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Synthesis of Oxacalixarene-Locked Bisporphyrins and Higher Oligomers

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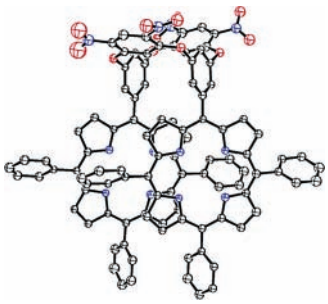

The efficient one-step synthesis of oxacalixarene-bisporphyrins and higher oligomers from readily available starting materials is described. The X-ray structure of one oxacalix[4]arene-locked cofacial bisporphyrin, prepared in 91% yield, shows an 1,3-alternate conformation of the molecule with partial overlap of the two porphyrin rings. ^{1}H NMR data supports a similar conformation in solution. The absorption and emission spectra of oxacalixarene-porphyrins are briefly discussed.

Multiporphyrin arrays have attracted much recent interest because they play important biological roles in diverse areas such as in light harvesting,[1] energy and electron transfer,[2] and multielectron redox catalysis.[3] Among the covalently linked porphyrin arrays, cofacial porphyrins (e.g., the so-called Pacman systems) have been the most investigated in the past decade.[4,5] However, the synthesis of cofacial porphyrins and cyclic porphyrin arrays[6,7] is still a challenge because they involve long reaction sequences and result in low overall yields. Calixarenes have also been extensively studied in the past decade because of their unique conformational flexibilities and recognition properties.[8] In particular, heteroatom-bridged calixarenes, such as the oxygen-bridged calix[4]arenes, are of special interest because they display unique chemical and physical properties.[9] Nevertheless the efficient availability of this type of compound in large amounts is still limited, and no large macrocycles, such as oxacalix[6]arene and oxacalix[8]arene, have yet been reported in the literature.

Porphyrin-calixarene conjugates have been previously synthesized by several groups and shown to have high conformational flexibility.[10−12] Because oxacalix[4]arenes usually adopt discrete 1,3-alternate conformations, we envisioned the design and synthesis of oxacalixarene-locked cofacial bisporphyrins and higher oligomers. Herein, we describe an efficient one-step synthesis and X-ray structure of a novel oxacalix[4]arene-locked cofacial bisporphyrin (**1**). We also report, for the first time, the formation of an oxacalix[6]arene **2** and an oxacalix[8]arene **3**, accessed by variation of the reaction conditions that give **1**.

As shown in Scheme 1, bisporphyrin **1** can be efficiently prepared in 91% yield by simply mixing equimolar amounts of **4** and **5** with finely ground K_2CO_3 (<80 μm) in DMSO at room temperature and atmospheric pressure. The reaction is complete in less than 20 min, and the product is purified simply by filtration through a pad of silica gel, eluting with dichloromethane. The starting porphyrin **4** was prepared in multigram scale by a mixed aldehyde condensation in propionic acid, followed by demethylation with BBr_3 in dichloromethane.[13] Unexpectedly, when the demethylation was carried out in pyridine hydrochloride at 200 °C under air, porphyrin **6** (bearing a fused five membered-ring between an *o*-phenyl and adjacent β-positions) was isolated in 84% yield, probably as a result of oxidation by air after cyclization. A similar reaction has been recently achieved via intramolecular Pd(0) catalysis.[14]

When granular K_2CO_3 (>250 μm) was used in the above reaction, macrocycles **2** and **3** were also formed, as detected by mass spectrometry (see Figure S1 in Supporting Information). Flash column separation of the mixture gave a 62% yield of bisporphyrin **1**, 21% of **2**, and 4% of **3**. Under high dilution conditions (0.1 mM) and/or in the presence of granular Na_2CO_3, similar yields of **1**−**3** were obtained. Using acetone

(1) (a) For a recent review: Choi, M.-S.; Yamazaki, T.; Yamazaki, I.; Aida, T. *Angew. Chem., Int. Ed.* **2004**, *43*, 150−158, (b) Recent example: Kuramochi, Y.; Satake, A.; Kobuke, Y. *J. Am. Chem. Soc.* **2004**, *126*, 8668−8669.

(2) Recent example: Faure, S.; Stern, C.; Guilard, R.; Harvey, P. D. *J. Am. Chem. Soc.* **2004**, *126*, 1253−1261.

(3) Recent example: Chang, C. J.; Loh, Z.-H.; Shi, C.; Anson, F. C.; Nocera, D. G. *J. Am. Chem. Soc.* **2004**, *126*, 10013−10020.

(4) Collman, J. P.; Wagenknecht, P. S.; Hutchison, J. E. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1537−1554.

(5) (a) Chng, L. L.; Chang, C. J.; Nocera, D. G. *J. Org. Chem.* **2003**, *68*, 4075−4078, (b) Fletcher, J. T.; Therien, M. J. *J. Am. Chem. Soc.* **2000**, *122*, 12393−12394, (c) Deng, Y.; Chang, C. J.; Nocera, D. G. *J. Am. Chem. Soc.* **2000**, *122*, 410−411, (d) Clement, T. E.; Nurco, D. J.; Smith, K. M. *Inorg. Chem.* **1998**, *37*, 1150−1160.

(6) Sanders, J. K. M. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, CA, 2000; Vol. 3, pp 347−368.

(7) Li, J.; Ambroise, A.; Yang, S. I.; Diers, J. R.; Seth, J.; Wack, C. R.; Bocian, D. F.; Holten, D.; Lindsey, J. S. *J. Am. Chem. Soc.* **1999**, *121*, 8927−8940.

(8) *Calixarenes 2001*; Asfari, Z., Böhmer, V., Harrowfiled, J., Vicens, J., Saadipui, M. Eds.; Kluwer Academic Publishers: The Netherlands, 2001.

(9) (a) For a review, see: König, B.; Fonseca, M. H. *Eur. J. Inorg. Chem.* **2000**, 2303−2310, (b) Lhoták, P. *Eur. J. Org. Chem.* **2004**, 1675−1692, (c) Wang, M.-X.; Yang, H.-B. *J. Am. Chem. Soc.* **2004**, *126*, 15412−15422, (d) Katz, J. L.; Feldman, M. B.; Conry, R. R. *Org. Lett.* **2005**, 91−94.

(10) (a) Khoury, R. G.; Jaquinod, L.; Aoyagi, K.; Olmstead, M. M.; Fisher, A. J.; Smith, K. M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2497−2500, (b) Jokic, D.; Asfari, Z.; Weiss, J. *Org. Lett.* **2002**, *4*, 2129−2132.

(11) (a) Tremblay-Morin, J.-P.; Faure, S.; Samar, D.; Stern, C.; Guilard, R.; Harvey, P. D. *Inorg. Chem.* **2005**, *44*, 2836−2842, (b) Baldini, L.; Ballester, P.; Casnati, A.; Gomila, R. M.; Hunter, C. A.; Sansone, F.; Ungaro, R. *J. Am. Chem. Soc.* **2003**, *125*, 14181−14189.

(12) Di Costanzo, L.; Geremia, S.; Randaccio, L.; Purrello, R.; Lauceri, R.; Sciotto, D.; Gulino, F. G.; Pavone, V. *Angew. Chem., Int. Ed.* **2001**, *40*, 4245−4247.

(13) Tanaka, T.; Endo, K.; Aoyama, Y. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 907−916.

(14) Fox, S.; Boyle, R. W. *Chem. Commun.* **2004**, 1322−1323.

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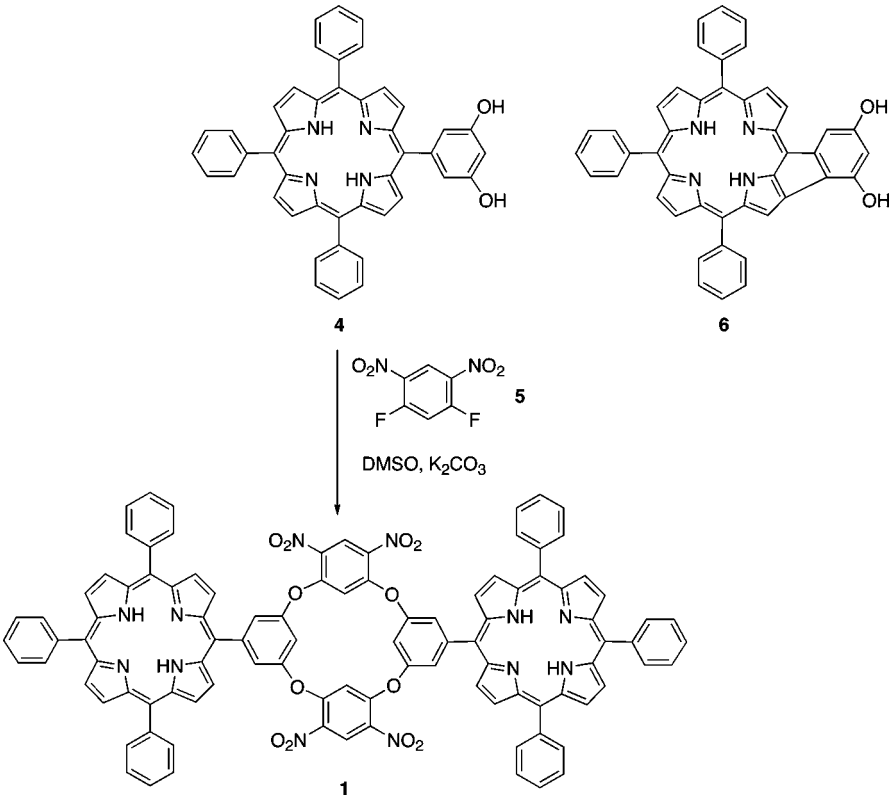
SCHEME 1. Synthesis of Bisporphyrin 1 and Chemical Structure of Porphyrin 6



in place of DMSO and either granular or finely ground K_2CO_3 gave compounds **1**, **2**, and **3** after longer reaction times (~10 h for complete disappearance of starting porphyrin by TLC). To the best of our knowledge, compounds **2** and **3** are the first examples of oxacalix[6]arene and oxacalix[8]arene and concomitantly are rare examples of heteroatom-bridged calix[6]-arenes (**2**) and calix[8]arenes (**3**). Interestingly, when porphyrin **6** reacted with **5** under the same conditions (DMSO, granular K_2CO_3), higher yields were isolated for the larger macrocycles: 45% of oxacalix[4]arene **7**, 27% of oxacalix[6]arene **8**, and 15% of oxacalix[8]arene **9** (see Supporting Information). Trace amounts of even larger macrocycles (oxacalix[10]arene and oxacalix[12]arene) were also detected by MALDI-TOF. The formation of the larger macrocycles is favored by reaction conditions that promote macrocyclic $\pi-\pi$ interactions; the use of granular versus finely ground K_2CO_3 and of acetone in place of DMSO are likely to increase the tendency for $\pi-\pi$ interactions. Steric hindrance may be also one of the reasons for the formation of larger macrocycles in this reaction and explains the higher yields obtained for the larger macrocycles from porphyrin **6**.

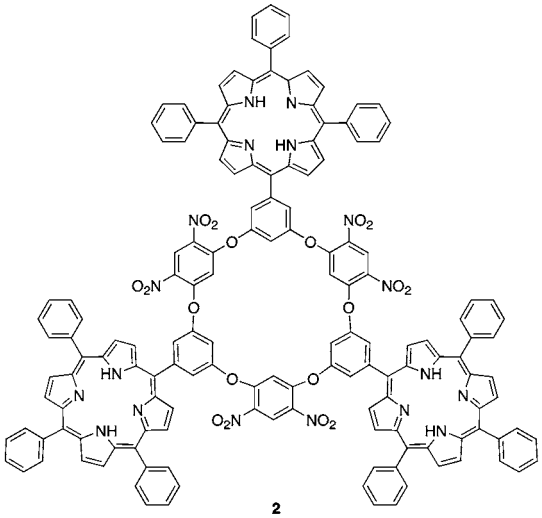
Small purple crystals of **1** were grown by slow diffusion of hexane into dichloromethane solution. Figure 1 shows the molecular structure of **1** (see Supporting Information). As expected, the oxacalix[4]arene adopts a 1,3-alternate conformation, with the two rings carrying nitro groups forming a dihedral angle of 60.6(2)°, and the two rings carrying porphyrins more nearly parallel, forming a dihedral angle of 8.7(3)°. The two porphyrin ring systems are thus also nearly parallel, forming a dihedral angle of 2.8(7)°. The two porphyrins have a plane-to-plane distance of 3.81 Å but are not perfectly face-to-face, being slipped by 4.11 Å, such that the N_4 centroid$-N_4$ centroid distance is 5.60 Å. Thus, they overlap minimally, similar to that seen in the special pair of the photoreaction center.[15] As can be seen in Figure 1 (side view), the porphyrins are not individually planar but twisted, showing deviations of up to 0.4 Å from their 24-atom best planes. This geometry may be the result of steric hindrance and the electrostatic π-stacking interactions of the two pendant porphyrins. Insertion of zinc(II) into compounds **1**, **2**, and **3** gave, in quantitative yields, the corresponding **1Zn$_2$**, **2Zn$_3$**, and **3Zn$_4$** derivatives. Compound **1H$_2$Zn** was also prepared in 29% yield by mono-metalation of bisporphyrin **1** using zinc(II) acetate in dilute solution.

^{1}H NMR analysis provided information about the structure of **1**, **1H$_2$Zn**, and **1Zn$_2$** in solution (see Supporting Information). The unusual high-field chemical shifts observed for the interior protons on the electrophilic aromatic rings (6.98 ppm for **1**, 6.99 ppm for **1H$_2$Zn**, and 7.11 ppm for **1Zn$_2$**) indicate a 1,3-alternate conformation of the oxacalix[4]arenes. However, the ^{1}H NMR spectra of **1**, **1H$_2$Zn**, and **1Zn$_2$** only show part of the expected number of signals for the porphyrin rings, which indicates the flexibility of these molecules; a very rapid (on the NMR time-scale) switching between conformations likely occurs in solution at room temperature.[16]

The electronic absorption spectrum of **1** (Supporting Information, Figure S2) shows a slightly split Soret band at ~406 and 416 nm in THF, whereas the absorption spectra of **2** and **3** (Supporting Information, Figure S3) show little electronic coupling between the porphyrin rings. Interestingly, porphyrin **6** shows a triply split Soret band, and its oxacalixarenes **7**, **8**, and **9** show strong electronic interactions (Supporting Information, Figure S4) due to their more rigid conformations.

(15) Deisenhofer, J.; Ep, O.; Miki, K.; Huber, R.; Michel, H. *Nature (London)* **1985**, *318*, 618−624.

(16) Osuka, A.; Nakajima, S.; Nagata, T.; Maruyama, K.; Toriumi, K. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 582−584.



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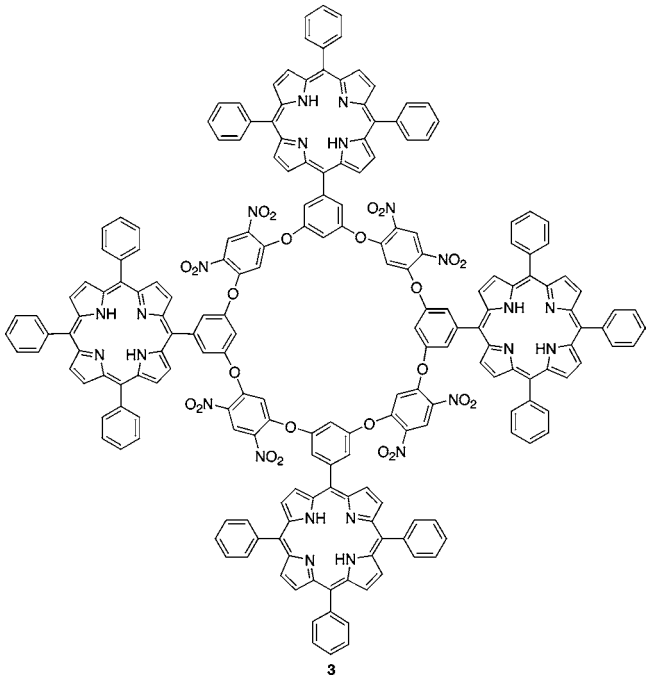

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Compounds **1**−**3** display strong fluorescence emissions at ∼650 and 720 nm. However, whereas **1H$_2$Zn** and **1Zn$_2$** exhibit strong fluorescence (Supporting Information, Figure S5), **2Zn$_3$** and **3Zn$_4$** show much weaker emissions (Supporting Information, Figure S6). Similar fluorescence quenching characteristics were found for the free-base oxacalixarenes **7**, **8**, and **9** and may indicate intermolecular aggregation, for which there is precedent.[10a]

In conclusion, oxacalixarene-bisporphyrins and higher oligomers can be synthesized in a single step, in high yields. This methodology is general for the preparation of a variety of cofacial multiporphyrin architectures, which will find applications in the area of multielectron redox catalysis and energy transfer.

Experimental Section

Commercially available anhydrous potassium carbonate (ACS grade) was further dried at 140 °C for 2 days prior to use. Granular anhydrous K_2CO_3 containing particle sizes larger than 250 μm was obtained by sieving dried commercially available K_2CO_3. Finely ground anhydrous K_2CO_3 containing particle sizes smaller than 80 μm, was obtained by grinding and sieving dried commercially available K_2CO_3. The synthesis of 5-(3,5-dimethoxyphenyl)-10,15,20-triphenylporphyrin and its demethylation were performed according to the literature procedure.[13]

Synthesis of Oxacalixarene Bisporphyrin 1. Porphyrin **4** (59.0 mg, 0.09 mmol), 1,5-difluoro-2,4-dinitrobenzene (18.6 mg, 0.09 mmol), and finely ground anhydrous K_2CO_3 (50.4 mg, 0.36 mmol) were combined in a 50-mL round-bottom flask. DMSO (10 mL) was added, and the reaction mixture was stirred vigorously for 1 h at room temperature and under atmospheric pressure. The reaction mixture was then partitioned between ethyl acetate (100 mL) and brine (100 mL). The resulting mixture was separated, and the aqueous layer was extracted until colorless. The combined organic layers were dried over anhydrous $NaSO_4$, filtered, and concentrated under vacuum. The resulting residue was purified by filtration through a pad of silica gel eluting with dichloromethane. The bisporphyrin fraction was collected, concentrated, and recrystallized from dichloromethane/hexane. The purple crystals were dried under vacuum, giving 67.1 mg (90.5% yield) of bisporphyrin **1**. HRMS (MALDI-TOF) *m*/*z* 1622.4569 $[M + H]^+$, calcd for $C_{100}H_{61}N_{12}O_{12}$ 1622.4563. Anal. Calcd for $C_{100}H_{60}N_{12}O_{12}\cdot 2H_2O$: C, 72.40; H, 3.95; N, 10.14. Found: C, 72.39; H, 3.94; N, 9.98. ^{1}H NMR ($CDCl_3$) δ 9.09 (s, 2H), 8.60−8.91 (br, 8H), 8.23 (m, 8H), 7.80 (m, 6H), 7.53 (s, 2H), 6.98 (s, 2H), −3.20 (s, 4H). UV−vis (THF) λ_{max} (log ϵ) 406 (5.4), 416 (5.4), 516 (4.2), 551 (3.9), 593 (3.8), 650 (3.5) nm.

Synthesis of Oxacalixarenes 2 and 3. The synthesis of **2** and **3** is similar to that of bisporphyrin **1** except for the use of granular K_2CO_3 (particle size > 250 μm) in place of finely ground K_2CO_3 (particle size < 80 μm) (see Figure S1). Porphyrin **4** (59.1 mg, 0.09 mmol), 1,5-difluoro-2,4-dinitrobenzene (18.6 mg, 0.09 mmol), and granular anhydrous K_2CO_3 (51.0 mg, 0.36 mmol) were combined in a 20-mL flask. DMSO (10 mL) was added, and the reaction mixture was stirred for 3 h at room temperature under atmospheric pressure. After the extractions, as described above, the mixture was purified by column chromatography on silica gel. Three fractions were collected: first, oxacalixarene **2** eluted using dichloromethane/hexane 5:1, followed by oxacalixarene **3** and finally bisporphyrin **1**, eluted using dichloromethane. Recrystallization from dichloromethane/hexane gave oxacalixarene **2** in 21% yield, oxacalixarene **3** in 4%, and bisporphyrin **1** in 62%. For oxacalixarene **2**: HRMS (MALDI-TOF) *m*/*z* 2430.6753, calcd for $C_{150}H_{90}N_{18}O_{18}$ 2430.6779. Anal. Calcd for $C_{150}H_{90}N_{18}O_{18}\cdot 2H_2O$: C, 72.97; H, 3.84; N, 10.21. Found: C, 72.80; H, 3.75; N, 10.09. $_1$H NMR (CD_2Cl_2/TFA) δ 9.27 (s, 3H), 8.90 (m, 6H), 8.69−8.75 (m, 18H), 8.52 (br, 6H), 8.43 (br, 12H), 8.37 (s, 6H), 8.04 (br, 9H), 7.93 (br, 18H), 7.66 (s, 3H), 7.32 (s, 3H). UV−vis (THF) λ_{max} (log ϵ) 417 (5.8), 514 (4.5), 547 (4.1), 590 (3.9), 647 (3.7) nm. For oxacalixarene **3**: HRMS (MALDI-TOF) *m*/*z* 3241.9020, calcd for $C_{200}H_{120}N_{24}O_{24}$ 3241.8983. Anal. Calcd for $C_{200}H_{120}N_{24}O_{24}$: C, 74.07; H, 3.88; N, 10.36. Found: C, 73.70; H, 3.88; N, 10.12. ^{1}H NMR (CD_2Cl_2) δ 8.63−8.67 (m, 16H), 8.38 (br, 8H), 8.28 (br, 8H), 8.10 (d, 8H, J = 6.9 Hz), 7.74−7.80 (m, 24H), 7.07−7.40 (m, 36H), 6.93 (br, 12H), −3.21 (s, 8H). UV−vis (THF) λ_{max} (log ϵ) 417 (6.0), 514 (4.7), 548 (4.3), 591 (4.1), 647 (3.9) nm.

Synthesis of Metal Complexes 1Zn$_2$, 2Zn$_3$, and 3Zn$_4$. Zinc(II) insertion into **1**, **2**, and **3** was performed in refluxing chloroform/methanol (v/v = 9/1) using excess zinc(II) acetate. The complexes **1Zn$_2$**, **2Zn$_3$**, and **3Zn$_4$** were obtained in quantitative yields. For **1Zn$_2$**: HRMS (MALDI-TOF) *m*/*z* 1748.2728, calcd for $C_{100}H_{56}N_{12}O_{12}Zn_2$ 1748.2715. Anal. Calcd for $C_{100}H_{56}N_{12}O_{12}Zn_2.2CH_3OH$: C, 67.59; H, 3.56; N, 9.28. Found: C, 67.65; H, 3.61; N, 9.14. ^{1}H NMR (THF-d_8) δ 9.06 (s, 2H), 8.71 (b, 8H), 8.41 (m, 4H), 8.23 (m, 6H), 7.83 (s, 2H), 7.78 (m, 6H), 7.11 (s, 2H). UV−vis (THF) λ_{max} (log ϵ) 421 (5.6), 557 (4.4), 598 (3.9) nm. For **2Zn$_3$**: HRMS (MALDI-TOF) *m*/*z* 2618.4257, calcd

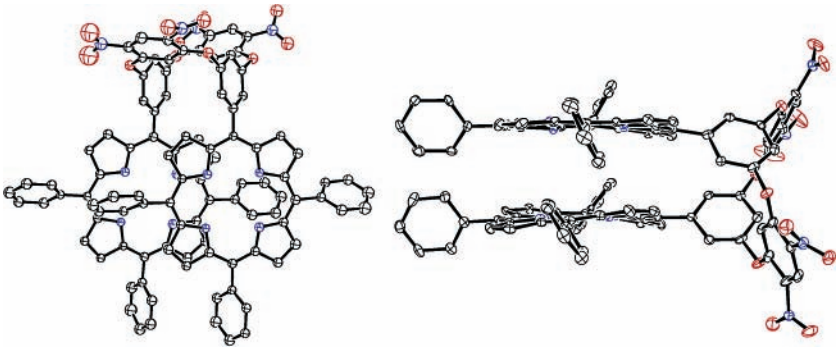

FIGURE 1. Two views of the X-ray structure of **1**. H atoms and solvent ($CHCl_3$) molecules are not included. The lowest NO_2 group in the right view is disordered into two orientations, only one of which is shown.

for $C_{150}H_{85}N_{18}O_{18}Zn_3$ 2618.4193. Anal. Calcd for $C_{150}H_{84}N_{18}O_{18}\cdot CH_2Cl_2$: C, 66.98; H, 3.20; N, 9.30. Found: C, 66.75; H, 3.45; N, 8.85. ^{1}H NMR (THF-d_8) δ 9.03 (s, 3H), 8.95 (d, 6H, J = 4.5 Hz), 8.76 (d, 6H), 8.69 (d, 12H, J = 3.5 Hz), 8.12 (m, 6H), 8.02 (s, 6H), 7.92 (br, 12H), 7.87 (s, 3H), 7.72 (m, 9H), 7.69 (s, 3H), 7.40 (m, 18H). UV−vis (THF) λ_{max} (log ϵ) 424 (5.8), 556 (4.7), 595 (4.2) nm. For **3Zn$_4$**: HRMS (MALDI-TOF) *m*/*z* 3497.5405, calcd for $C_{200}H_{112}N_{24}O_{24}Zn_4$ 3497.5444. Anal. Calcd for $C_{200}H_{112}N_{24}O_{24}Zn_4\cdot CHCl_3\cdot H_2O$: C, 66.43; H, 3.19; N, 9.25. Found: C, 66.07; H, 3.42; N, 9.00. ^{1}H NMR (THF-d_8) δ 10.87 (s, 4H), 8.83 (d, 8H, J = 4.4 Hz), 8.69 (d, 8H, J = 4.4 Hz), 8.58 (br, 16H), 8.09 (m, 8H), 7.90 (s, 8H), 7.69 (m, 24H), 7.61 (br, 4H), 7.45 (br, 4H), 7.37 (m, 12H), 7.22 (br, 16H). UV−vis (THF) λ_{max} (log ϵ) 425 (6.0), 556 (4.8), 596 (4.3) nm.

Synthesis of 1H$_2$Zn. Bisporphyrin **1** (28.2 mg, 0.0174 mmol) was dissolved in dichloromethane (80 mL) and heated to reflux. Zinc(II) acetate (4.8 mg, 0.26 mmol) in methanol (10 mL) was added dropwise during 1 h, and the reaction was followed by TLC (R_f order: **1** > **1H$_2$Zn** > **1Zn$_2$**). The reaction was stopped after 4 h, and the solvents removed under vacuum. The residue was purified by column chromatography on silica gel using dichloromethane/hexane (v/v = 9/1) for elution. The second porphyrin band was collected and recrystallized from dichloromethane/hexane to give 8.5 mg (29% yield) of **1H$_2$Zn**. HRMS (MALDI-TOF) *m*/*z* 1683.3672, calcd for $C_{100}H_{59}N_{12}O_{12}Zn$ 1683.3666. Anal. Calcd for $C_{100}H_{58}N_{12}O_{12}Zn\cdot 2CH_3OH$: C, 70.04; H, 3.80; N, 9.60. Found: C, 70.02; H, 3.61; N, 9.29. ^{1}H NMR (THF-d_8) 9.06 (s, 2H), 8.68 (b, 8H), 8.45 (m, 8H), 8.24 (m, 6H), 7.89 (s, 2H), 7.80 (m, 12H), 6.99 (s, 2H), −3.09 (s, 2H). UV−vis (THF) λ_{max} (log ϵ) 417 (5.5), 516 (3.6), 556 (4.3), 597 (3.9), 648 (3.4) nm.

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Supporting Information Available: Crystallographic data (in CIF format) and X-ray data for bisporphyrin **1**, MALDI-TOF, ^{1}H NMR and UV−vis supplementary spectra, and detailed syntheses of compounds **6**−**9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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