Synthesis of Tetrameric and Hexameric *Cyclo*-Porphyrins

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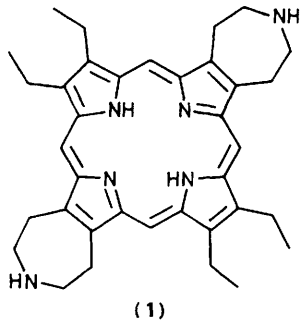
The synthesis of tetrameric and hexameric porphyrin derivatives is reported; these species can act as models of multi-tetrapyrrole aggregates in biological systems.

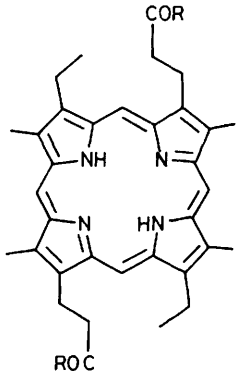
The enforced aggregation of several metal ions or prosthetic groups is an important device in biological structures for the formation of catalytically active centres. For instance, the bacterial photosynthetic reaction centre from *Rhodopseudomonas viridis* has recently been shown to contain six closely coupled tetrapyrroles (four bacteriochlorophyll and two bacteriopheophytin)[1] as the primary photoactive unit. Similarly cytochrome C_3 (ref. 2) and the cytochromes C553 and C558 in bacterial reaction centres[1] contain four interacting haem groups in close proximity to each other. In recent years there has been much interest in the preparation of synthetic models of these, and other, multicentre active sites.[3] The primary goals in these studies are to understand the unique properties of the aggregate above and beyond those of the monomeric unit and to develop synthetic catalysts for multi-electron- and photo-redox processes inspired by the biological system. Crucial to this is an understanding of the importance of distance, orientation, and number of the pigments in the aggregate. To this end a number of synthetic tetrapyrrole dimers[3a,4] and trimers[5] have been prepared.

We now report a new strategy for the construction of large, multi-tetrapyrrole species as models for biochemical aggregates. By using rigid and doubly functionalized porphyrin spacers we have prepared covalently linked tetrameric and hexameric porphyrin derivatives with an overall macrocyclic structure. This arrangement was chosen to provide (i) symmetrical structures in which all the porphyrins (and their chelated metals) can interact, (ii) a cavity at the centre of the model potentially capable of host–guest binding to organic substrates, and (iii) a contrast to the cofacial topology of earlier oligomers.[5b–d]

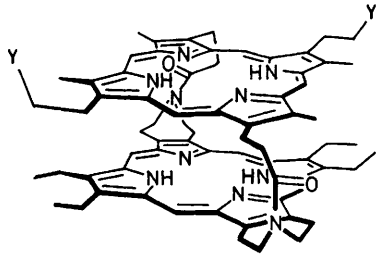
The key building blocks, porphyrin diamine (**1**),[4d] diacid (**2**),[6] and dimer diacid (**3a**)[5d] were prepared as previously described. Reaction of diacid (**2**) with oxalyl chloride (CH_2Cl_2) gave porphyrin diacid chloride (**4**) which was used without further purification. The macrocyclization of (**1**) and (**4**) was carried out under high-dilution conditions[7] (10^{-3} M, CH_2Cl_2, Et_3N) to encourage intramolecular condensation. The primary products in this reaction are expected to result from both 1 + 1 and 2 + 2 condensation; however, the formation of tetramer over dimer could be enhanced by careful control of the reactant concentrations. By maintaining an excess of diamine (**1**) (~2 equiv.) at the beginning of the reaction it was possible to promote formation of the intermediate trimeric diamine diamide and thus to favour the tetra-amide.† The tetrameric tetra-amide (**5**) was isolated by silica gel chromatography (CH_2Cl_2,MeOH) and recrystallization from methanol in 25% yield.‡ The structural assignment of (**5**) is based on its high resolution mass (M^+ + H, 2182.2650; $C_{140}H_{156}N_{20}O_4$ requires 2182.2696),§ ^{1}H n.m.r., and u.v.–visible spectra. In particular the ^{1}H n.m.r. spectrum of (**5**)



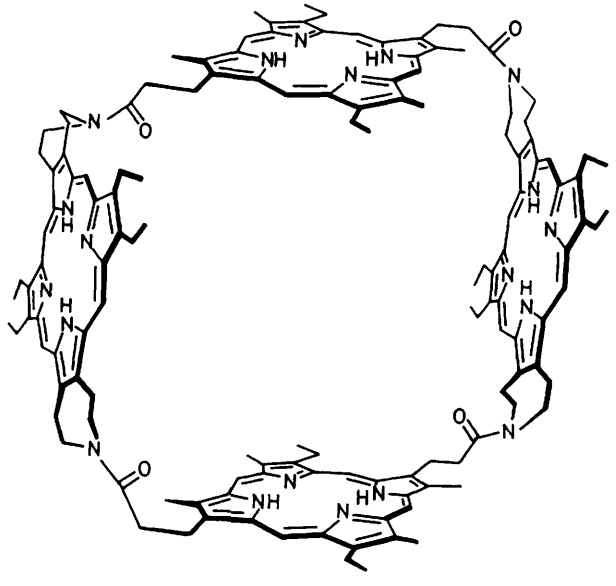
(**1**)



(**2**); R = OH
(**4**); R = Cl



(**3**) **a**; Y = CO_2H
b; Y = H



(**5**)

† An alternative strategy would be to mono-protect diamine (**1**).

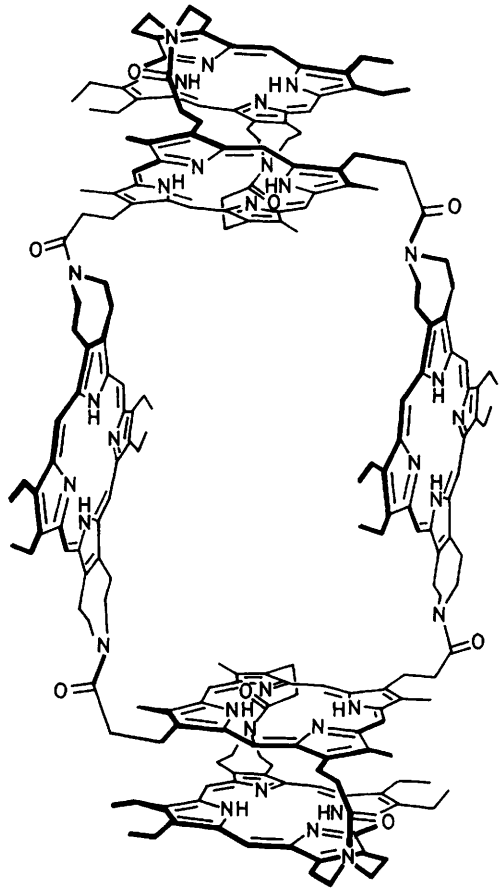
‡ The tetramer was easily separated from the cofacial dimeric product also formed in this reaction. The properties of this material are discussed in ref. 4d.

§ Fast atom bombardment mass spectrum at 8 keV accelerating voltage with triethanolamine as the matrix.

Table 1. U.v.–visible data for oligomeric porphyrins.

Porphyrin	$\lambda_{max.}$/nm(log ε) Soret (B)	Long wavelength (Q)
(**5**)	391 (5.97)	504 (4.90), 539 (4.81), 571 (4.71), 624 (4.47)
Zn_4 (**5**)	398 (6.06)	540 (4.91), 575 (4.97)
(**6**)	378 (6.08), 400 (sh)	503 (5.02), 537 (4.93), 570 (4.79), 624 (4.50)
Zn_6 (**6**)	386 (6.18), 402 (sh)	538 (5.17), 574 (5.23)
OEP[a]	398 (5.23)	497 (424), 538 (4.13), 566 (3.96), 619 (3.86)
Zn–OEP	400 (5.52)	531 (4.17), 568 (4.33)
(**3a**)	374 (5.68)	506 (4.47), 541 (4.32), 572 (4.25), 626 (4.02)
Zn_2 (**3a**)	386 (5.62)	538 (4.29), 573 (4.36)

[a] OEP = octaethylporphyrin.



(**6**)

clearly shows 8 NH protons as a broad singlet at δ −6.3. This falls midway between the NH chemical shifts for a monomeric porphyrin (δ *ca.* −3.8)[8] and a closely spaced cofacial porphyrin dimer (**3b**) (δ *ca.* −8).[4d] Similarly, the Soret absorbance of (**5**) at 391 nm is intermediate between that of a monomer (*ca.* 398 nm) and a cofacial dimer (*ca.* 374 nm[4d]) (Table 1).

Cyclo-porphyrin (**5**) is a large and somewhat flexible structure that can exist in a number of possible conformations. The upfield shift of the NH protons (~2.5 p.p.m.) and the blue shift of the Soret band (~7 nm) are comparable to those of a cofacially linked dimer with an interplane separation of 6 Å.[9] This suggests that in chloroform the central cavity in (**5**) has collapsed to a 'folded' or rhombohedral structure in which the two pairs of adjacent rings closely interact. *Cyclo*-porphyrin (**5**) will also show diastereoisomerism due to the two opposite porphyrins derived from (**2**) (with C_{2h} symmetry) taking up a *syn* (as shown) or *anti* (by rotating one of these by 180° relative to the other three) relationship.¶ The barrier to ring rotation, and thus diastereoisomer interconversion, is likely to be high in the folded form. Further stereoisomers will result from restricted rotation of the four amide bonds. The relative orientations of the C=O groups in a cofacial dimer have already been shown to lead to different conformations.[4d] In *cyclo*-porphyrin (**5**) the different stereoisomers lead to a complex ^{1}H n.m.r. spectrum, particularly in the CH_2 and CH_3 regions which show broad resonances at δ 1—1.8 and 3—4.5.** However, that these different stereoisomers have very similar (folded) conformations is seen by the single NH signal at −6.3.

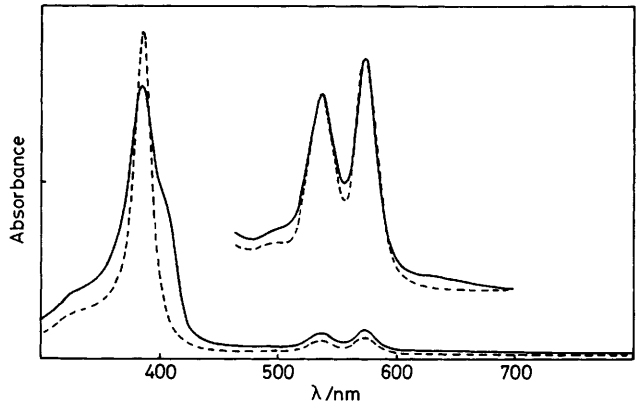


Figure 1. U.v.–visible spectrum of hexa-zinc hexamer (**6**) (——) compared to bis-zinc dimer (**3a**) (- - - - -) in CH_2Cl_2 at 25 °C.

A hexameric analogue of (**5**) can be prepared by a related route. Reaction of the diacid chloride of dimer (**3a**) with diamine (**1**) gave hexamer (**6**) in 35% yield (M + H^+ 3406.9 $C_{216}H_{237}N_{32}O_8$ requires 3406.9).§ Despite its size the solubility properties of (**6**) were quite normal,[4d,5d] ($CHCl_3$, CH_2Cl_2 *etc.*) and purification was achieved as for (**5**). The ^{1}H n.m.r. spectrum of (**6**) shows two sets of NH protons at δ −4.4 (integrating for 4H) and −8 (8H) due to the linking monomer and dimer environments respectively. The structural possibili-

¶ As seen in closely spaced dimers, ref. 4a, c.

** The conformational homogeneity of these derivatives should greatly increase on reduction of the amide groups. Conditions are currently being sought for this transformation.

ties for (**6**) are similar to those for (**5**) with the added influences of the two cofacial dimers (*e.g.* upfield-shifted NH resonances, blue-shifted Soret band to 378 nm, and amide carbonyl isomerism).[4d] An additional conformation of (**6**) is possible in which one of the linked dimers rotates 180° to fill the central cavity. This would prevent a folded structure from forming and may account for the small upfield shift of the NH protons (at δ −4.3) of the linking diamine porphyrin in (**6**) relative to those in (**5**) (at δ −6.3).

Tetramer (**5**) and hexamer (**6**) are interesting as photoactive ligands capable of binding 4 and 6 metal atoms, respectively, within a single molecular unit. Treatment of (**5**) and (**6**) with $Zn(OAc)_2$ (CH_2Cl_2–MeOH) provides both Zn_4 (**5**) (M^+ 2428.9; $C_{140}H_{148}N_{20}O_4Zn_4$ requires 2428.9) and Zn_6 (**6**) (M^+ 3786; $C_{216}H_{224}N_{32}O_8Zn_6$ requires 3786) in quantitative yield. The u.v.–visible spectrum of Zn_6 (**6**) (Figure 1) clearly shows both porphyrin environments, the Soret band at 386 nm being from the dimers and the shoulder at 405 nm from the linking monomers.

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