'Caged' Porphyrin: the First Dendritic Molecule having a Core Photochemical Functionality

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Alkali-mediated reaction of 5,10,15,20-tetrakis(3',5'-dihydroxyphenyl)porphine with dendritic bromide gives the novel porphyrin covalently encapsulated into a huge dendritic cage ('caged' porphyrin).
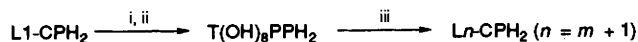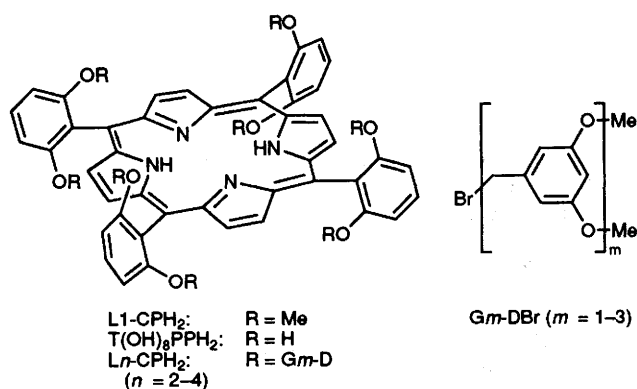
In order to mimic biological functions of haemoproteins and chlorophylls, a variety of metalloporphyrins with sterically hindered faces have been designed, which include 'picket fence', 'pocket', 'capped', 'crowned', 'strapped' and 'basket handle' porphyrins.[1] More recent examples, including the metalloporphyrins linked to polypeptide chains,[2] cyclocholate units,[3] steroid units[4] and cyclodextrin units,[5] suggest the importance of steric isolation of the metalloporphyrin nucleus for realizing certain biological functions.

We report here the synthesis of a novel porphyrin covalently encapsulated into a huge dendritic cage ['caged' porphyrin; Ln-CPH$_2$. *n* represents the number of the aromatic layers (L) of the cage, Fig. 1].

The synthetic route makes use of the alkali-mediated coupling reaction (Scheme 1) of 5,10,15,20-tetrakis(3',5'-dihydroxyphenyl)porphine [T(OH)$_8$PPH$_2$]† with dendritic bromide [a 3,5-dialkoxybenzyl bromide, G*m*-DBr, *m* represents the number of generation (G)], which was prepared according to the Frechet's method.[6] Typically, the four-layered 'caged' porphyrin (L4-CPH$_2$) was synthesized as follows: T(OH)$_8$PPH$_2$ (0.035 g, 0.047 mmol) and G3-DBr (0.56 g, 0.54 mmol) were dissolved in acetone (15 ml) containing K$_2$CO$_3$ (0.279 g, 2 mmol) and 18-crown-6 (0.013 g, 0.067 mmol), and the mixture was allowed to reflux with vigorous stirring under N$_2$. After 9 days, the reaction mixture was evaporated to dryness under reduced pressure. The

residue, after the removal of inorganic salts, was chromatographed thrice on silica gel using CHCl$_3$ as eluent, and the first fraction was collected and subjected to repeated reprecipitations (10 times) from CHCl$_3$-hexane, affording L4-CPH$_2$ in 46% yield (0.182 g) based on T(OH)$_8$PPH$_2$. Likewise, L2-CPH$_2$ and L3-CPH$_2$ were obtained in 88 and 61% yields, respectively.

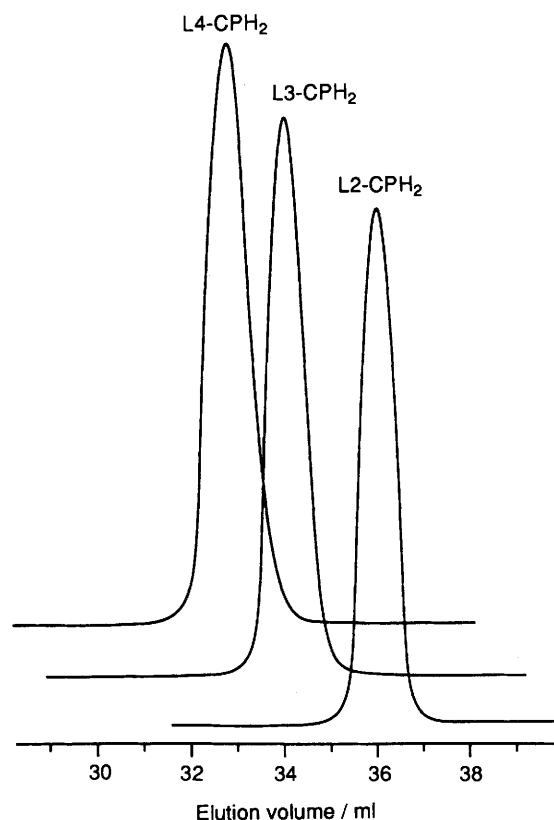The 'caged' porphyrins (Ln-CPH$_2$) were unambiguously characterized: In the SEC (size-exclusion chromatography)

L1-CPH$_2$:   R = Me
T(OH)$_8$PPH$_2$:   R = H
L*n*-CPH$_2$:   R = G*m*-D
(*n* = 2–4)

G*m*-DBr (*m* = 1–3)

$$\text{L1-CPH}_2 \xrightarrow{\text{i, ii}} \text{T(OH)}_8\text{PPH}_2 \xrightarrow{\text{iii}} \text{L}n\text{-CPH}_2 \ (n = m + 1)$$

Scheme 1. *Reagents*: i, BBr$_3$; ii, H$_2$O; iii, G*m*-DBr, K$_2$CO$_3$-18-crown-6 in acetone under reflux

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† FAB HRMS: Calc. for C$_{52}$H$_{46}$O$_8$N$_4$ *m/z* 743.2142 [MH]$^+$, obs. 743.2100.
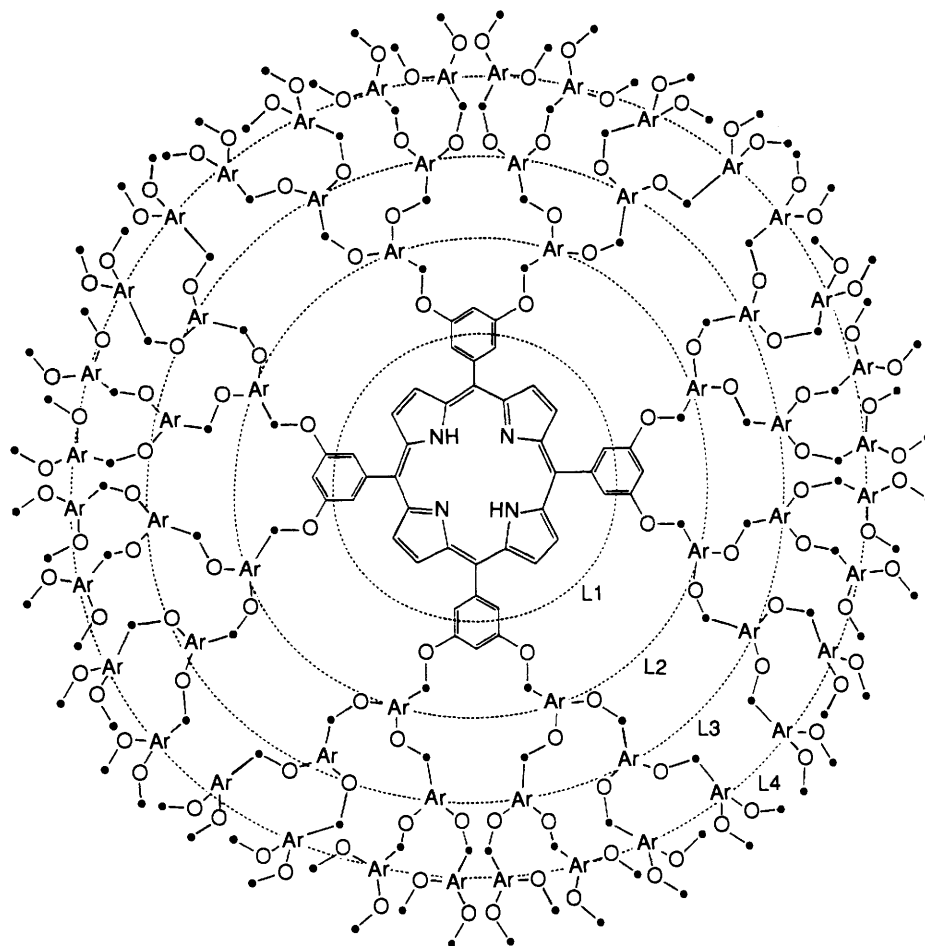
Fig. 1 Schematic illustration of L4-CPH$_2$

profiles (Fig. 2), a single, sharp elution peak was observed for each Ln-CPH$_2$ without any peak due to the parent dendritic component.‡ As expected from the theory of SEC, the elution volume of Ln-CPH$_2$ is smaller as the number of the layers (n) is higher. FABMS analyses of Ln-CPH$_2$ showed the parent peaks at the expected m/z ratios of 1944 for L2-CPH$_2$ [$C_{116}H_{110}O_{24}N_4$] (exact mass 1943.8 calc. for [MH]$^+$), 4120 for L3-CPH$_2$ [$C_{244}H_{238}O_{56}N_4$] (exact mass 4120.6 calc. for [MH]$^+$) and 8480 for L4-CPH$_2$ [$C_{500}H_{494}O_{120}N_4$] (exact mass 8479.3 calc. for [M + 6H]$^+$, molecular mass 8480.4 calc. for [MH]$^+$). In each case no other peaks due to the starting dendrimer and partially substituted intermediate were observed at the lower m/z field. Accordingly, the ^{1}H NMR spectrum of e.g. L4-CPH$_2$ in CDCl$_3$ showed single signals at δ 8.95 (s) and 5.10 (s) [CHCl$_3$ (δ 7.28) as internal standard] due respectively to the protons at the pyrrole-β positions and the connecting methylene moieties {porphine-[Ph(OCH_2-G3-D)$_2$]$_4$}, and their relative intensity satisfied the required ratio of 8 : 16. Although L1-CPH$_2$ does not melt below 300 °C, the melting point of Ln-CPH$_2$ decreased steeply as the number of the aromatic layers (n) was increased: 175–178 °C for L2-CPH$_2$ and 58–61 °C for L3-CPH$_2$ and L4-CPH$_2$.

In the Ln-CPH$_2$ family, the number of the MeO groups (F) in the outer layer is increased as a function of the number of the aromatic layers (n), according to F = 2^{n+2}. Surprisingly, in the ^{1}H NMR spectrum of L4-CPH$_2$ in CDCl$_3$ at 22 °C, all the 64 MeO groups in the outer layer appeared as a sharp singlet signal (δ 3.65) in the upfield region relative to that of the parent dendrimer (G3-DBr, δ 3.80). The same was true for

‡ The elution volumes of G2-DBr and G3-DBr were 39.5 and 37.7 ml, respectively.

Fig. 2 SEC profiles of 'caged' porphyrins (Ln-CPH$_2$); tetrahydrofuran as eluent; 35 °C

the ^{1}H NMR profile at $-40\,^{\circ}$C (MeO : δ 3.70). Thus, L4-CPH$_2$ may take a nearly globular shape on the NMR timescale,[7] where the huge dendritic substituents are situated above and below the core porphyrin plane.

All the Ln-CPH$_2$ free bases were quantitatively converted into the corresponding Zn complexes [Ln-CP)Zn] upon refluxing overnight with Zn(OAc)$_2$ in CHCl$_3$–MeOH (3:1). A preliminary fluorescence quenching study was carried out for (L4-CP)Zn (2.0 $\times$ 10^{-6} mol dm^{-3}) in deaerated MeCN at 20$\,^{\circ}$C using vitamin K$_3$ (2-methyl-1,4-naphthoquinone, 5.8 $\times$ 10^{-4} mol dm^{-3}) and L1-CPH$_2$ (2.0 $\times$ 10^{-6} mol dm^{-3}) as quenchers;§ the fluorescence of (L1-CP)Zn, a reference complex, was quenched by 14.1 and 11.9% in the presence of vitamin K$_3$ and L1-CPH$_2$, respectively. However, as for (L4-CP)Zn, the fluorescence was more significantly quenched (42.5%) by vitamin K$_3$, but not quenched at all by L1-CPH$_2$. These contrasting results indicate that the dendritic substituents in (L4-CP)Zn cooperatively serve as a barrier for the access of a large quencher molecule (L1-CPH$_2$) to the metalloporphyrin core, but behave as a trap for a small quencher molecule (vitamin K$_3$). This is a unique feature of the 'caged' metalloporphyrin.

Further studies on the synthesis and photochemical application of 'caged' metalloporphyrins are now in progress.

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§ Both (L1-CP)Zn and (L4-CP)Zn emitted at 604 and 659 nm upon excitation at 423 nm. The quenching efficiencies were evaluated based on the emission intensity at 659 nm, since the emission at 604 nm was overlapped by that of L1-CPH$_2$.

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