ($SiMe_4$, ^{1}H and ^{13}C = 0 ppm) or the solvent residue peak ($CDCl_3$; ^{1}H = 7.26 and ^{13}C = 77.16 ppm) as the internal standard. Temperature was controlled by a Bruker B-VT 2000 variable temperature unit. For spectra recorded at temperatures other than 300 K either tetramethylsilane or a residual "silicon grease" peak (^{1}H = 0.07 ppm) were used as internal references. ^{13}C NMR spectra were acquired on either a Bruker AC-200F (50 MHz) or a Bruker DPX-400 (100 MHz) spectrometer as stated and are reported as the fully decoupled spectra assigned with the aid of DEPT analysis.

Matrix assisted laser desorption ionisation time of flight (MALDI-TOF) mass spectra were recorded on a VG TofSpec spectrometer. For most porphyrins under study, no matrix was required but when necessary α-cyano-4-hydroxycinnamic acid was used as the matrix. Mass spectra were obtained as an envelope of the isotope peaks of the molecular ion. The mass corresponding to the envelope's maximum is reported and was compared with the maximum of a simulated spectrum. Electrospray ionisation (ESI) mass spectra were recorded on a ThermoQuest Finnigan LCQ Deca mass spectrometer. High resolution fast atomic bombardment (HRFAB) mass spectra were acquired at the Research School of Chemistry, Australian National University. The HRFAB mass spectra were obtained as an envelope of the isotope peaks of the molecular ion and calibrated against an external CsI standard. For heavy molecules (> 2000 amu) the mass of individual peaks in the envelope were reported and compared to a simulated spectrum. Fourier transform matrix assisted laser desorption ionisation time of flight (FT-MALDI-TOF) were acquired at the School of Chemistry, The University of New South Wales.

Column chromatography with flash silica was performed using Merck silica gel 60, Type 9385 (230–400 mesh) with the stated solvent systems. Analytical thin layer chromatography (TLC) was performed on Merck silica gel 60 F_{254} precoated sheets (0.2 mm) in the stated solvents. Preparative TLC plates (1 mm thick) were prepared from a slurry of Merck silica gel 60, Type 7747 in water according to instructions from the manufacturer. Alumina refers to Merck aluminium oxide 90 active neutral I, Type 1077 (63–200 mesh). Class IV alumina refers to the water content (10% water added).[31] Analytical alumina TLC was performed on Merck alumina 60 F_{254} precoated sheets (0.2 mm) in the stated solvents. Size-exclusion chromatography was conducted using gravity feed columns containing BioBeads (S–X1 polystyrene based size-exclusion particles) using toluene as the eluent. Analytical high performance liquid chromatography (HPLC) was performed with a Waters 510EF pump, U6K injector and a 490E multiwavelength detector (set at wavelengths 280 and 428 nm) controlled by Millennium software. The column used was Zorbax RX-SIL (4.6 mm id × 250 mm) eluting at a rate of 1.5 cm^3 min^{-1} in the stated solvent systems. Preparative HPLC was performed with a Waters 510EF pump, U6K injector, a Waters 481 ultraviolet detector (set at a wavelength of 280 nm) and a Waters R403 refractive index detector. The columns used were either a Whatman Partisil M20 10/50 (22 mm id × 50 mm) or Zorbax RX-SIL (21.2 mm id × 25 mm, 7 μm particle size).

The solvent systems used were as stated eluting at a rate of 13.5 cm^3 min^{-1}.

Light petroleum refers to the fraction of bp 60–80 °C. Chloroform and dichloromethane were typically distilled from potassium carbonate prior to use as HPLC solvents. Other chemicals were used as obtained from commercial sources.

The synthesis of [5,5′,10,10′,15,15′,20,20′-octakis(3,5-di-*tert*-butylphenyl)-1″,4″,6″,9″-tetraazaanthraceno[2,3-*b*:2′,3′-*e*]-bisporphyrinato]dizinc(II) **14** was carried out according to a previously published procedure.[26]

Synthesis and separation of [2-nitro-5,10,15,20-[pyromellitoyl-(tetrakis-*o*-oxyethoxyphenyl)]porphyrinato]zinc(II) 3 and [7-nitro-5,10,15,20-[pyromellitoyl(tetrakis-*o*-oxyethoxy-phenyl)]chlorinato]zinc(II) 4 mixture

Starting from C_2-capped porphyrin[20,21,32] **1** the mixture of the two isomeric zinc(II) nitro-C_2-capped porphyrins **3** and **4** was obtained in 94% yield following the method of Baldwin and co-workers.[20,21,24,25] The crude mixture of the two isomeric zinc(II) nitro-C_2-capped porphyrins **3** and **4** (260 mg) was separated by preparative HPLC (toluene–ethyl acetate; 17 : 3).[25] The combined less polar fractions were evaporated to give **4** (92 mg, 71% recovered of this isomer) which co-chromatographed with an authentic sample and had an identical ^{1}H NMR spectrum to that reported in the literature.[25] The combined more polar fractions were evaporated to give **3** (100 mg, 77% recovered of this isomer) which co-chromatographed with an authentic sample and had an identical ^{1}H NMR spectrum to that reported in the literature.[25]

Synthesis and separation of [2,3-dioxo-5,10,15,20-[pyromellitoyl-(tetrakis-*o*-oxyethoxyphenyl)]chlorinato]zinc(II) 7 and [7,8-dioxo-5,10,15,20-[pyromellitoyl(tetrakis-*o*-oxyethoxy-phenyl)]chlorinato]zinc(II) 8 mixture

Method 1. A mixture of **3** and **4** (389 mg, 0.340 mmol) was dissolved in a mixture of dry dichloromethane (40 cm^3) and dry methanol (30 cm^3) under an argon atmosphere in a round bottom flask (100 cm^3) shielded from light. The solution was purged with argon for 20 min and then 10% palladium on carbon (281 mg) was added. Sodium borohydride (305 mg, 8.06 mmol) was added in portions over 5 min. The reaction mixture was stirred and monitored by TLC analysis (the product appeared as a reddish spot just underneath the green starting material). After 7 min, when all the starting material had been consumed, the mixture was filtered through a small plug of celite and the filtrate evaporated to dryness. The resultant solid was dissolved in dichloromethane (100 cm^3) and then washed with water (100 cm^3). The aqueous layer was extracted with dichloromethane (2 × 30 cm^3) and the combined organic layers were dried over anhydrous sodium sulfate and filtered to yield the crude mixture of **5** and **6**. [This compound was unstable and converted slowly to **7** and **8** upon standing. A reasonably pure sample of the mixture of zinc(II) 2- and 7-amino-C_2-capped porphyrins **5** and **6** was obtained by column chromatography over flash silica (dichloromethane–methanol; 100 : 1) to give a dark green-purple solid, mp > 300 °C. ν_{max} ($CHCl_3$)/cm^{-1} 3389, 3013, 2931, 2872, 1731, 1614w, 1578, 1490, 1443, 1378, 1337, 1320, 1284 and 1243; λ_{max} ($CHCl_3$)/nm 407.5sh (log ε 4.94), 423 (5.19), 473.5 (4.16), 553 (3.95), 603 (3.66) and 653 (3.52); *m*/*z* (MALDI-TOF) 1114.3 (simulated maximum requires 1114.7).

The mixture of **5** and **6** was immediately diluted with dichloromethane (to 250 cm^3) and photo-oxidised. The reaction was monitored by TLC analysis. Rose Bengal (5 mg) was added to the solution and after 1 h more Rose Bengal (5 mg) was added. After 2.5 h, no starting material remained and the solvent was removed under vacuum and the residue purified by column chromatography over flash silica (dichloromethane–methanol; 100 : 0.75). The main fraction yielded a mixture (310 mg) of the products **7** and **8** [267 mg, 69% (yield calculated for conversion from a mixture of **3** and **4**)] contaminated with porphyrin **2** (15%) as a dark brown–green–purple solid, mp > 300 °C. The ^{1}H NMR spectrum showed a 1 : 1 mixture of **7** and **8**.

A portion of the crude mixture of **7** and **8** (54 mg) was separated by preparative HPLC (dichloromethane–methanol; 100 : 0.5). Samples (25–30 mg) of the above mixture in chloroform (1.0 cm^3) were applied to the column. A less polar fraction (R_t = 16–21 min) and a more polar fraction (R_t = 30–54 min) was collected.

The combined less polar fractions (which have a bronze hue) yielded **8** (17.6 mg, 65% recovery of this isomer) as a brown–red–purple solid, mp > 300 °C (Found: C, 64.2; H, 3.45; N, 4.7. $C_{62}H_{40}N_4O_{14}Zn$ + 0.5 CH_2Cl_2 requires C, 64.0; H, 3.5; N, 4.8%); ν_{max} ($CHCl_3$)/cm^{-1} 2931, 2849, 1731, 1602, 1578, 1490, 1443, 1337, 1284 and 1243; λ_{max} ($CHCl_3$)/nm 416.5 (log ε 5.14), 493 (4.28), 613.5sh (3.51), 638.5sh (3.68) and 713.5 (3.75); δ_H (400 MHz, $CDCl_3$) 3.84 (2 H, ddd, *J* = 11.5, 6.1 and 2.2, CH_2), 4.06–4.45 (12 H, m, CH_2), 4.64–4.72 (2 H, m, CH_2), 5.81 (2 H, s, capping H), 7.24 (2 H, ddd, *J* 7.5, 7.4 and 0.8, Ar–H_5), 7.31 (2 H, dd, *J* 8.0 and 0.9, Ar–H_3), 7.35 (2 H, ddd, *J* 7.5, 7.4 and 0.8, Ar–H_5), 7.42 (2 H, dd, *J* 8.4 and 0.8, Ar–H_3), 7.46 (2 H, dd, *J* 7.5 and 1.6, Ar–H_6), 7.66 (2 H, ddd, *J* 8.4, 7.4 and 1.6, Ar–H_4), 7.72 (2 H, ddd, *J* 8.0, 7.4 and 1.7, Ar–H_4), 7.80 (2 H, dd, *J* 7.5 and 1.7, Ar–H_6), 8.30 and 8.48 (4 H, ABq, *J* 4.7, β-pyrrolic H-2, H-3, H-12 and H-13) and 8.40 (2 H, s, β-pyrrolic H-17 and H-18); δ_C (100 MHz, $CDCl_3$) 62.68 (4 × CH_2), 66.46 (2 × CH_2), 68.20 (2 × CH_2), 110.12 (2 × *meso*-C), 113.32 (2 × Ar–CH), 116.54 (2 × Ar–CH), 120.88 (2 × Ar–CH), 121.49 (2 × Ar–CH), 122.39 (2 × *meso*-C), 127.19 (2 × capping Ar–CH), 129.47 (2 × Ar–CH), 130.13 (2 × Ar–CH), 130.19 (2 × β-pyrrolic CH), 131.19 (2 × β-pyrrolic CH), 131.30 (2 × Ar–C), 130.51 (2 × Ar–C), 131.82 (2 × α-pyrrolic C), 131.89 (2 × β-pyrrolic CH), 133.92 (2 × capping Ar–C), 135.27 (2 × Ar–CH), 135.59 (2 × Ar–CH), 138.17 (2 × capping Ar–C), 149.16 (2 × α-pyrrolic C), 150.44 (2 × α-pyrrolic C), 154.14 (2 × α-pyrrolic C), 157.36 (2 × Ar–C), 157.38 (2 × Ar–C), 163.52 (4 × C=O) and 188.03 (2 × β-pyrrolic C-7 and C-8); *m*/*z* (FT-MALDI-TOF) 1129.36 (simulated maximum requires 1129.3); *m*/*z* (MALDI-TOF) 1129.9 (simulated maximum requires 1129.3); *m*/*z* (ESI) 1151.0 ($M(Zn^{64})^+ + Na^+$ requires 1151.2), 1130.0 ($M(Zn^{66})^+$ requires 1130.2).

The combined more polar fractions (which have a brown hue) yielded **7** (20.4 mg, 76% recovery of this isomer) as a brown–green–purple solid, mp > 300 °C (Found: C, 65.7; H, 3.4; N, 5.05. $C_{62}H_{40}N_4O_{14}Zn$ requires C, 65.9; H, 3.6; N, 5.0%); ν_{max} ($CHCl_3$)/cm^{-1} 2932, 2851, 1726, 1601, 1581, 1490, 1445, 1339, 1264 and 1244; λ_{max} ($CHCl_3$)/nm 417 (log ε 5.12), 501 (4.30), 605.5sh (3.34), 652.5sh (3.53) and 735 (3.76); δ_H (400 MHz, $CDCl_3$) 3.85–3.93 (2 H, m, CH_2), 4.08–4.45 (14 H, m, CH_2), 5.82 (1 H, s, capping H), 6.37 (1 H, s, capping H), 7.24 (2 H, ddd, *J* 7.6, 7.4 and 0.8, Ar–H_5), 7.34 (2 H, ddd, *J* 7.6, 7.4 and 0.9, Ar–H_5), 7.40 (2 H, dd, *J* 8.7 and 0.8, Ar–H_3), 7.43 (2 H, dd, *J* 8.8 and 0.9, Ar–H_3), 7.47 (2 H, dd, *J* 7.4 and 1.6, Ar–H_6), 7.67 (2 H, ddd, *J* 8.8, 7.4 and 1.8, Ar–H_4), 7.72 (2 H, ddd, *J* 8.7, 7.4 and 1.6, Ar–H_4), 7.74 (2 H, dd, *J* 7.6 and 1.8, Ar–H_6), 8.26 and 8.45 (4 H, ABq, *J* 4.7, β-pyrrolic H-7, H-8, H-17 and H-18) and 8.33 (2 H, s, β-pyrrolic H-12 and H-13); δ_C (100 MHz, $CDCl_3$) 62.80 (2 × CH_2), 63.27 (CH_2), 63.46 (CH_2), 67.38 (2 × CH_2), 68.46 (2 × CH_2), 110.80 (2 × *meso*-C), 115.44 (2 × Ar–CH), 116.40 (2 × Ar–CH), 121.45 (2 × Ar–CH), 121.70 (2 × Ar–CH), 122.54 (2 × *meso*-C), 126.84 (capping Ar–CH), 127.51 (capping Ar–CH), 129.17 (2 × Ar–C), 129.76 (2 × Ar–CH), 130.23 (2 × Ar–CH), 130.47 (2 × β-pyrrolic CH), 130.65 (2 × β-pyrrolic CH), 131.52 (2 × Ar–C), 132.02 (2 × α-pyrrolic C), 132.70 (2 × β-pyrrolic CH), 133.44 (2 × capping Ar–C), 134.36 (2 × Ar–CH),135.70 (2 × Ar–CH), 137.90 (2 × capping Ar–C), 149.30 (2 × α-pyrrolic C), 150.42 (2 × α-pyrrolic C), 154.39 (2 × α-pyrrolic C), 157.24 (2 × Ar–C), 157.35 (2 × Ar–C), 163.04 (2 × C=O), 163.89 (2 × C=O) and 188.77 (2 ×

β-pyrrolic C-2 and C-3); *m*/*z* (FT-MALDI-TOF) 1130.37 (simulated maximum requires 1129.3); *m*/*z* (MALDI-TOF) 1129.7 (simulated maximum requires 1129.3); *m*/*z* (ESI) 1130.9 ($M(Zn^{66})^+$ requires 1130.2), 1128.7 and 1128.0 ($M(Zn^{64})^+$ requires 1128.2).

Method 2 for the synthesis of 8. Porphyrin **4** (62 mg, 0.054 mol) was reduced to give crude **6** using sodium borohydride as in Method 1 and **6** was then immediately dissolved in dichloromethane (300 cm^3) and photo-oxidised. The reaction was monitored by TLC analysis and after 3 h when no starting material remained, the solvent was removed. The residue was purified by two preparative TLC plates (20 cm × 20 cm × 1 mm) using toluene–ethyl acetate (7 : 3) as the solvent system. Dichloromethane–methanol (100 : 3) was used to extract the compound from the silica. The main band yielded **8** [22 mg, 36% (yield calculated for conversion from **4**)], which co-chromatographed with and had identical spectroscopic properties to the compound obtained by Method 1.

Method 2 for the synthesis of 7. Porphyrin **3** (18 mg, 0.016 mol) was reduced to give crude **5** using sodium borohydride as in Method 1 and **5** was then immediately dissolved in dichloromethane (300 cm^3) and photo-oxidised. The reaction was monitored by TLC analysis and after 4 h when no starting material remained, the solvent was removed. The residue was purified by column chromatography over flash silica (ethyl acetate–toluene; 1 : 1) to yield zinc(II) C_2-capped porphyrin-2,3-dione **7** [8 mg, 45% (yield calculated for conversion from **3**)], which co-chromatographed with and had identical spectroscopic properties to the compound **7** obtained by Method 1.

Synthesis and separation of *syn*- and *anti*-[5,5′,10,10′,15,15′,-20,20′-di[pyromellitoyl(tetrakis-*o*-oxyethoxyphenyl)]-1″,4″,6″,9″-tetraazaanthraceno[2,3-*b*:2′,3′-*e*]bisporphyrinato]dizinc(II) 9 and 10

A flask containing a mixture of **7** (40 mg, 0.035 mmol) and 1,2,4,5-benzenetetramine tetrahydrochloride (6.8 mg, 0.024 mmol) under a nitrogen atmosphere was charged with dry pyridine (10 cm^3) which had previously been degassed with nitrogen by cannula. The reaction was shielded from light and the mixture heated at reflux for 3 days. The mixture was diluted with toluene (70 cm^3) and dichloromethane (20 cm^3) and the solvents removed. The crude residue was dissolved in toluene (100 cm^3) and the solvent removed again. Then the residue was dissolved in dichloromethane (75 cm^3), heated to reflux and a solution of zinc(II) acetate dihydrate (17 mg, 0.077 mmol) in methanol (15 cm^3) was added. The mixture was heated at reflux for 30 min. The solvents were removed and the residue was dissolved in a mixture of dichloromethane–methanol (9 : 1) and filtered through a plug of flash silica and the solvent removed. The crude mixture was purified by column chromatography over flash silica (chloroform changing to chloroform–methanol; 100 : 6) giving several fractions. The solvent was removed and the fractions purified by BioBeads size-exclusion chromatography (2.5 cm id × 90 cm, toluene) to give a crude mixture of *syn* and *anti* dizinc(II) bis(2,3-C_2-capped porphyrins) **9** and **10** (29 mg, 70%) as a dark brown-purple solid, mp > 300 °C. The ^{1}H NMR spectrum showed a 1 : 1 mixture of **9** and **10** (see below). *m*/*z* (MALDI-TOF) 2326.9 (simulated maximum requires 2326.5).

A portion of the mixture of **9** and **10** (2.86 mg) was separated by preparative HPLC (chloroform). The sample was dissolved in chloroform (1 cm^3) and prefiltered through a membrane filter (Millipore™, Type FH, 0.5 μm). The filtrate was applied to the column. A less polar fraction (R_t = 3.7–4 min) and a more polar fraction (R_t = 4–4.5 min) were collected. The precipitate collected on the membrane was washed off with chloroform and analysed by TLC and showed a major band of the less polar fraction with minor contamination of the more polar fraction. The washings were sonicated and then applied on the HPLC column as above.

The less polar fractions were evaporated to give the *anti*-isomer **10** (1.07 mg, 74% recovery of this isomer) as a brown–purple solid, mp > 300 °C. ν_{max} ($CHCl_3$)/cm^{-1} 3506, 2931, 2860, 1731, 1602, 1578, 1490, 1443, 1337, 1279 and 1243; λ_{max} ($CHCl_3$)/nm 426 (log ε 5.39), 457 (5.24), 515.5sh (4.68), 548 (4.70), 604.5sh (4.08) and 678.5 (4.16); δ_H (600 MHz, $CDCl_3$) 3.92–3.97 (8 H, m, CH_2), 4.30–4.38 (8 H, m, CH_2), 4.40–4.45 (4 H, m, CH_2), 4.45–4.50 (4 H, m, CH_2), 4.51–4.55 (4 H, m, CH_2), 4.60–4.65 (4 H, m, CH_2), 5.59 (2 H, s, capping H), 5.62 (2 H, s, capping H), 7.41 (4 H, ddd, *J* 7.3, 7.2 and 0.8, Ar–H_5 at $C_{10,15}$), 7.49 (4 H, ddd, *J* 7.7, 7.1 and 0.6, Ar–H_5 at $C_{5,20}$), 7.58 (4 H, dd, *J* 8.7 and 0.8, Ar–H_3 at $C_{10,15}$), 7.72 (4 H, dd, *J* 7.1 and 1.5, Ar–H_6 at $C_{5,20}$), 7.81 (4 H, ddd, *J* 8.7, 7.3 and 1.6, Ar–H_4 at $C_{10,15}$), 7.85 (4 H, dd, *J* 7.2 and 1.6, Ar–H_6 at $C_{10,15}$), 7.87 (4 H, dd, *J* 8.7 and 0.6, Ar–H_3 at $C_{5,20}$), 8.13 (4 H, ddd, *J* 8.7, 7.7 and 1.5, Ar–H_4 at $C_{5,20}$), 8.72 (4 H, s, β-pyrrolic H-12 and H-13), 8.84 (2 H, s, bridging H-5″ and H-10″), 8.90 and 8.98 (8 H, ABq, *J* 4.5, β-pyrrolic H-7, H-8, H-17 and H-18); *m*/*z* (LRFAB) 2326.6 (simulated maximum requires 2326.5); *m*/*z* (MALDI-TOF) 2327.3 (simulated maximum requires 2326.5).

The more polar fractions were evaporated to give the *syn*-isomer **9** (1.15 mg, 80% recovery of this isomer) as a red–purple solid, mp > 300 °C (Found: C, 66.15; H, 3.65; N, 6.9. $C_{130}H_{82}N_{12}O_{16}Zn_2$ + 0.5 CH_2Cl_2 requires C, 66.15; H, 3.5; N, 7.1%); ν_{max} ($CHCl_3$)/cm^{-1} 3433, 2925, 2852, 1730, 1600, 1491, 1455, 1278 and 1237; λ_{max} ($CHCl_3$)/nm 427.5 (log ε 5.44), 459.5 (5.32), 495sh (4.58), 539.5 (4.71), 614sh (4.16), 678.5 (4.23) and 681 (4.23); δ_H (600 MHz, $CDCl_3$) 3.92–3.98 (8 H, m, CH_2), 4.29–4.37 (8 H, m, CH_2), 4.45–4.55 (12 H, m, CH_2), 4.60–4.64 (4 H, m, CH_2), 5.61 (4 H, s, capping H), 7.41 (4 H, ddd, *J* 7.8, 7.1 and 0.9, Ar–H_5 at $C_{10,15}$), 7.49 (4 H, ddd, *J* 7.7, 7.1 and 0.9, Ar–H_5 at $C_{5,20}$), 7.57 (4 H, dd, *J* 8.7 and 0.9, Ar–H_3 at $C_{10,15}$), 7.71 (4 H, dd, *J* 7.1 and 1.6, Ar–H_6 at $C_{5,20}$), 7.80 (4 H, ddd, *J* 8.7, 7.8 and 1.6, Ar–H_4 at $C_{10,15}$), 7.85 (4 H, dd, *J* 7.1 and 1.6, Ar–H_6 at $C_{10,15}$), 7.87 (4 H, dd, *J* 8.8 and 0.9, Ar–H_3 at $C_{5,20}$), 8.14 (4 H, ddd, *J* 8.8, 7.7 and 1.6, Ar–H_4 at $C_{5,20}$), 8.72 (2 H, s, β-pyrrolic H-12 and H-13), 8.83 (2 H, s, bridging H-5″ and H-10″), 8.89 and 8.97 (8 H, ABq, *J* 4.4, β-pyrrolic H-7, H-8, H-17 and H-18); *m*/*z* (HRFAB) Envelope (M^+ requires): 2322.45/22% (2322.42/33%), 2323.45/48 (2323.418/50), 2324.47/60 (2324.416/80), 2325.45/80 (2325.417/89), 2326.46/90 (2326.416/100), 2327.45/100 (2327.416/94), 2328.46/98 (2328.416/80), 2329.46/67 (2329.416/60), 2330.46/49 (2330.416/40) and 2331.44/29 (2331.416/29); *m*/*z* (ESI) 2326.4 (simulated maximum requires 2326.5); *m*/*z* (MALDI-TOF) 2326.7 (simulated maximum requires 2326.5).

Synthesis and separation of *syn*- and *anti*-[5,5′,10,10′,15,15′,-20,20′-di[pyromellitoyl(tetrakis-*o*-oxyethoxyphenyl)]-1″,4″,6″,9″-tetraazaanthraceno[7,8-*b*:7′,8′-*e*]bisporphyrinato]dizinc(II) 11 and 12

A flask containing a mixture of **8** (52 mg, 0.046 mmol) and 1,2,4,5-benzenetetramine tetrahydrochloride (9.2 mg, 0.032 mmol) under a nitrogen atmosphere was charged by cannula with dry pyridine (10 cm^3) which had previously been degassed with nitrogen. The reaction was shielded from light and the mixture heated at reflux for 2 days. The mixture was then diluted with toluene (70 cm^3) and dichloromethane (20 cm^3) and the solvents removed. The crude residue was dissolved in toluene (50 cm^3) and the solvent removed again. The residue was dissolved in dichloromethane (50 cm^3) and a solution of zinc(II) acetate dihydrate (26 mg, 0.118 mmol) in methanol (15 cm^3) was added and the mixture heated at reflux for 30 min. The crude product obtained from evaporation of the solvent was purified by BioBeads size-exclusion chromatography (2.5 cm id

× 90 cm, toluene). The front-running main fraction was collected. A considerable amount of material had precipitated at the top of the BioBeads column. The top 5 cm of the BioBeads was carefully removed and extracted with toluene and chloroform. Filtration and evaporation of the solvent yielded a solid which was purified by column chromatography over flash silica (chloroform–methanol; 100 : 1). One main fraction was collected. The crude residue was rechromatographed over BioBeads size-exclusion chromatography (2.5 cm id × 90 cm, toluene) and the main front-running band combined with the previously obtained fraction to yield a crude mixture of **11** and **12** (23 mg, 42%) as a dark brown–purple solid, mp > 300 °C. The ^{1}H NMR spectrum showed a 1:1 mixture of **11** and **12**. *m*/*z* (MALDI-TOF) 2326.9 (simulated maximum requires 2326.5).

A portion of the mixture of **11** and **12** (20.3 mg) was separated by preparative HPLC (chloroform–dichloromethane; 1 : 1). Samples (2.5–3 mg) of the above mixture in chloroform (1.0 cm^3) were applied to the column. A less polar fraction (R_t = 6–7 min) and a more polar fraction (R_t = 8–9 min) was collected.

The less polar fractions were evaporated to give the *anti*-isomer **12** (9.25 mg, 91% recovery of this isomer) as a brown–purple solid, mp > 300 °C (Found: C, 63.1; H, 3.85; N, 6.2. $C_{130}H_{82}N_{12}O_{16}Zn_2$ + 2 CH_2Cl_2 requires C, 63.5; H, 3.5; N, 6.7%); ν_{max} ($CHCl_3$)/cm^{-1} 3600, 2931, 2861, 1731, 1602, 1578, 1490, 1443, 1337, 1279 and 1243; λ_{max} ($CHCl_3$)/nm 425.5 (log ε 5.36), 456 (5.23), 521sh (4.70), 538.5 (4.71), 624.5 (4.28) and 666 (4.32); δ_H (600 MHz, $CDCl_3$) 3.82–3.86 (4 H, m, CH_2), 3.91–3.98 (8 H, m, CH_2), 4.28–4.37 (16 H, m, CH_2), 4.46–4.50 (4 H, m, CH_2), 5.69 (4 H, s, capping H), 7.43 (4 H, ddd, *J* 7.6, 7.1 and 0.9, Ar–H_5 at $C_{15,20}$), 7.54 (4 H, dd, *J* 8.7 and 0.9, Ar–H_3 at $C_{15,20}$), 7.61 (4 H, ddd, *J* 7.7, 7.0 and 0.8, Ar–H_5 at $C_{5,10}$), 7.66 (4 H, dd, *J* 8.7 and 0.8, Ar–H_3 at $C_{5,10}$), 7.81 (4 H, ddd, *J* 8.7, 7.6 and 1.5, Ar–H_4 at $C_{15,20}$), 7.92 (4 H, dd, *J* 7.0 and 1.6, Ar–H_6 at $C_{5,10}$), 7.93 (4 H, dd, *J* 7.1 and 1.5, Ar–H_6 at $C_{15,20}$), 8.13 (4 H, ddd, *J* 8.7, 7.7 and 1.6, Ar–H_4 at $C_{5,10}$), 8.75 (4 H, s, β-pyrrolic H-17 and H-18), 8.84 (2 H, s, bridging H-5″ and H-10″), 8.87 and 8.96 (8 H, ABq, *J* 4.4, β-pyrrolic H-2, H-3, H-12 and H-13); *m*/*z* (HRFAB) Envelope (M^+ requires): 2323.49/43% (2323.418/50%), 2324.49/50 (2324.416/80), 2325.44/52 (2325.417/89), 2326.49/90 (2326.416/100), 2327.49/100 (2327.416/94), 2328.52/76 (2328.416/80), 2329.49/64 (2329.416/60), 2330.48/38 (2330.416/40) and 2331.53/32 (2331.416/29); *m*/*z* (FT-MALDI-TOF) 2327.85 (simulated maximum requires 2326.5); *m*/*z* (MALDI-TOF) 2326.3 (simulated maximum requires 2326.5).

The more polar fractions were evaporated to give the *syn*-isomer **11** (10.0 mg, 98% recovery of this isomer) as a red–purple solid, mp > 300 °C (Found: C, 65.9; H, 3.9; N, 6.9. $C_{130}H_{82}N_{12}O_{16}Zn_2$ + 0.5 $CHCl_3$ requires C, 65.7; H, 3.5; N, 7.1%); ν_{max} ($CHCl_3$)/cm^{-1} 3601, 2954, 2931, 2872, 1731, 1602, 1578, 1490, 1443, 1337, 1284 and 1243; λ_{max} ($CHCl_3$)/nm 425.5 (log ε 5.52), 455.5 (5.40), 511.5sh (4.74), 533.5 (4.77), 624sh (4.16) and 666 (4.28); δ_H (600 MHz, $CDCl_3$) 3.86–3.91 (4 H, m, CH_2), 3.95–4.00 (4 H, m, CH_2), 4.17–4.24 (4 H, m, CH_2), 4.30–4.35 (4 H, m, CH_2), 4.37–4.48 (8 H, m, CH_2), 4.48–4.54 (4 H, m, CH_2), 5.70 (4 H, s, capping H), 7.43 (4 H, ddd, *J* 7.7, 7.1 and 1.0, Ar–H_5 at $C_{15,20}$), 7.54 (4 H, ddd, *J* 7.7, 7.1 and 0.9, Ar–H_5 at $C_{5,10}$), 7.55 (4 H, dd, *J* 8.8 and 1.0, Ar–H_3 at $C_{15,20}$), 7.73 (4 H, dd, *J* 8.8 and 0.9, Ar–H_3 at $C_{5,10}$), 7.81 (4 H, ddd, *J* 8.8, 7.7 and 1.6, Ar–H_4 at $C_{15,20}$), 7.83 (4 H, dd, *J* 7.1 and 1.6, Ar–H_6 at $C_{5,10}$), 7.92 (4 H, dd, *J* 7.1 and 1.6, Ar–H_6 at $H_{15,20}$), 8.11 (4 H, ddd, *J* 8.8, 7.7 and 1.6, Ar–H_4 at $C_{5,10}$), 8.75 (4 H, s, β-pyrrolic H-17 and H-18), 8.81 (2 H, s, bridging H-5″ and H-10″), 8.87 and 8.96 (8 H, ABq, *J* 4.4, β-pyrrolic H-2, H-3, H-12 and H-13); *m*/*z* (HRFAB) Envelope (M^+ requires): 2322.37/24% (2322.42/33%), 2323.36/50 (2323.418/50), 2324.38/72 (2324.416/80), 2325.37/86 (2325.417/89), 2326.37/98 (2326.416/100), 2327.37/100 (2327.416/94), 2328.36/89 (2328.416/80), 2329.37/78 (2329.416/60), 2330.36/58 (2330.416/40), 2331.36/29 (2331.416/29) and 2332.36/22 (2332.42/16); *m*/*z* (FT-MALDI-TOF) 2327.86 (simulated maximum requires 2326.5); *m*/*z* (MALDI-TOF) 2326.5 (simulated maximum requires 2326.5).

Synthesis of [2,3-dioxo-5,10,15,20-tetrakis(3,5-di-*tert*-butylphenyl)chlorinato]zinc(II) 13

A mixture of 2,3-dioxo-5,10,15,20-tetrakis(3,5-di-*tert*-butylphenyl)chlorin[29] (317 mg, 0.290 mmol) and zinc(II) acetate dihydrate (291 mg, 1.33 mmol) in dichloromethane (250 cm^3) and methanol (20 cm^3) was heated at reflux for 3 h. The solvent was removed and the residue purified by column chromatography over flash silica (dichloromethane–light petroleum; 1 : 2 changing to 1 : 1) to yield [2,3-dioxo-5,10,15,20-tetrakis(3,5-di-*tert*-butylphenyl)chlorinato]zinc(II) (zinc(II) porphyrin-dione) **13** (270 mg, 80%) as a green–grey solid, mp > 300 °C. δ_H (400 MHz, $CDCl_3$) 1.44 (36 H, s, *t*-butyl H), 1.48 (36 H, s, *t*-butyl H), 7.63 (4 H, d, *J* 1.8, Ar–H_o at $C_{5,20}$), 7.69 (2 H, t, *J* 1.8, Ar–H_p at $C_{5,20}$), 7.73 (2 H, t, *J* 1.8, Ar–H_p at $C_{10,15}$), 7.90 (4 H, d, *J* 1.8, Ar–H_o at $C_{10,15}$), 8.32 and 8.58 (4 H, ABq, *J* 4.7, β-pyrrolic H-7, H-8, H-17 and H-18) and 8.50 (2 H, s, β-pyrrolic H-12 and H-13); *m*/*z* (MALDI-TOF) 1159.3 (M^+ requires 1157.0).

Synthesis of {5,10,15,20-[pyromellitoyl(tetrakis-*o*-oxyethoxyphenyl)]-6′,7′-diaminoquinoxalino[7,8-*b*]porphyrinato}zinc(II) 17

A flask containing a mixture of zinc(II) C_2-capped porphyrin-7,8-dione **8** (20 mg, 0.018 mmol) and 1,2,4,5-benzenetetramine tetrahydrochloride (31 mg, 0.11 mmol) under a nitrogen atmosphere was charged by cannula with dry pyridine (50 cm^3) which had previously been degassed with nitrogen. The reaction was shielded from light and the mixture heated at reflux for 20 h. The mixture was cooled and diluted with dichloromethane (50 cm^3) and water (250 cm^3). The aqueous phase was extracted with dichloromethane (2 × 25 cm^3). The combined organic extracts were washed with water (3 × 250 cm^3), dried over anhydrous sodium sulfate and evaporated to dryness. The residue was dissolved in toluene (50 cm^3) and the solvent removed again. The residue was dissolved in dichloromethane (75 cm^3) and a solution of zinc(II) acetate dihydrate (16 mg, 0.073 mmol) in methanol (20 cm^3) was added and the mixture heated at reflux for 1 h. The crude product obtained from evaporation of the solvent was purified by column chromatography over flash silica (dichloromethane–methanol; 100 : 0.8 changing to 100 : 4). The main fraction yielded crude {5,10,15,20-[pyromellitoyl-(tetrakis-*o*-oxyethoxyphenyl)]-6′,7′-diaminoquinoxalino-[7,8-*b*]porphyrinato}zinc(II) [zinc(II) C_2-capped 6′,7′-diaminoquinoxalino-porphyrin] **17** (14 mg, 66%) as a dark purple solid, mp > 300 °C. δ_H (400 MHz, $CDCl_3$) 2.60–3.00 (4 H, br s, NH_2 protons), 3.76–3.85 (4 H, m, CH_2), 3.86–3.96 (4 H, m, CH_2), 4.25–4.41 (8 H, m, CH_2), 4.44–4.56 (4 H, m, CH_2), 5.57 (2 H, s, capping H), 6.51 (2 H, s, quinoxalino H), 7.36 (2 H, dd, *J* 7.6 and 1, Ar–H), 7.39–7.46 (2 H, m, Ar–H), 7.55 (2 H, dd, *J* 8.3 and 1.0, Ar–H), 7.70 (2 H, dd, *J* 6.9 and 1.0, Ar–H), 7.72–7.83 (6 H, m, Ar–H), 8.74 (2 H, s, β-pyrrolic H-17 and H-18), 8.77 and 8.82 (4 H, ABq, *J* 4.6, β-pyrrolic H-2, H-3, H-12 and H-13).

Exemplary procedure for self-replication studies

The chloroform used in this experiment had been dried and deacidified by filtering the solvent through a plug of alumina and then purged with argon for at least 10 min. Zinc(II) C_2-capped porphyrin-7,8-dione **8** (13.4 mg, 0.0118 mmol) and zinc(II) C_2-capped 6′,7′-diaminoquinoxalino-porphyrin **17** (14.4 mg, 0.0117 mmol) were dissolved in chloroform (7.0 cm^3). A portion (1 cm^3) of the stock solution was then added to seven small (5–10 cm^3) round-bottom flasks labelled no. 1–7. A solution of 1,3-bis(4-pyridyl)propane **16** (8.9 mg, 0.0449 mmol) in chloroform (1.02 cm^3) was prepared and aliquots (0.038 cm^3,

0.0017 mmol) were added to flasks no. 1, 2, 3 and 5. A solution of pyridine (0.007 cm^3, 0.0865 mmol) in chloroform (1.00 cm^3) was prepared and a portion of that solution (0.020 cm^3, 0.0017 mmol) was added to flask no. 4. *anti* Dizinc(II) bis(7,8-C_2-capped porphyrin) **12** (0.9 mg, 0.0004 mmol) was then added to flask no. 1. *syn* Dizinc(II) bis(2,3-C_2-capped porphyrin) **9** (0.99 mg, 0.0004 mmol) was added to flask no. 2. *syn* Dizinc(II) bis(7,8-C_2-capped porphyrin **11** (1.0 mg, 0.0004 mmol) was added to flask no. 3. To flasks no. 5 and 6, dizinc(II) bis-porphyrin **14** (0.9 mg, 0.0004 mmol) was added to each flask. After all the reagents had been added, chloroform was added to each flask so that the total volume was close to 1.2 cm^3. Argon was briefly blown over the solution and the flasks then stoppered with a septum and the solutions stirred in the dark. After 3 days, a 0.005 cm^3 aliquot was removed from each flask by a syringe and analysed by analytical HPLC (dichloromethane–methanol; 100 : 0.65). After 7 days, dichloromethane (20 cm^3) was added to each flask and a small aliquot (*ca.* 0.01 cm^3) of that solution analysed by analytical HPLC column as above. Each reaction mixture (no. 1–7) was then washed with aqueous hydrochloric acid (0.001 M, 30 cm^3), water (30 cm^3), dried over anhydrous sodium sulfate and evaporated to dryness. The crude residues were analysed by ^{1}H NMR spectroscopy. Each crude product mixture was then purified by BioBeads size-exclusion chromatography (1.5 cm id × 35 cm, toluene) to give two main fractions. The first main fraction, consisted mostly of the bis-porphyrin templates and products; *anti* dizinc(II) bis(7,8-C_2-capped porphyrin) **12**, *syn* dizinc(II) bis(7,8-C_2-capped porphyrin **11**, *syn* dizinc(II) bis(2,3-C_2-capped porphyrin) **9** and dizinc(II) bis-porphyrin **14** which were then analysed as above by analytical HPLC and ^{1}H NMR spectroscopy to determine their ratios. The second fraction was also analysed by ^{1}H NMR and consisted mostly of unreacted starting materials (monomers) **8** and **17**.

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References

1 N. Lahav, In *Biogenesis: Theories of Life's Origin*, Oxford University Press, New York, 1999.
2 G. von Kiedrowski, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 932–935.
3 T. Tjivikua, P. Ballester and J. Rebek Jr., *J. Am. Chem. Soc.*, 1990, **112**, 1249–1250.
4 J. S. Nowik, Q. Feng, T. Tjivikua, P. Ballester and J. Rebek Jr., *J. Am. Chem. Soc.*, 1991, **113**, 8831–8839.
5 G. von Kiedrowski, B. Wlotzka, J. Helbing, M. Matzen and S. Jordan, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 423–426.
6 C. Bohler, W. Bannwarth and P. L. Luisi, *Helv. Chim. Acta*, 1993, **76**, 2313–2320.
7 T. Li and K. C. Nicolaou, *Nature*, 1994, **369**, 218–221.
8 D. Sievers and G. von Kiedrowski, *Nature*, 1994, **369**, 221–224.
9 D. H. Lee, J. R. Granja, J. A. Martinez, K. Severin and M. R. Ghadiri, *Nature*, 1996, **382**, 525–528.
10 K. Severin, D. H. Lee, J. A. Martinez and M. R. Ghadiri, *Chem. Eur. J.*, 1997, **3**, 1017–1024.
11 B. Wang and I. O. Sutherland, *Chem. Commun.*, 1997, 1495–1496.
12 K. Severin, D. H. Lee, J. A. Martinez, M. Vieth and M. R. Ghadiri, *Angew. Chem., Int. Ed.*, 1998, **37**, 126–128.
13 D. Sievers and G. von Kiedrowski, *Chem. Eur. J.*, 1998, **4**, 629–641.
14 E. A. Wintner and J. Rebek Jr., *Acta Chem. Scand.*, 1996, **50**, 469–485.
15 S. Shinkai, M. Ikeda, A. Sugasaki and M. Takeuchi, *Acc. Chem. Res.*, 2001, **34**, 494–503.
16 S. Anderson, H. L. Anderson and J. K. M. Sanders, *Acc. Chem. Res.*, 1993, **26**, 469–475.
17 J. K. M. Sanders, in *Comprehensive Supramolecular Chemistry*, ed. J.-P. Sauvage and M. W. Hosseini, Oxford, 1996, Vol 9, pp. 131–164.
18 M. J. Crossley and P. Thordarson, *Angew. Chem., Int. Ed.*, 2002, **41**, 1709–1712.
19 P. Thordarson, A. Marquis and M. J. Crossley, unpublished results.
20 J. Almog, J. E. Baldwin, R. L. Dyer and M. Peters, *J. Am. Chem. Soc.*, 1975, **97**, 226–227.
21 J. Almog, J. E. Baldwin, M. J. Crossley, J. F. DeBernardis, R. L. Dyer, J. R. Huff and M. K. Peters, *Tetrahedron*, 1981, **37**, 3589–3601.
22 J. Almog, J. E. Baldwin and J. Huff, *J. Am. Chem. Soc.*, 1975, **97**, 227–228.
23 T. Hashimoto, R. L. Dyer, M. J. Crossley, J. E. Baldwin and F. Basolo, *J. Am. Chem. Soc.*, 1982, **104**, 2101–2109.
24 J. E. Baldwin and J. F. DeBernardis, *J. Org. Chem.*, 1977, **42**, 3986–3987.
25 J. E. Baldwin, M. J. Crossley and J. DeBernardis, *Tetrahedron*, 1982, **38**, 685–692.
26 M. J. Crossley and P. L. Burn, *J. Chem. Soc., Chem. Commun.*, 1987, 39–40.
27 M. J. Crossley, P. L. Burn, S. J. Langford, S. M. Pyke and A. G. Stark, *J. Chem. Soc., Chem. Commun.*, 1991, 1567–1568.
28 M. J. Crossley, L. J. Govenlock and J. K. Prashar, *J. Chem. Soc., Chem. Commun.*, 1995, 2379–2380.
29 M. J. Crossley and L. G. King, *J. Chem. Soc., Chem. Commun.*, 1984, 920–922.
30 Hyperchem 6.0, Hypercube Inc., Gainesville, FL, 2000.
31 A. I. Vogel, in *Vogel's Handbook of Practical Organic Chemistry*, ed. B. S. Furniss, A. J. Hannaford, P. W. G. Smith and A. R. Tatcher, Longman Scientific, London, 1989, pp. 199–208.
32 M. J. Crossley, P. Thordarson, J. P. Bannerman and P. J. Maynard, *J. Porphyrins Phthalocyanines*, 1998, **2**, 511–516.