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Preliminary communication

A 'calix[4]arened' porphyrin as a new host and an oxygen carrier model

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Abstract

A calix[4]arene capped porphyrin **4** and its iron complex Fe**4** have been prepared in high yields using calix[4]arene as a template. The former is a new host compound and the latter functions as an oxygen carrier when iron is in the divalent state and in the presence of a base.

Keywords: Calix[4]arene; Porphyrin; Host; Oxygen carrier

A principal theme of bioinorganic chemistry is the design of metal complexes which mimic active sites in functional metalloproteins. As synthetic models for the oxygen-binding hemoproteins, for example, compounds such as those named 'picket fence' [1], 'capped' [2], 'crowned' [3] and 'pocket' [4] porphyrins have been reported from the early 1970s to the mid 1980s. In these complexes, attention has been paid to create, on one side, a non-proteic cavity for the coordination of small ligands while also protecting such ligands from bimolecular reactions. However, research on oxygen carrier models appears to have faded in recent years.

In contrast, interest in the *p*-alkylphenol-derived cyclic oligomers called calixarenes [5] has been increasing, and these compounds are now recognized as molecular baskets. Metal cations, organic cations and anions, and neutral organic molecules are known to fill the basket by making complexes. In this communication, we report the synthesis and intriguing properties of compounds containing both a porphyrin and a calix[4]arene moiety, i.e. a 'calix[4]arened' porphyrin, **4**, and its iron complex, Fe**4**. As shown below, **4** functions as a new host and Fe^{II}**4** is an oxygen carrier.

Our strategy is the same as that reported for a 'capped' porphyrin [2] (Scheme 1). Thus, an aldehyde **2** [6] was linked to a calix[4]arene **1**, under the condition which maintains the cone conformation [5b], to provide tetraaldehyde **3** in 40.8% yield where four aldehyde units are equidistant from the rim of the calix[4]arene[1]. After attachment of long alkyl chains (longer than propyl) or bulky alkyl groups such as **2**, calix[4]arenes do not change conformation [7]. Hence, condensation of **3** (1 equiv.) with pyrrole (11.5 equiv., [pyrrole] = 0.028 M) [8] was performed in refluxing propionic acid for 3.5 h. After removing the solvent in vacuo, the black residue was chromatographed on silica gel using meth-

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[1] Analytical and spectroscopic data of new compounds. **3**: highly viscous liquid. *Anal.* Found: C, 77.07; H, 7.33. Calc. for $C_{80}H_{88}O_{12}$: C, 77.39; H, 7.14%. 60 MHz ^1H NMR ($CDCl_3$): δ 0.8–1.4 (36H, m, $C(CH_3)_3$, 3.31 and 4.60 (4H each, d each ($J = 13$ Hz), $ArCH_2Ar$), 4.20 and 4.40 (8H each, s each, OCH_2CH_2O), 6.4–8.1 (24H, m, Ar*H*), 10.63 (4H, s, C*H*O). **4**: *Anal.* Found: C, 79.97; H, 6.84; N, 3.58. Calc. for $C_{96}H_{94}N_4O_8$; C, 80.53; H, 6.62; N, 3.91%. *m/z* (FAB): 1431 ($M+1$). λ_{max} (CH_2Cl_2): 418 nm ($\epsilon = 323000$), 515 (16200), 548 (6700), 590 (6200), 644 (2600). 90 MHz ^1H NMR (CD_2Cl_2): δ −2.78 (2H, s, N*H*), 0.46–1.40 (36H, m, $C(CH_3)_3$), 3.07 and 4.20 (4H each, d each ($J = 12$ Hz), $ArCH_2Ar$), 3.53 and 3.98 (8H each, s each, OCH_2CH_2O), 6.3–7.5 (20H, m, Ar*H*), 7.70 (4H, s, *ortho H* of phenyl), 8.67 (8H, s, βH of pyrrole). In compounds **3** and **4**, the splitting pattern for the $ArCH_2Ar$ protons in the NMR spectra (a pair of doublets with $\delta = 1.29$ and 1.13 ppm, respectively) indicates that they adopt a cone conformation [5]. Fe^{III}**4**Cl: *Anal.* Found: C, 75.40; H, 6.32; N, 3.47; Cl, 2.06. Calc. for $C_{96}H_{92}N_4O_8ClFe$: C, 75.80; H, 6.10; N, 3.68; Cl, 2.33%.

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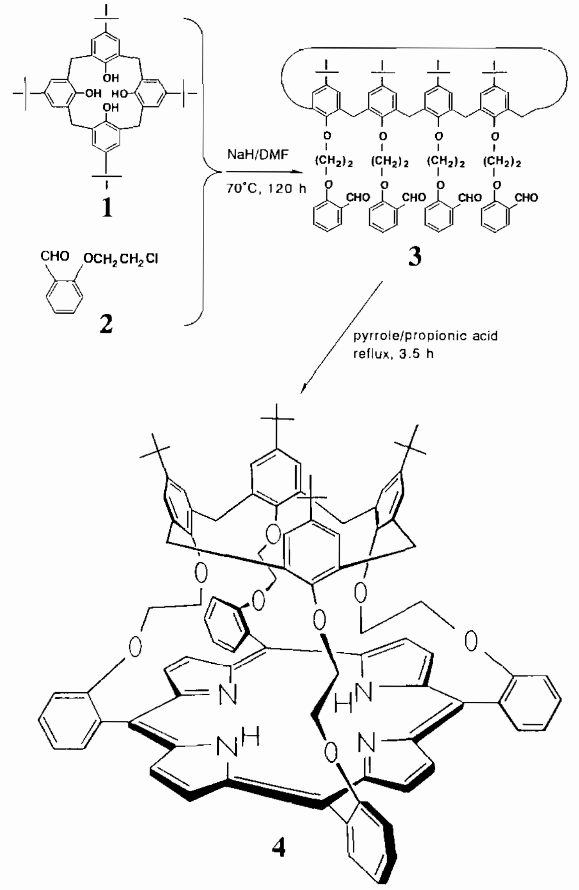

Scheme 1.

ylene chloride (CH_2Cl_2)–benzene. A part of the resultant crude porphyrin was treated with dichlorodicyanobenzene (DDQ) in benzene–CH_2Cl_2 to oxide traces of chlorine [9]. However, the FAB mass spectrum of the purified compound gave a parent ion peak of 1658, which corresponds to the sum of the molecular weights of **3** and DDQ. Accordingly, the rest of the crude porphyrin was chromatographed on silica gel again, and portions which did not show the 655 nm band of chlorine [9] in the electronic absorption spectrum were carefully collected. Double crystallization from ethyl acetate–methanol gave the calix[4]arened porphyrin **4** as lustrous purple crystals (25% yield). The structure assigned to **4** is based on its constitution and spectral properties (see footnote on p. 1). Reaction of **4** with anhydrous ferrous chloride in the presence of sodium acetate in acetic acid [10] under nitrogen provided a moderate yield (19% after chromatography) of ferric porphyrin chloride, Fe^{III}**4**Cl, λ_{max} ($CHCl_3$) 508 nm, μ 5.86 βM (Evans method [11] in $CHCl_3$). (The analogous tetraphenylporphinatoiron(III) chloride has λ_{max} ($CHCl_3$) 509.5 nm, μ 5.87 βM [12].)

In order to confirm the capability of **4** as a new host, fluorescence quenching of **4** and tetraphenylporphyrin (H_2TPP) by benzoquinone (Q) was compared. It is well-known that quinone quenches the fluorescence of porphyrins [13]. Accordingly, more efficient quenching is expected for **4** than H_2TPP if Q is trapped in the cavity of **4**. Both **4** and H_2TPP showed an S_1 emission peak at 652 nm when excited at 456 nm in CH_2Cl_2, whose intensity decreased on addition of Q (Fig. 1(a), left). The Stern–Volmer plots [14] from these experiments are shown in Fig. 1(a), right hand side. Since the slopes of these plots are equal to the product of the lifetime (τ) and the bimolecular quenching constant, k_2 [15], τ values of **4** (9.50 ns) and H_2TPP (9.40 ns) were determined from the decay curves in order to estimate the k_2 values. The k_2 values for **4** and H_2TPP were found to be 7.41×10^{10} and 2.13×10^{10} dm^3 mol^{-1} s^{-1}, respectively, indicating that quenching in the **4** system occurs about 3.5 times more efficiently than the system without the calix[4]arened moiety in methylene chloride.

Reduction of Fe^{III}**4**Cl was carried out using the Na mirror method [16] in an all-glass apparatus equipped

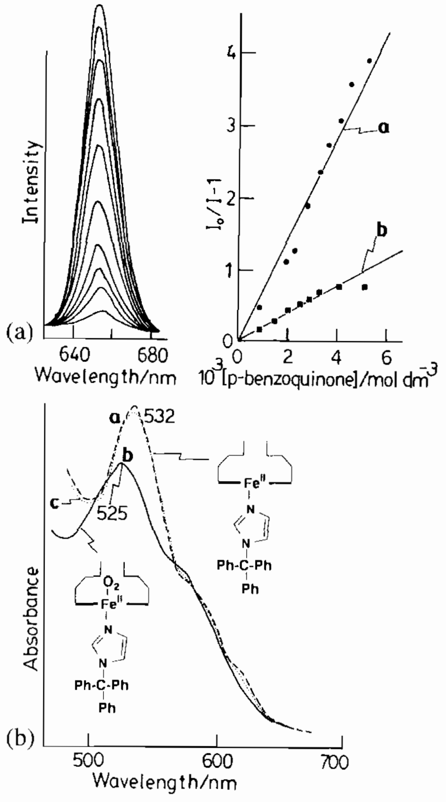

Fig. 1. (a) Emission spectra of **4** in the absence or presence of varying concentrations of *p*-benzoquinone (Q) in CH_2Cl_2 (left) and Stern–Volmer plot therefrom (right, line a). Line b is the plot of the H_2TPP system, obtained in a similar manner. Excitation was at 546 nm, and [**4**] = [H_2TPP] = 1.0×10^{-6} M and [Q] = 1.0×10^{-3}–5.3×10^{-3} M. Quenching in the H_2TPP system saturated at [Q] ≅ 4.1×10^{-3} M. (b) Electronic absorption spectra of Fe^{II}**4** (curve a) and Fe^{II}**4**–O_2 (curve b) in the presence of 1-triphenylmethylimidazole in chloroform. Curve c (dotted line) was obtained after two oxygenated cycles. [1-triphenylmethylimidazole] = 4.1×10^{-3} M.

with a cell for measuring the absorption spectra [17]. Fe^{III}**4**Cl was dissolved in $CHCl_3$ ([Fe^{III}**4**Cl] = ~10^{-4} M), and triphenylmethylimidazole [3] in $CHCl_3$ was added using a microsyringe. After confirming five-coordination from the spectroscopic change (λ_{max} 507 nm, which is the same as that of Fe^{III}**4**Cl, but lower in intensity), this solution was transferred to the above apparatus. After several freeze–thaw cycles under rigorous anaerobic conditions, this solution was touched with an Na mirror, and the Fe^{III} to Fe^{II} process was monitored using the absorption spectroscopic changes. The final Fe^{II}**4** spectrum with a peak at 532 nm is shown in Fig. 1(b), curve a. Exposure of this solution to oxygen at 20 °C was accompanied by an immediate change in the spectrum (curve b with a peak at 525 nm)[2]. Deaeration by freeze–thawing restored the spectrum of the ferrous complex, curve a. Since the stability of a dioxygen adduct (curve b) is known to depend on the concentration of coordinating base [2a], the above experiments were conducted by changing the concentration of 1-triphenylmethylimidazole. At [1-triphenylmethylimidazole] = 4.1×10^{-2} and 4.1×10^{-3} M, the dioxygen adduct was stable for ~5.5 and 1 h, respectively, at 20 °C in chloroform.

In summary, the above results indicate that the calix[4]arened porphyrin **4** can acts as a new host compound, and its ferrous derivative is found to function as an oxygen carrier.

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[2] Similar spectroscopic change was observed in the case of the 'capped' porphyrin iron complex. Thus, the absorption maximum of Fe^{II} porphyrin (545 nm) shifts to shorter wavelength (537 nm) with concomitant decrease in intensity in pyridine [2a].

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