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Tetrahedron
Tetrahedron 63 (2007) 4011–4017

Syntheses and properties of functionalized oxacalix[4]arene porphyrins

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Received 6 November 2006; revised 16 February 2007; accepted 1 March 2007
Available online 6 March 2007

Abstract—Six new functionalized oxacalix[4]arene porphyrins have been synthesized via a high-yielding '3+1' condensation between *meso*-(3,5-dihydroxyphenyl)triphenylporphyrin and readily available new fluorodinitrobenzene-containing trimers. The X-ray structure of one linear trimer is presented. The synthesis of a porphyrin containing two oxacalix[4]arene moieties is also reported using a similar strategy. ^{1}H NMR data and computer calculations using the AM1 semiempirical method incorporated into the Spartan program indicate that the oxacalix[4]arene porphyrins adopt 1,3-alternating conformations. The photophysical properties of the oxacalix[4]arene porphyrins were investigated.

1. Introduction

The mechanisms of proton-coupled electron transfer (PCET) processes, which occur in many natural systems,[1–3] have been the subject of several investigations using model porphyrin-based compounds.[4,5] Such studies indicate that either a face-to-face or side-to-side arrangement of the acid–base and redox sites are crucial for efficient proton and electron transfers.[6] On the other hand, the recognition that the hydrogen-bond framework in heme model systems is a determinant of heme structure and function has resulted in the targeted synthesis of model systems containing one or more hydrogen-bond functionalities.[7–10] Some such porphyrins were found to have interesting structural and electronic properties, particularly the so-called 'hangman' porphyrins, which are potential model systems for investigations of both hydrogen-bond frameworks and energy transfer agents in natural systems.[6,11–19] Hangman porphyrins bearing hydrogen synthons with different pK_a values have been reported[6,13–19] and the acidity of these systems was found to influence both the speed and the stability of the catalyst in proton-coupled O–O activation reactions.[6,15c] These types of porphyrins are attractive PCET model systems since they allow the control of both the proton and electron transfers while providing the opportunity to introduce a hydrogen-bond active group with specific proton-donating ability and arrangement relative to the metalloporphyrin redox site.[6] However, the synthesis of such models presents several challenges due to very long and tedious synthetic routes currently available and the lack of susceptibility to modular modifications of the target systems.[14]

Calixarenes have been extensively studied in recent years because of their interesting chemical and physical properties.[20–32] However, heterocalixarenes are far less prevalent in the chemical literature. Among those, oxacalixarenes are especially scarce, despite the fact that their modest yield synthesis was first reported in 1966.[26] Although this flexible route based on a nucleophilic aromatic substitution can be used to efficiently synthesize highly functionalized oxacalixarenes, it requires high temperature with extended reaction time. Recently, Katz et al.[30] made a significant improvement in oxacalixarene synthesis by choosing selective bases and solvents to let the reaction proceed at room temperature and in high yields. We have recently reported the synthesis of calixarene-locked bisporphyrins via the nucleophilic aromatic substitution reaction of 1,5-difluoro-2,4-dinitrobenzene with a 3,5-dihydroxyphenyl-containing porphyrin.[33] Synthetic routes to the unsymmetric heterocalixarenes are few, especially for oxacalixarenes, although Wang and Yang[24] recently developed a fragment-coupling synthesis of O- and N-bridged calixarenes using triazine; the reaction in general needs a long time to go to completion.

Herein we report the first efficient preparation and properties of functionalized unsymmetrical oxacalixarene porphyrins via a '3+1' condensation of readily available aryl trimers with *meso*-(3,5-dihydroxyphenyl)porphyrins. Due to the unique discrete 1,3-alternating conformations of oxacalix[4]arenes,[20–33] we envisioned the design and synthesis of porphyrin-oxacalix[4]arene systems containing hydrogen

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0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.03.005

synthons in a face-to-face arrangement relative to the porphyrin macrocycle, for application as heme model systems. Our synthetic strategy involves the preparation of a series of novel unsymmetrical oxacalix[4]arenes by nucleophilic aromatic substitution of functionalized *meta*-dihydroxybenzenes with 1,5-difluoro-2,4-dinitrobenzene.

2. Results and discussion

The synthesis of functionalized oxacalix[4]arene porphyrins **1a–c** from readily available dihydroxybenzenes **2a–c** is shown in Scheme 1. The linear aryl trimers **3a–c** were readily prepared on a multi-gram scale in 75–85% yield, by reacting **2a–c** with 3 equiv of 1,5-difluoro-2,4-dinitrobenzene and 4 equiv of finely ground K_2CO_3 (<80 μm) in acetone at room temperature for 1–2 h. The amount of symmetrical oxacalix[4]arene byproducts resulting from this reaction was minimized by using acetone as the solvent and 3 equiv (rather than two) of 1,5-difluoro-2,4-dinitrobenzene. The linear trimers **3a–c** shared characteristic ^{1}H NMR spectra, showing two downfield singlets (around 8.9 ppm) for the protons next to the carbons bearing the NO_2 groups, and two upfield singlets (around 6.9 ppm) for the protons next to the carbons bearing the fluorines. The structure of trimer **3c** was further confirmed by crystallography at T=150 K (see Fig. 1). The crystals were destroyed by cooling to temperatures lower than 150 K, apparently as a result of a phase change. The C–F distances are 1.331(2) and 1.334(2) Å.

The reaction of *meso*-(dihydroxyphenyl)triphenylporphyrin **2d** (obtained by a mixed aldehyde condensation followed by demethylation using BBr_3 according to the literature)[35] and trimers **3a–c** produced the target functionalized oxacalix[4]arene porphyrins in 80–86% yields (Scheme 1); 4 equiv of finely ground K_2CO_3 in DMSO were required, at room temperature, for 30 min to 3 h (until complete

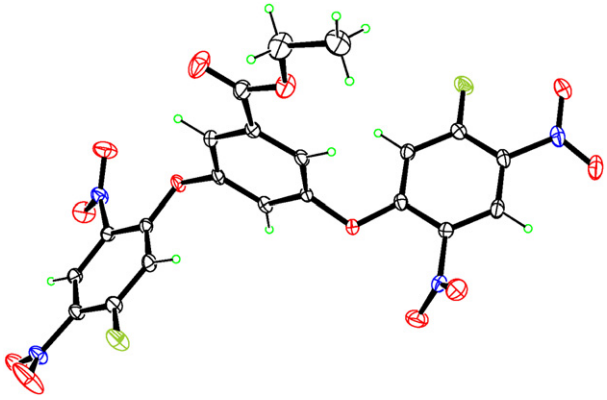
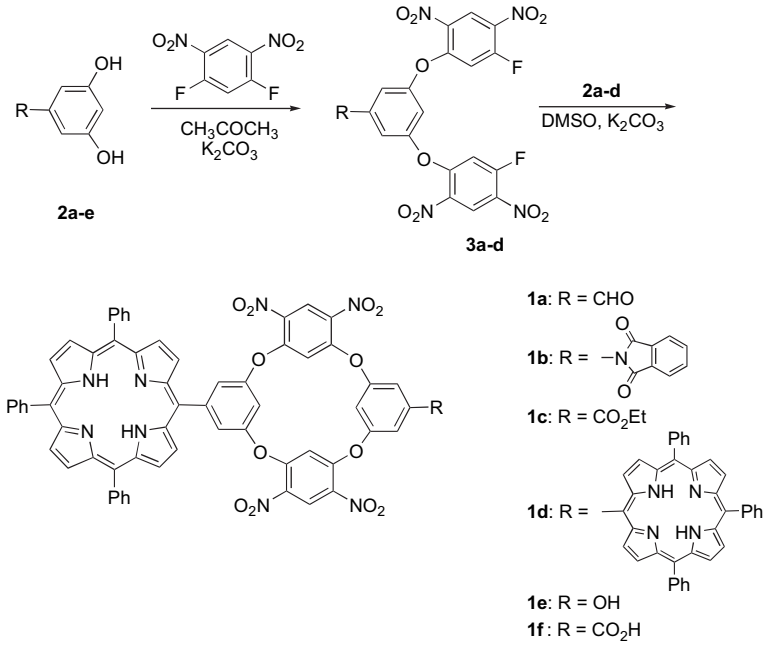


Figure 1. Molecular structure of trimer **3c**.

disappearance of the starting materials as monitored by TLC). These fragment-coupling reactions are very efficient and no higher analogs were detected compared with other fragment-coupling reactions reported in the literature.[20–25] The porphyrin-containing trimer **3d** was also prepared in 80% yield from the reaction of porphyrin **2d** with an excess of 1,5-difluoro-2,4-dinitrobenzene in acetone at room temperature. A side product in this reaction was the symmetric oxacalix[4]arene bisporphyrin **1d**. Using DMSO as the solvent in place of acetone resulted in a lower yield of the trimer product and increased the yield of bisporphyrin **1d**. However, the coupling of porphyrin-containing trimer **3d** with **2a–c** and **2e** in DMSO, in the presence of finely ground K_2CO_3, resulted in low yields (10–25%) of the corresponding oxacalix[4]arene porphyrins **1a–c** and **1e**. The major product from these reactions was invariably the symmetric oxacalix[4]arene bisporphyrin **1d**,[33] obtained from scrambling of trimer **3d** under the reaction conditions. The thermodynamic reversibility of oxacalixarene formation during nucleophilic substitution has been studied and confirmed



Scheme 1. Synthesis of functionalized oxacalix[4]arene porphyrins.

recently by Katz et al.;[30] their results are also in agreement with studies reported for thiocalixarenes[34] and with our own observations. Hydrolysis of the ester functionality in **1c**, upon refluxing in THF/4 M aqueous HCl (v/v=1/2) for 3 days, provided **1f** in 95% yield. The functionalized oxacalix[4]arenoporphyrins **1a–c** and **1e**,**f** were characterized by HRMS, UV–vis, fluorescence, and by ^{1}H NMR spectroscopy.

In order to prepare bis(oxacalix[4]areno)porphyrin **4**, 5,15-di(3,5-hydroxyphenyl)porphyrin **5** (prepared by mixed aldehyde condensation under Lindsey conditions[36] followed by demethylation with BBr_3) was used in the coupling reaction along with 2 equiv of trimer **3c** (Scheme 2). The presence of the four *tert*-butyl groups in porphyrin **4** induced high solubility in organic solvents; an analog of porphyrin **4** without the *tert*-butyl groups was also prepared separately (as confirmed by MALDI-MS) but it was poorly soluble and difficult to purify and characterize. Porphyrin **4** was isolated in 84% yield and its structure was confirmed by HRMS (a molecular ion peak was observed at 1923.5460), UV–vis, fluorescence, and ^{1}H NMR spectroscopy.

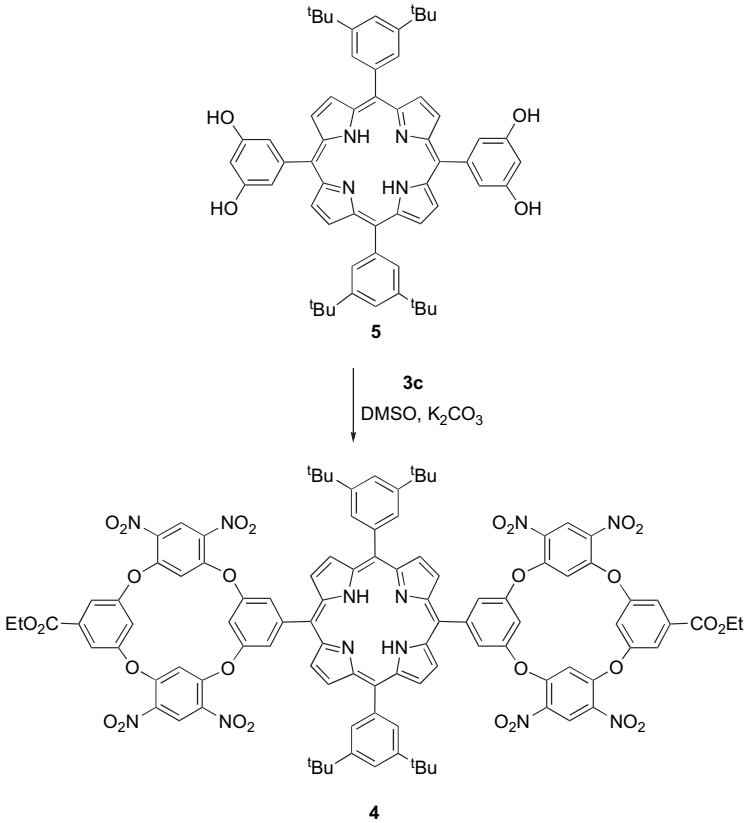
Based on the characteristic upfield chemical shifts observed in the ^{1}H NMR spectra of oxacalix[4]arenes for the interior protons on the electrophilic (NO_2-bearing) aromatic rings,[28] it is believed that these compounds adopt 1,3-alternating structures in solution.[20–33] Recent X-ray structures[26–33] have confirmed this conformation of oxacalix[4]arenes in the solid state. Table 1 shows the ^{1}H NMR shifts observed for these protons on porphyrins **1a–c**,**e**,**f** and **4**. These results

Table 1. ^{1}H NMR shifts for the interior protons on the NO_2-bearing benzene rings of porphyrins **1a–c**,**e**,**f** and **4**

Porphyrin	**1a**	**1b**	**1c**	**1e**	**1f**	**4**
^{1}H NMR shift (ppm)	6.77	6.70	6.43	6.87	6.70	6.49

suggest that our functionalized oxacalix[4]arene porphyrins also adopt 1,3-alternating conformations in solution, in agreement with results reported for symmetrical oxacalix[4]arenes.[26–33] Furthermore, computer calculations using the AM1 theoretical model incorporated into the Spartan program were performed to determine the minimum energy conformations for oxacalix[4]arene porphyrins **1a–f**. Such calculations have been found reliable for the determination of geometrical parameters in porphyrin arrays.[37–40] Similar optimized geometries were found for all oxacalix[4]arene porphyrins (see Fig. 2) and the calculated structure obtained for bisporphyrin **1d** was in agreement with the crystal data.[33] These results suggest, as seen in Figure 2, favorable 1,3-alternating conformations for all oxacalix[4]arene porphyrins, with the hydrogen-bond synthons hanging over an adjacent pyrrole ring. Such a conformation would provide a face-to-face structural arrangement for the porphyrin macrocycles and hydrogen-bond synthons, therefore making these compounds suitable as model systems for PCET and hydrogen-bond investigations.

The photophysical properties of porphyrins **1a–c**,**e**,**f** and **4** are summarized in Table 2. The long wavelength absorption and fluorescence emission bands for all porphyrins except **1f** were observed between 646–652 and 652–658 nm,



Scheme 2. Synthesis of a bis(oxacalix[4]arene)porphyrin.

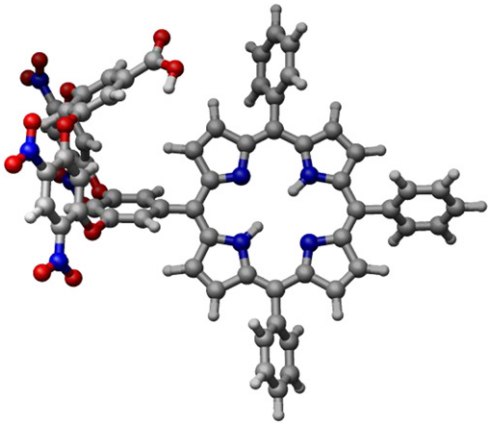


Figure 2. Optimized geometry for porphyrin **1f** calculated using the AM1 semiempirical method.

Table 2. Spectral properties of porphyrins **1a–c,e,f** and **4** in degassed CH_2Cl_2 at room temperature

Porphyrin	Absorption λ_{max} (nm)	Emission[a] λ_{max} (nm)	Fluorescence[b] quantum yield
1a	418, 514, 548, 591, 647	652	0.13
1b	418, 515, 550, 591, 652	658	0.15
1c	418, 513, 548, 591, 649	652	0.13
1e	417, 513, 548, 591, 646	655	0.17
1f	418, 514, 548	600, 646	0.03
4	422, 518, 553, 592, 650	656	0.22

[a] Excitation at 415 nm.
[b] Calculated using 5,10,15,20-tetraphenylporphyrin as the standard.

respectively. The carboxyl group in porphyrin **1f** is probably involved in intermolecular hydrogen-bonding, resulting on its distinct absorbance and emission spectra compared with the other porphyrins, as well as its reduced fluorescence quantum yield (0.03). All other oxacalix[4]arene porphyrins showed quantum yields between 0.13 and 0.22.

3. Conclusions

An efficient and convenient stepwise fragment-coupling approach to the synthesis of unsymmetrical architectures composed of porphyrins and hydrogen-bond functionalities anchored to an oxacalix[4]arene spacer is reported. Spectroscopic data and computer calculations indicate that these oxacalix[4]arene porphyrins adopt 1,3-alternating conformations. These novel, high-yield syntheses of unsymmetrical oxacalix[4]arenes will find applications in supramolecular chemistry and molecular design.

4. Experimental

4.1. General

Silica gel (32–63 μm) was used for flash column chromatography. All reactions were monitored by TLC using 0.25 mm silica gel plates with or without UV indicator (60F-254). ^1H and ^{13}C NMR spectra were obtained on either a DPX-250 or a ARX-300 Bruker spectrometer. Chemical shifts (δ) are given in ppm relative to $CDCl_3$, acetone-d_6, DMSO-d_6 or THF-d_8 as indicated. Electronic absorption spectra were measured on a Perkin Elmer Lambda 35 UV–vis spectrophotometer in the 300–800 nm wavelength region with 0.1 nm accuracy. Fluorescence spectra were measured on a Perkin Elmer LS55 spectrometer in the 500–800 nm wavelength region with 1 nm accuracy. The fluorescence quantum yields were measured using the standard method and 5,10,15,20-tetraphenylporphyrin as the standard (quantum yield is 0.11), according to the literature.[41] Mass spectra were obtained on Applied Biosystems QSTAR XL. High-resolution mass spectra were obtained on a Q-TOF2 eletrospray at the mass spectrometry facility of Ohio State University. All solvents were obtained from Fisher Scientific (HPLC grade, Houston, TX) and used without further purification unless indicated. Acetone (reagent plus, phenol free, ≥99.5%) and DMSO (Biotech grade solvent, 99.8%) were purchased from Sigma–Aldrich and used without further purification. K_2CO_3 was ground and dried at 140 °C. Compounds **2b**[42] and **2d**[35] were synthesized according to literature procedures. Solvents were dried according to literature procedures.[43] The computational simulations used the AM1 semiempirical Hamiltonian method[44] incorporated into the quantum mechanical Spartan program.[45] The coordinates used to build the porphyrins in this study were based on the X-ray crystal structure of **1d**.[33]

4.1.1. Aryl trimer 3a. 3,5-Dihydroxybenzaldehyde (**1a**) (276.7 mg, 2.0 mmol) was mixed with 1,5-difluoro-2,4-dinitrobenzene (816.5 mg, 4.0 mmol) and K_2CO_3 (561.4 mg, 4 mmol) in 10 mL of acetone at room temperature under air. When the reaction was complete, acetone was removed under vacuum. The resulting residue was purified by silica gel column chromatography using CH_2Cl_2/ethyl acetate (v/v=20/1) for elution. After removal of the solvent under vacuum and washing with hexane (2×10 mL), pure trimer **3a** was obtained as a white solid in 85% yield (860.0 mg). ^1H NMR (300 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.98 (s, 1H), 8.95 (s, 1H), 7.58 (d, 2H, J=2.25 Hz), 7.30 (s, 1H), 7.06 (s, 1H), 7.02 (s, 1H). ESI-MS calcd for $C_{19}H_8F_2N_4O_{11}$ m/z 506.3, found: 506.5.

4.1.2. Aryl trimer 3b. Compound **2b** (510.4 mg, 2 mmol) was mixed with 1,5-difluoro-2,4-dinitrobenzene (1.63 g, 8.0 mmol) and K_2CO_3 (2.21 g, 16 mmol) in 20 mL of acetone at room temperature under air. When the reaction was complete, acetone was removed under vacuum. The resulting residue was purified by silica gel column chromatography using CH_2Cl_2 to CH_2Cl_2/ethyl acetate (v/v=20/1) for elution. After removal of the solvent under vacuum and washing with hexane (2×10 mL), trimer **3b** was obtained as a white solid in 75% yield (935.0 mg). ^1H NMR (300 MHz, acetone-d_6) δ 8.93 (d, 2H, J=7.67 Hz), 7.93 (m, 4H), 7.69 (s, 1H), 7.65 (s, 1H), 7.60 (d, 2H, J= 2.21 Hz), 7.48 (s, 1H). ESI-MS calcd for $C_{26}H_{11}F_2N_5O_{12}$ m/z 623.4, found: 623.8.

4.1.3. Aryl trimer 3c. Ethyl 3,5-dihydroxybenzoate (**2c**) (182.0 mg, 1 mmol) was mixed with 1,5-difluoro-2,4-dinitrobenzene (408.0 mg, 2 mmol) and K_2CO_3 (560.0 mg, 4 mmol) in 10 mL of acetone at room temperature under air. When the reaction was complete, acetone was removed under vacuum. The resulting residue was purified by silica gel column chromatography using CH_2Cl_2 for elution. After removal of the solvent and washing with hexane (2×10 mL),

trimer **3c** was obtained as a white solid in 82% yield (451.0 mg). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.91 (s, 1H), 7.74 (d, 2H, J=2.34 Hz), 7.19 (s, 1H), 6.96 (s, 1H), 6.92 (s, 1H), 4.39 (q, 2H), 1.38 (t, 3H). Anal. Calcd for $C_{21}H_{12}F_2N_4O_{12}$: C, 45.83; H, 2.20; N, 10.18. Found: C, 45.79; H, 2.26; N, 9.98. ESI-MS calcd for $C_{21}H_{12}F_2N_4O_{12}$ m/z 550.3, found: 549.8.

4.1.4. Aryl trimer 3d. 5-(3,5-Dihydroxyphenyl)triphenylporphyrin (**2d**) (32.8 mg, 0.05 mmol) was mixed with 1,5-difluoro-2,4-dinitrobenzene (81.6 mg, 0.2 mmol) and K_2CO_3 (56.0 mg, 0.4 mmol) in 20 mL of acetone at room temperature under air. After the reaction was complete, acetone was removed under vacuum. The resulting residue was purified by silica gel column chromatography using CH_2Cl_2/hexane (v/v=10/1) for elution. Pure trimer **3d** was isolated in 80% yield (40.6 mg) after recrystallization from hexane and CH_2Cl_2. ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.84 (m, 6H), 8.68 (d, 2H, J=2.37 Hz), 8.19 (m, 8H), 7.73 (m, 11H), 7.05 (m, 1H), 6.80 (m, 2H), −3.03 (s, 2H). HRMS (MALDI-TOF) calcd for $[M+H]^+$ $C_{56}H_{33}F_2N_8O_{10}$ m/z 1015.2288, found: 1015.2265. UV–vis (CH_2Cl_2) λ_{max} (log ε) 417 (5.84), 513 (4.47), 548 (4.03), 590 (3.85), 646 (3.58) nm.

4.1.5. Porphyrin 1a. Trimer **3a** (50.1 mg, 0.1 mmol) was mixed with **2d** (64.1 mg, 0.1 mmol) and K_2CO_3 (60.3 mg, 0.44 mmol) in 20 mL of DMSO at room temperature under air for 1 h (until TLC showed the complete disappearance of starting material). HCl (0.1 M, 40 mL) was used to quench the reaction. The water layer was extracted with 100 mL of ethyl acetate, and the organic layer was washed once with water and dried over anhydrous Na_2SO_4. The resulting residue was purified by silica gel column chromatography using CH_2Cl_2 for elution. Pure porphyrin **1a** was obtained as a purple solid in 83% yield (92.1 mg) after recrystallization from CH_2Cl_2/hexane. ^{1}H NMR (250 MHz, THF-d_8) δ 10.07 (s, 1H), 8.98 (s, 2H), 8.84 (m, 6H), 8.66 (s, 2H), 8.20–8.21 (m, 6H), 8.13 (d, 2H, J=2.10 Hz), 8.00 (d, 2H, J=2.16 Hz), 7.81–7.82 (m, 9H), 7.64 (s, 1H), 7.52 (s, 1H), 6.77 (s, 2H), −2.76 (s, 2H). MALDI-TOF-MS calcd for $[M+H]^+$ $C_{63}H_{37}N_8O_{13}$ m/z 1114.0, found: 1114.0. HRMS (ESI) calcd for $[M+H]^+$ $C_{63}H_{37}N_8O_{13}$ m/z 1113.2480, found: 1113.2501. UV–vis (CH_2Cl_2) λ_{max} (log ε) 418 (5.88), 514 (4.50), 548 (4.11), 591 (3.93), 647 (3.72) nm.

4.1.6. Porphyrin 1b. Trimer **3b** (63.3 mg, 0.1 mmol) was mixed with **2d** (65.7 mg, 0.1 mmol) and K_2CO_3 (60.0 mg, 0.43 mmol) in 10 mL of DMSO at room temperature under air for 3 h (until TLC showed the complete disappearance of starting material). HCl (0.1 M, 40 mL) was used to quench the reaction. The water layer was extracted with 100 mL of ethyl acetate, and the organic layer was washed once with water and dried over anhydrous Na_2SO_4. The resulting residue was purified by silica gel column chromatography using CH_2Cl_2 for elution. Pure porphyrin **1b** was obtained as a purple solid in 83% yield (102.0 mg) after recrystallization from CH_2Cl_2/hexane. ^{1}H NMR (300 MHz, THF-d_8) δ 8.98 (s, 2H), 8.90 (br s, 2H), 8.82 (br s, 4H), 8.20 (br s, 4H), 8.17 (s, 3H), 8.14 (s, 3H), 7.79–7.81 (m, 9H), 7.63 (s, 2H), 7.56 (s, 1H), 7.35 (s, 1H), 6.95 (d, 4H, J=2.55 Hz), 6.70 (s, 2H), −2.84 (s, 2H). MALDI-TOF calcd for $[M+H]^+$ $C_{70}H_{40}N_9O_{14}$ m/z 1230.3, found: 1230.8. HRMS (ESI) calcd for $[M+H]^+$ $C_{70}H_{40}N_9O_{14}$ m/z 1230.2694, found: 1230.2700. UV–vis (CH_2Cl_2) λ_{max} (log ε) 418 (5.57), 515 (4.20), 550 (3.79), 591 (3.49), 652 (3.43) nm.

4.1.7. Porphyrin 1c. Trimer **3c** (55.0 mg, 0.1 mmol) was mixed with **2d** (64.6 mg, 0.1 mmol) and K_2CO_3 (56.0 mg, 0.44 mmol) in 20 mL of DMSO at room temperature under air (the reaction was considered complete after TLC showed the complete disappearance of the starting material). HCl (0.1 M, 40 mL) was used to quench the reaction. The water layer was extracted with 100 mL of ethyl acetate, and the organic layer was washed once with water and dried over anhydrous Na_2SO_4. The resulting residue was purified by silica gel column chromatography using CH_2Cl_2 for elution. Pure porphyrin **1c** was obtained as a purple solid in 86% yield (100.1 mg) after recrystallization from CH_2Cl_2/hexane. ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.93 (s, 2H), 8.82 (m, 6H), 8.41 (s, 4H), 8.16 (m, 6H), 8.04 (d, 2H, J=2.22 Hz), 7.99 (d, 2H, J=2.22 Hz), 7.71 (m, 9H), 6.43 (s, 2H), 4.01 (q, 2H), 1.11 (m, 3H), −2.88 (s, 2H). MALDI-TOF calcd for $C_{65}H_{40}N_8O_{14}$ m/z 1157.058, found: 1159.198. HRMS (MALDI-TOF) calcd for $[M+H]^+$ $C_{65}H_{41}N_8O_{14}$ m/z 1157.2742, found: 1157.2787. HRMS (ESI) calcd for $[M+H]^+$ $C_{65}H_{41}N_8O_{14}$ m/z 1157.2742, found: 1157.2799. UV–vis (CH_2Cl_2) λ_{max} (log ε) 418 (5.89), 513 (4.51), 548 (4.09), 591 (3.88), 649 (3.76) nm.

4.1.8. Bisporphyrin 1d. This compound was synthesized and characterized as previously reported.[33]

4.1.9. Porphyrin 1e. Trimer **3d** (20.3 mg, 0.02 mmol) was mixed with **2e** (2.5 mg, 0.02 mmol) and K_2CO_3 (11.0 mg, 0.08 mmol) in 5 mL of DMSO at room temperature under air for 40 min. HCl (0.1 M, 20 mL) was used to quench the reaction. The water layer was extracted with 50 mL of ethyl acetate, and the organic layer was washed once with water and dried over anhydrous Na_2SO_4. The resulting residue was purified by silica gel column chromatography using THF/hexane for elution. Porphyrin **1e** was obtained in 20% yield (4.5 mg). ^{1}H NMR (300 MHz, THF-d_8) δ 9.95 (br s, 1H), 9.06 (d, 2H, J=3.90 Hz), 8.93 (s, 2H), 8.84 (s, 4H), 8.71 (d, 2H, J=2.0 Hz), 8.20–8.28 (m, 6H), 8.13 (d, 2H, J=4.58 Hz), 7.79–7.81 (m, 9H), 7.61 (s, 1H), 6.86 (s, 2H), 6.75 (s, 1H), 6.70 (d, 2H, J=6.93 Hz), −2.75 (s, 2H). MALDI-TOF calcd for $[M+H]^+$ $C_{62}H_{36}N_8O_{13}$ m/z 1102.0, found: 1103.3. HRMS (ESI) calcd for $[M+H]^+$ $C_{62}H_{37}N_8O_{13}$ m/z 1101.2480, found: 1101.2545. UV–vis (CH_2Cl_2) λ_{max} (log ε) 417 (5.75), 513 (4.37), 548 (3.92), 591 (3.71), 646 (3.43) nm.

4.1.10. Porphyrin 1f. Hydrolysis of **1c** was achieved by dissolving **1c** (24.6 mg, 0.02 mmol) in 10 mL of THF, followed by addition of 4 M HCl (20 mL). The reaction mixture was refluxed at 60 °C in an oil bath for 3 days. After completion of the reaction, the mixture was extracted with ethyl acetate and the organic layer washed with brine. The resulting residue was purified by silica gel column chromatography using CH_2Cl_2/ethyl acetate (v/v=20/1) for elution. Pure porphyrin **1f** was obtained in 95% yield (21.5 mg) after recrystallization from CH_2Cl_2/hexane. ^{1}H NMR (300 MHz, THF-d_8) δ 8.97 (s, 1H), 8.93 (d, 2H, J=4.40 Hz), 8.83 (s, 6H), 8.77 (s, 2H), 8.21 (m, 6H), 8.14 (d, 2H, J=1.98 Hz), 8.03 (d, 2H, J=2.06 Hz), 7.79 (d, 9H), 7.53 (s, 1H), 7.49 (s, 1H), 6.87 (s, 2H), −2.74 (s, 2H). MALDI-TOF calcd for

$[M+H]^+$ $C_{63}H_{37}N_8O_{14}$ *m/z* 1129.2, found: 1130.2. HRMS (ESI) calcd for $[M+H]^+$ $C_{63}H_{37}N_8O_{14}$ *m/z* 1129.2429, found: 1129.2405. UV–vis (CH_2Cl_2) λ_{max} (log ε) 418 (5.43), 514 (3.90), 548 (3.32) nm.

4.1.11. 5,15-Di(3,5-dihydroxyphenyl)-10,20-di(3,5-di-*tert*-butylphenyl)porphyrin (5). 3,5-Dimethylbenzaldehyde (0.83 g, 5.0 mmol), 3,5-di-*tert*-butylbenzaldehyde (1.09 g, 5.0 mmol), and pyrrole (0.70 mL, 10 mmol) were mixed in a 2 L flask. Dry CH_2Cl_2 (1000 mL) was added and the solution was stirred for 10 min under argon before 0.4 mL of 2.5 M $BF_3\cdot OEt$ in CH_2Cl_2 was added. The reaction mixture was stirred under argon and in the dark for 2 h. DDQ (1.64 g) was added and the mixture stirred for 45 min. The reaction mixture was concentrated to give a residue that was purified by silica gel column chromatography using a mixture of hexane and CH_2Cl_2 for elution. The third eluted purple fraction contained 5,15-di(3,5-dimethoxyphenyl)-10,20-di(3,5-di-*tert*-butylphenyl)porphyrin. The solvent was removed under vacuum to give 192 mg (7.9% yield) of this porphyrin as a purple powder. MALDI-TOF-MS calcd for $[M+H]^+$ $C_{64}H_{71}N_4O_4$ *m/z* 960.25, found: 960.17. ^{1}H NMR ($CDCl_3$) δ 9.07 (d, 4H, J=4.70 Hz), 9.01 (d, 4H, J=4.70 Hz), 8.20 (d, 4H, J=1.68 Hz), 7.91–7.90 (m, 2H), 7.53 (d, 4H, J=2.24 Hz), 6.97–6.99 (m, 2H), 1.63 (s, 36H), −2.63 (s, 2H). To a solution of 5,15-di(3,5-dimethoxyphenyl)-10,20-di(3,5-di-*tert*-butylphenyl)porphyrin (0.096 g, 0.1 mmol) in dry CH_2Cl_2 (20 mL) at −20 °C was added dropwise a solution of BBr_3 (0.3 mL, 3.1 mmol) in CH_2Cl_2 (1 mL) with vigorous stirring under argon over a period of 30 min. The reaction mixture was stirred at room temperature for 24 h and then poured into water and extracted with ethyl acetate (3×50 mL). The combined organic layers were washed successively with brine and aqueous $NaHCO_3$ solutions. The organic solution was dried over Na_2SO_4 and evaporated to dryness, giving the title porphyrin (82.7 mg, 0. 092 mmol) as purple crystals in 91.6% yield. MALDI-TOF-MS calcd for $[M+H]^+$ $C_{60}H_{63}N_4O_4$ *m/z* 904.14, found: 904.21. ^{1}H NMR (CD_2Cl_2) δ 9.04 (d, 4H, J=4.80 Hz), 8.90 (d, 4H, J=4.75 Hz), 8.70 (s, 4H), 8.15 (d, 4H, J=1.81 Hz), 7.96–7.94 (m, 2H), 7.26 (d, 4H, J=2.18 Hz), 6.84–6.82 (m, 2H), 1.56 (s, 36H), −2.75 (s, 2H).

4.1.12. Porphyrin 4. 5,15-Di(3,5-dihydroxyphenyl)-10,20-di(3,5-di-*tert*-butylphenyl)porphyrin **5** (36.1 mg, 0.04 mmol) was mixed with trimer **3c** (44.0 mg, 0.08 mmol) and K_2CO_3 (33.6 mg, 0.24 mmol) in 10 mL of DMSO at room temperature under air for 3 h. Dilute HCl (0.1 M×40 mL) was used to quench the reaction and ethyl acetate (2×25 mL) was used to extract the water layer. The resulting organic phase was dried over anhydrous Na_2SO_4 and purified by alumina column chromatography using CH_2Cl_2/ethyl acetate (v/v=100/1) for elution. Porphyrin **4** was obtained in 84% yield (64.7 mg). ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.95 (br s, 8H), 8.46 (br s, 4H), 8.09 (s, 4H), 8.05 (d, J=1.86 Hz, 4H), 8.02 (d, J=1.82 Hz, 4H), 7.92 (s, 2H), 7.25 (br s, 4H), 6.49 (s, 4H), 3.98–4.06 (m, 4H), 1.56 (s, 36H), 1.27 (t, 6H). MALDI-TOF-MS calcd for $[M+H]^+$ $C_{102}H_{83}N_{12}O_{28}$ *m/z* 1923.5, found: 1923.1. HRMS (ESI) calcd for $[M+H]^+$ $C_{102}H_{83}N_{12}O_{28}$ *m/z* 1923.5440, found: 1923.5460. UV–vis (CH_2Cl_2) λ_{max} (log ε) 422 (5.79), 518 (4.40), 553 (4.08), 592 (3.87), 650 (3.85) nm.

4.1.13. Molecular structures. The crystal structure of trimer **3c** was determined using data collected at T=150 K to θ=31.5° with Mo Kα radiation on a Nonius KappaCCD diffractometer. The X-ray crystallographic data for **3c** can be found in supplementary publication CCDC-626294 available from the Cambridge Crystallographic Data Centre.

Acknowledgements

The work described was supported by the National Science Foundation, grant number CHE-304833.

References and notes

1. Dismukes, G. C. *Science* **2001**, *292*, 447–448.
2. Tommos, C.; Babcock, G. T. *Acc. Chem. Res.* **1998**, *31*, 18–25.
3. Yocum, C. F.; Pecoraro, V. L. *Curr. Opin. Chem. Biol.* **1999**, *3*, 182–187.
4. (a) Dawson, J. H. *Science* **1988**, *240*, 433–439; (b) Sono, M.; Roach, M. P.; Coulter, E. D.; Dawson, J. H. *Chem. Rev.* **1996**, *96*, 2841–2887.
5. Ozaki, S.-I.; Roach, M. P.; Matsui, T.; Watanbe, Y. *Acc. Chem. Res.* **2001**, *34*, 818–825.
6. Chang, C. J.; Chng, L. L.; Nocera, D. G. *J. Am. Chem. Soc.* **2003**, *125*, 1866–1876.
7. Mims, M. P.; Porras, A. G.; Olson, J. S.; Noble, R. W.; Peterson, J. A. *J. Biol. Chem.* **1983**, *258*, 14219–14232.
8. Rohlfs, R. J.; Mathaws, A. J.; Carver, T. E.; Olson, J. S.; Springer, B. A.; Egeberg, K. D.; Sligar, S. G. *J. Biol. Chem.* **1990**, *265*, 3168–3176.
9. Momenteau, M.; Reed, C. A. *Chem. Rev.* **1994**, *94*, 659–698.
10. Chang, C. K.; Kondylis, M. P. *J. Chem. Soc., Chem. Commun.* **1986**, 316–318.
11. Chang, C. J.; Brown, J. D. K.; Chang, M. C. Y.; Baker, E. A.; Nocera, D. G. *Electron Transfer in Chemistry*; Balzani, V., Ed.; Wiley-VCH: Weinheim, Germany, 2001; Vol. 3.2.4, pp 409–461.
12. (a) Deng, Y.; Roberts, J. A.; Peng, S.-M.; Chang, C. K.; Nocera, D. G. *Angew. Chem., Int. Ed.* **1997**, *36*, 2124–2127; (b) Cukier, R. I.; Nocera, D. G. *Annu. Rev. Phys. Chem.* **1998**, *49*, 337–369.
13. Chang, C. K.; Liang, Y.; Aviles, G. *J. Am. Chem. Soc.* **1995**, *117*, 4191–4192.
14. Liu, S. Y.; Nocera, D. G. *J. Am. Chem. Soc.* **2005**, *127*, 5278–5279.
15. (a) Yeh, C. Y.; Chang, C. J.; Nocera, D. G. *J. Am. Chem. Soc.* **2001**, *123*, 1513–1514; (b) Chang, C. J.; Yeh, C. Y.; Nocera, D. G. *J. Org. Chem.* **2002**, *67*, 1403–1406; (c) Chng, L. L.; Chang, C. J.; Nocera, D. G. *Org. Lett.* **2003**, *5*, 2421–2424.
16. Zhang, X. X.; Lippard, S. J. *J. Org. Chem.* **2000**, *65*, 5298–5305.
17. Liang, Y.; Chang, C. K. *Tetrahedron Lett.* **1995**, *36*, 3817–3820.
18. Chang, C. K.; Bag, N.; Guo, B. M.; Peng, S. M. *Inorg. Chim. Acta* **2003**, *351*, 261–268.
19. Arimura, T.; Brown, C. T.; Springs, S. L.; Sessler, J. L. *Chem. Commun.* **1996**, 2293–2294.
20. König, B.; Fonseca, M. H. *Eur. J. Inorg. Chem.* **2000**, 2303–2310.
21. Lhoták, P. *Eur. J. Org. Chem.* **2004**, 1675–1692.
22. Chambers, R. D.; Hoskin, P. R.; Kenwright, A. R.; Khalil, A.; Richmond, P.; Sandford, G.; Yufit, D. S.; Howard, J. A. K. *Org. Biomol. Chem.* **2003**, *1*, 2137–2147.

23. Li, X.; Upton, T. G.; Gibb, C. L. D.; Gibb, B. C. *J. Am. Chem. Soc.* **2003**, *125*, 650–651.
24. (a) Wang, M.-X.; Yang, H.-B. *J. Am. Chem. Soc.* **2004**, *126*, 15412–15422; (b) Wang, M.-X.; Zhang, X.-H.; Zheng, Q.-Y. *Angew. Chem., Int. Ed.* **2004**, *43*, 838–842.
25. Yang, F.; Yan, L.; Ma, K.; Yang, L.; Li, J.; Chen, L.; You, J. *Eur. J. Org. Chem.* **2006**, 1109–1112.
26. Sommer, N.; Staab, H. A. *Tetrahedron Lett.* **1966**, *25*, 2837–2841.
27. Lehmann, F. P. A. *Tetrahedron* **1974**, *30*, 727–733.
28. Gilbert, E. E. *J. Heterocycl. Chem.* **1974**, *11*, 899–904.
29. Bottino, F.; Foti, S.; Pappalardo, S. *Tetrahedron* **1976**, *32*, 2567–2570.
30. (a) Katz, J. L.; Feldman, M. B.; Conry, R. R. *Org. Lett.* **2005**, *7*, 91–94; (b) Katz, J. L.; Geller, B. J.; Conry, R. R. *Org. Lett.* **2006**, *8*, 2755–2758; (c) Katz, J. L.; Selby, K. J.; Conry, R. R. *Org. Lett.* **2005**, *7*, 3505–3507.
31. Maes, W.; Rossom, W. V.; Hecke, K. V.; Meervelt, L. V.; Dehaen, W. *Org. Lett.* **2006**, *8*, 4161–4164.
32. Konishi, H.; Tanaka, K.; Teshima, Y.; Mita, T.; Morikawa, O.; Kobayashi, K. *Tetrahedron Lett.* **2006**, *47*, 4041–4044.
33. Hao, E.; Fronczek, F. R.; Vicente, M. G. H. *J. Org. Chem.* **2006**, *71*, 1233–1236.
34. For reversibility in thiocalixarene formation by nucleophilic substitution, see: Freund, T.; Kübel, C.; Baumgarten, M.; Enkelmann, V.; Gherghel, L.; Reuter, R.; Müllen, K. *Eur. J. Org. Chem.* **1998**, *63*, 555–564.
35. Tanaka, T.; Endo, K.; Aoyama, Y. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 907–916.
36. Lindsey, J. S.; Schreiman, I. C.; Hsu, H. C.; Kearney, P. C.; Marguerettaz, A. M. *J. Org. Chem.* **1987**, *52*, 827–836.
37. Jollife, K. A.; Langford, S. J.; Oliver, A. M.; Shephard, M. J.; Paddon-Row, M. N. *Chem.—Eur. J.* **1999**, *5*, 2518–2530.
38. Parusel, A. *J. Mol. Model.* **1998**, *4*, 366–378.
39. Hermann, D. T.; Schindler, A. C.; Polborn, K.; Gompper, G.; Stark, S.; Parusel, A.; Grabner, G.; Kohler, G. *Chem.—Eur. J.* **1999**, *5*, 3208–3220.
40. Odobel, F.; Suresh, S.; Blart, E.; Nichlas, Y.; Quintard, J.-P.; Janvier, P.; Questel, J.-Y.; Illien, B.; Rondeau, D.; Richomme, P.; Haupl, T.; Wallin, S.; Hammarstrom, L. *Chem.—Eur. J.* **2002**, *8*, 3027–3046.
41. Fery-Forgues, S.; Lavabre, D. *J. Chem. Educ.* **1999**, *76*, 1260–1264.
42. Thorn, M. A.; Denny, G. H.; Babson, R. D. *J. Org. Chem.* **1975**, *40*, 1556–1558.
43. Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon: Oxford, 1988.
44. Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902–3909.
45. *Spartan, version 2.0*; Wavefunction: Irvine, CA, 2001.