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SYNTHESIS AND MOLECULAR STRUCTURE OF CYCLO[8](9,10-DIHYDRO-9,10-ANTHRACENO)PYRROLE

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Dedicated to Professor Victor Snieckus on the occasion of his 77th birthday

Abstract – Cyclo[8]pyrrole with eight 9,10-dihydroanthracene wings was synthesized by oxidative coupling of the corresponding 2,2'-bipyrrole in good yield. The molecular structure was determined by single crystal X-ray analysis. The three-dimensionally structured cyclo[8]pyrrole possessed a cavity created by a pair of slip-stacked cyclo[8]pyrroles.

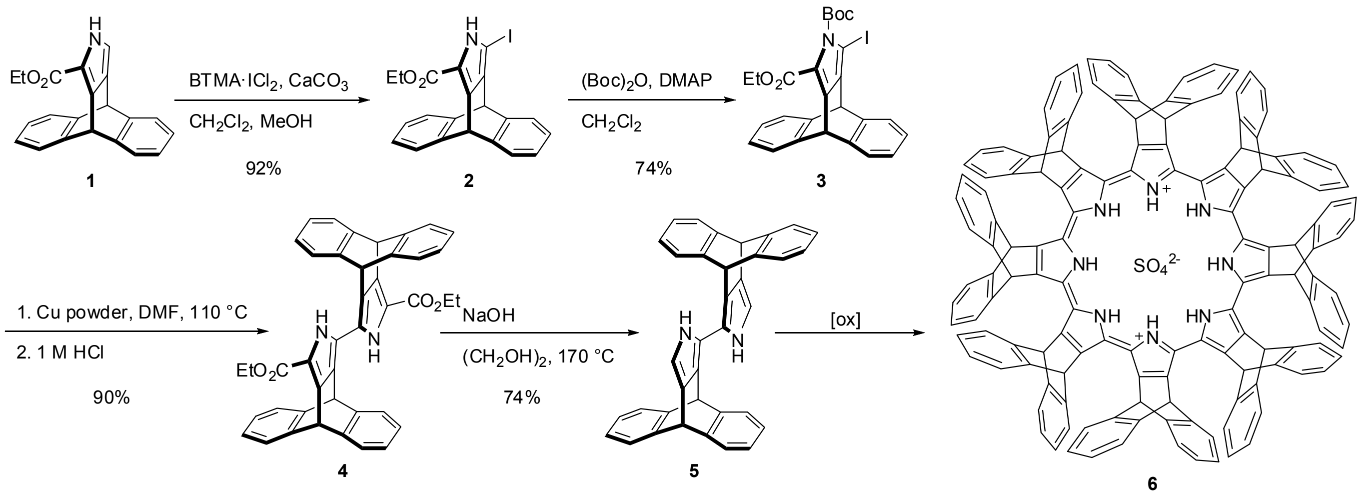
INTRODUCTION

Cyclo[n]pyrroles (n = 6, 7 and 8) belong to a family of ring-expanded porphyrins with no *meso*-bridges which was first reported as β-alkyl cyclo[8]pyrroles by Sessler and co-workers in 2002.[1] The photophysical, anion–binding and liquid crystal properties have been studied in-depth, along with their electronic structures.[2] Recently, some preparative examples of cyclo[8]pyrrole have been reported for derivatization at β-pyrrolic positions. For example, introduction of fused aromatic-rings resulted in the dramatic shift of the absorption bands, while the intense band was observed at around 1000 nm. The longest wavelength absorptions of cyclo[8]isoindole,[3] cyclo[4]naphthobipyrrole,[4] and cyclo[8]acenaphthopyrrole[5] appeared at 1078, 1334 and 1515 nm with large absorption coefficient, ε, respectively. On the other hand, Sessler has reported the liquid crystalline cyclo[8]pyrroles self-organized by donor–acceptor interaction with trinitrobenzenes or trinitrofluorenone in 2007.[2] We report herein the synthesis of biconcave cyclo[8]pyrrole, which possesses two wide cavities created by eight

9,10-dihydro-9,10-anthraceno moieties above and below porphyrin plane, for the purpose of the construction of the host–guest system by multi-pyrrolic macrocycles.

RESULTS AND DISCUSSION

The preparation of cyclo[8]pyrrole **6** is summarized in Scheme 1. Pyrrole **1** was prepared according to the literature procedure.[6] After iodination of **1** by treating with benzyltrimethylammonium dichloroiodate (BTMA·ICl_2), the protection of pyrrolic NH with di-*t*-butyl dicarbonate ($(Boc)_2O$) gave pyrrole **3**. Pyrrole **3** was dimerized by the Ullmann coupling reaction followed by deprotection with 1 M HCl and deesterification by heating with NaOH at 170 °C to give 2,2'-bipyrrole **5**. Oxidative coupling of **5** afforded cyclo[8]pyrrole **6**. Reaction conditions similar to those reported by Sessler[1] were adopted with a 1 M H_2SO_4 solution of $FeCl_3$ used as the oxidant. After purification by silica gel column chromatography and recrystallization, **6** was obtained in 61% yield as a sulfate similar to the reported cyclo[8]pyrroles (Table 1).[1–5] The MALDI–TOF mass spectrum displays molecular ion peaks at *m*/*z* 2026. Cyclo[8]pyrrole **6** was characterized by physical and spectral methods including the X-ray crystallographic analysis. The nitrosonium ion generated from $NaNO_2$ and acid was used as a mild oxidant to give **6** in 59% yield. When the reaction was carried out using $Ce(SO_4)_2$ as an oxidant together with H_2SO_4, Na_2SO_4, tetra(*n*-butyl)ammonium bisulfate ($TBAHSO_4$),[3] the best yield of 65% was obtained.



Scheme 1. Synthesis of cyclo[8]pyrrole **6**

Table 1. Oxidative homo-coupling of **5**

entry	oxidant	acid	additive	yield
1	$FeCl_3·6H_2O$	1 M H_2SO_4	none	61%
2	$NaNO_2$	conc. H_2SO_4	none	59%
3	$Ce(SO_4)_2$	conc. H_2SO_4	$TBAHSO_4$, Na_2SO_4	65%

A single crystal of **6** suitable for X-ray structure determination was obtained after recrystallization from $CHCl_3$/methanol. The crystal structure is shown in Figures 1 and 2, and the crystallographic data[7–10] are summarized in experimental section. Cyclo[8]pyrrole **6** crystallized in a monoclinic cell, space group $P2_1/c$ with $Z = 4$. The resulting structure was similar to those of bicyclo[2.2.2]octadiene-fused cyclo[8]pyrrole reported by our group[3] and β-alkyl substituted ones by Sessler's group.[1] Alternating pyrrole moieties tilt above and below the plane formed by the 16 α carbons with a mean deviation of 0.2133 Å. In contrast, displacements for bicyclo[2.2.2]octadiene-fused[3] and β-alkyl substituted[1] cyclo[8]pyrroles are 0.1891 and 0.4603 Å, respectively. Fused bicyclic-rings at β-pyrrolic positions resulted in a very flat conformation due to relatively small steric-hindrance between the neighboring bicyclo[2.2.2]octadiene moieties. Dihedral angles of 21.6–28.6° are observed between adjacent pyrrole moieties, while the inner SO_4^{2-} ion is bound by hydrogen-bonding interactions with NH···O distances ranging from 1.921 to 2.426 Å. Distances between the opposite anthracene wings are ca. 14.6 and 16.8 Å (Figure 2b). In the molecular packing, there is a cavity between the slip-stacked cyclo[8]pyrrole planes. The distance between these planes is ca. 8.3 Å as shown in Figure 2c. Although solvent molecules were caged in the similar cavity of tetrakis(6,13-dihydro-6,13-pentaceno)porphyrins,[11] no caged-solvent molecules were observed in this crystal.

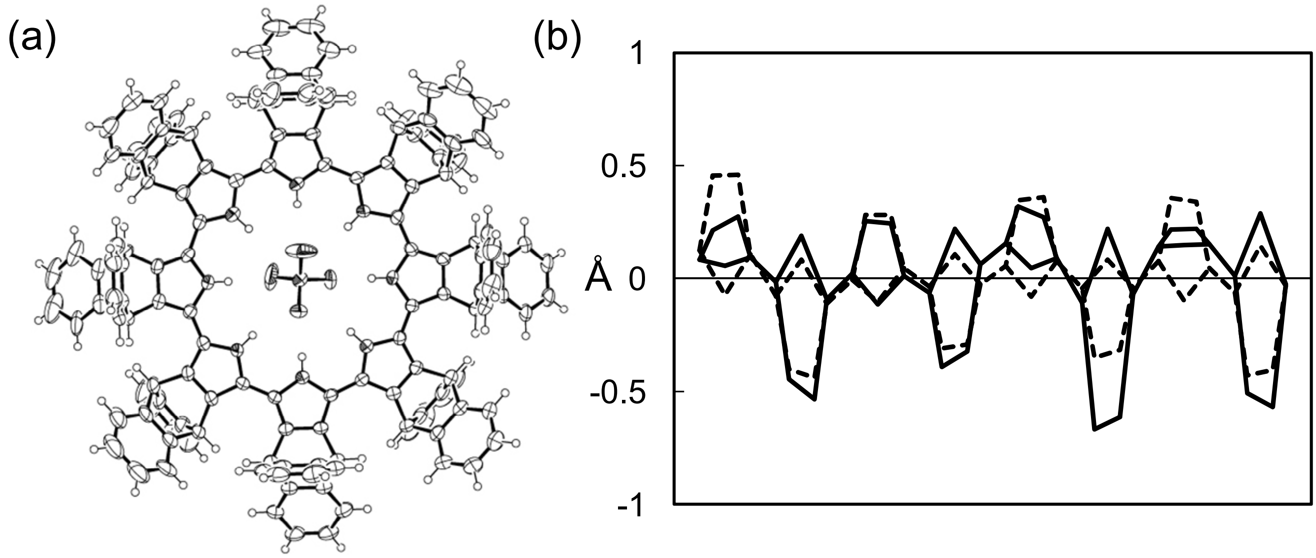


Figure 1. (a) ORTEP drawing of **6**. (b) Deviation from the mean cyclo[8]pyrrole planes of **6** (solid) and bicyclo[2.2.2]octadiene-fused cyclo[8]pyrrole[3] (dotted line)

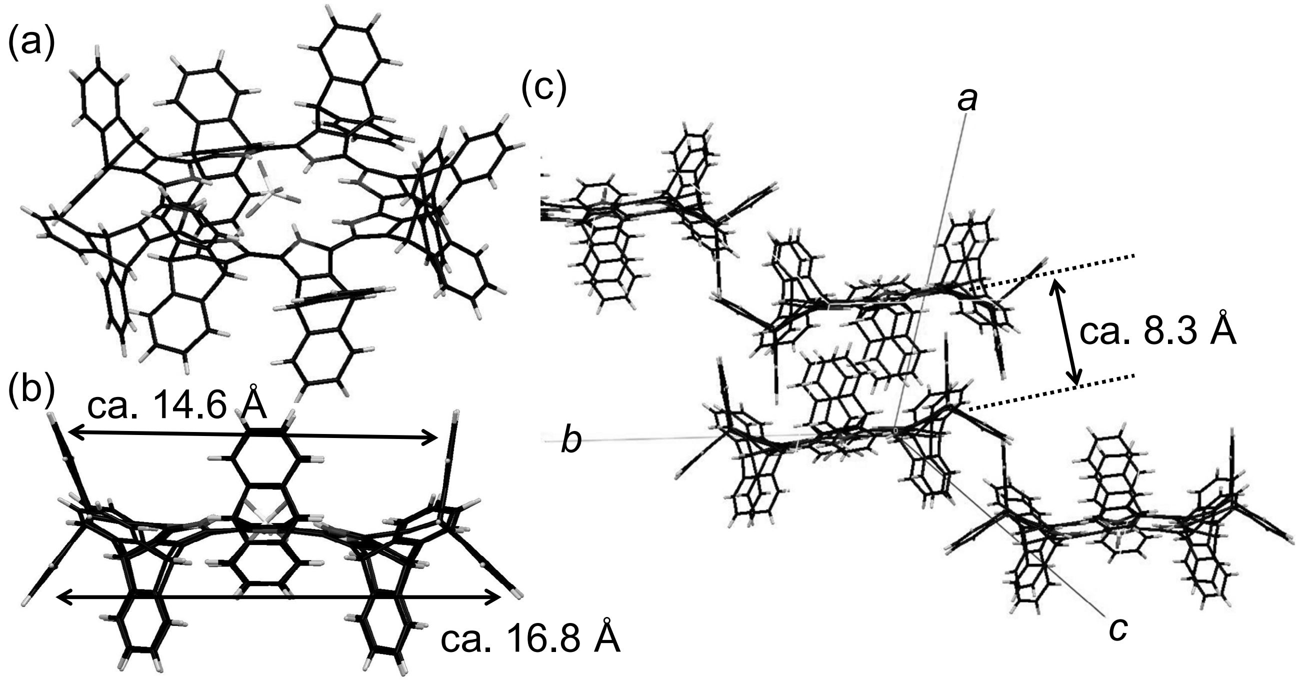


Figure 2. (a) Top and (b) side views and (c) packing diagram of **6**

The absorption spectrum of **6** is shown in Figure 3. The Soret and Q bands were observed at 467 nm (ε = 170,700 M^{-1} cm^{-1}) and 1087 nm (ε = 330,800 M^{-1} cm^{-1}). The Soret band was slightly blue-shifted whereas the Q band was red-shifted by ca. 50 nm compared to those of bicyclo[2.2.2]octadiene-fused cyclo[8]pyrrole. Inclusion behavior of **6** with π-systems in solution was examined by the measurement of the absorption spectra. When a solution of octaethylporphyrin (OEP) in $CHCl_3$ was added dropwise to this yellow solution of **6**, absorption spectra of OEP and **6** were observed independently. Novel absorptions arising from the formation of an adduct of **6** with OEP were not observed. Recrystallization from a 1 : 1 mixture in $CHCl_3$/methanol afforded only crystals of **6**. Crystals of **6** including OEP in their cavity were not obtained under these conditions.

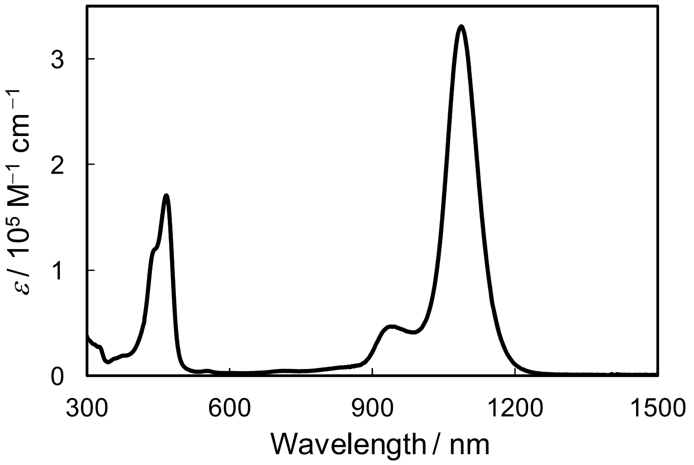


Figure 3. Absorption spectrum of **6** in $CHCl_3$

In summary, we succeeded in synthesis and characterization of three-dimensionally structured cyclo[8]pyrrole **6**, which exhibited the Soret band at visible region and the intense Q band at NIR region. X-Ray crystallographic analysis revealed that alternating pyrrole moieties tilted above and below the mean cyclo[8]pyrrole plane with the small deviation similar to the flat conformation of bicyclo[2.2.2]octadiene-fused cyclo[8]pyrrole.[3] 9,10-Dihydro-9,10-anthraceno moieties at β-pyrrolic positions created the cavities with a diameter of ca. 15 Å. A pair of slip-stacked cyclo[8]pyrroles was observed in the molecular packing. The further investigations for the formation of adduct of **6** with other π-systems are under way.

EXPERIMENTAL

General. Melting points were determined on a Yanaco micro melting point apparatus MP500D and are uncorrected. DI–EI and FAB mass spectra were measured on a JEOL JMS-700. MALDI–TOF mass spectra were measured on an Applied Biosystems Voyager-DE Pro. IR spectra were measured on a Horiba FT-720 infrared spectrophotometer, and UV–vis–NIR absorption spectrum was measured on a JASCO V-570 spectrophotometer. ^{1}H NMR spectra (^{13}C NMR spectra) were recorded on a JEOL AL-400 at 400 MHz (100 MHz). Elemental analyses were performed at the Integrated Center for Sciences, Ehime University.

Crystallographic analysis. X-Ray diffraction data were recorded at 100 K on a Rigaku CCD detector (Saturn 724) mounted on a Rigaku rotating anode X-ray generator (MicrMax-007HF) using Mo–Kα radiation from the corresponding set of confocal optics. *Crystallographic data of* ***6***: $C_{144}H_{88}N_8O_4S$, FW 2026.39, monoclinic, $P2_1/c$, $Z = 2$, $a = 21.816(5)$ Å, $b = 32.473(6)$ Å, $c = 22.067(5)$ Å, $\alpha = 90.00^\circ$, $\beta = 104.147(4)^\circ$, $\gamma = 90.00^\circ$, $V = 15159(5)$ Å^3, μ (Mo$_{K\alpha}$) = 0.067 mm^{-1}, unique 34678, R_{int} 0.1195, obs. 19084, param. 1415, R_1 (I > 2σ(I)) 0.0958, $_wR_2$ (all data) 0.1848, GOF 1.013, CCDC No. 946058.

Ethyl 5-iodo-3,4-(9,10-dihydro-9,10-anthraceno)-1*H*-pyrrole-2-carboxylate 2

A solution of **1** (3.75 g, 11.9 mmol), BTMA·ICl_2 (4.14 g) and $CaCO_3$ (2.37 g) in CH_2Cl_2 (120 mL) and MeOH (60 mL) was refluxed for 3 h. After the reaction mixture was filtered through a Celite pad, the filtrate was washed successively with sat. aqueous Na_2SO_3, water and brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with CH_2Cl_2 and washing with MeOH to give **2** (4.85 g, 92%).

White powder; mp 224.4–225.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (brs, 1H, NH), 7.36 (m, 4H, H-1',4',5',8'), 6.99 (m, 4H, H-2',3',6',7'), 5.76 (s, 1H, H-9'), 5.07 (s, 1H, H-10'), 4.35 (q, 2H, J = 7.1 Hz, CO_2Et), 1.42 (t, 3H, J = 7.1 Hz, CO_2Et); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 145.9, 145.5, 139.8, 138.8, 125.2, 125.2, 123.9, 123.6, 120.1, 62.7, 60.5, 47.9, 47.8, 14.6; IR (KBr disk) $\nu_{\max}$ 3396, 3255, 1697, 1683 cm^{-1}; MS (EI) *m*/*z* (rel intensity) 441 (M$^+$, 100), 315 (6); Anal. Calcd for $C_{21}H_{16}INO_2$: C, 57.16; H, 3.65; N, 3.17. Found: C, 57.43; H, 3.77; N, 3.13.

1-*t*-Butyl 2-ethyl 5-iodo-3,4-(9,10-dihydro-9,10-anthraceno)-1*H*-pyrrole-1,2-carboxylate 3

To a solution of **2** (1.50 g, 3.40 mmol) and DMAP (20 mg) in dry CH_2Cl_2 (20 mL) was added $(Boc)_2O$ (1.0 mL) at room temperature under an Ar atmosphere. The mixture was stirred at same temperature for 21 h, then washed successively with water and brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with $CHCl_3$ followed by recrystallization from $CHCl_3$/hexane to give **3** (1.36 g, 74%).

White powder; mp 163.5–166.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 4H, H-1',4',5',8'), 7.02 (m, 4H, H-2',3',6',7'), 5.67 (s, 1H, H-9'), 5.10 (s, 1H, H-10'), 4.37 (q, 2H, *J* = 7.1 Hz, CO_2Et), 1.54 (s, 9H, CO_2*t*-Bu), 1.44 (t, 3H, *J* = 7.1 Hz, CO_2Et); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 148.6, 144.8, 144.4, 141.3, 140.5, 125.6, 125.5, 124.1, 123.7, 121.5, 85.4, 66.6, 60.7, 47.9, 47.8, 27.6, 14.6; IR (KBr disk) ν_{max} 1751, 1718 cm^{-1}; MS (EI) *m*/*z* (rel intensity) 541 (M$^+$, 11), 441 (100); Anal. Calcd for $C_{26}H_{24}INO_4$: C, 57.68; H, 4.47; N, 2.59. Found: C, 57.69; H, 4.19; N, 2.54.

Diethyl 1*H*,1'*H*-2,2'-bis[3,4-(9,10-dihydro-9,10-anthraceno)pyrrole]-1,1'-dicarboxylate 4

A mixture of **3** (1.34 g, 2.48 mmol) and Cu powder (1.23 g) in dry DMF (20 mL) was heated at 110 °C for 18 h. The reaction mixture was filtered through a Celite pad to remove the copper and washed with CH_2Cl_2. The filtrate was extracted with CH_2Cl_2, washed successively with 1 M HCl, water and brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with 30% EtOAc/CH_2Cl_2 followed by recrystallization from $CHCl_3$/hexane to give **4** (697 mg, 90%).

White powder; mp >300 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (brs, 2H, NH), 7.44 (m, 8H, H-1',4',5',8'), 7.04 (m, 8H, H-2',3',6',7'), 5.84 (s, 2H, H-9'), 5.54 (s, 2H, H-10'), 4.33 (q, 4H, *J* = 7.1 Hz, CO_2Et), 1.40 (t, 6H, *J* = 7.1 Hz, CO_2Et); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 146.0, 145.8, 139.0, 131.7, 125.2, 125.1, 124.0, 123.3, 119.4, 115.5, 60.4, 47.8, 47.1, 14.4; IR (KBr disk) ν_{max} 3308, 1684 cm^{-1}; MS (FAB) *m*/*z* 628 [M]$^+$; Anal. Calcd for $C_{42}H_{32}N_2O_4\cdot 1/4H_2O$: C, 79.66; H, 5.17; N, 4.42. Found: C, 79.88; H, 5.20; N, 4.39.

1*H*,1'*H*-2,2'-Bis[3,4-(9,10-dihydro-9,10-anthraceno)pyrrole] 5

A mixture of **4** (320 mg, 0.509 mmol) and NaOH (0.26 g) in ethylene glycol (10 mL) was heated at 170 °C for 2 h under an Ar atmosphere. The reaction mixture was poured into water and extracted with $CHCl_3$. The organic layer was washed successively with water and brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was rinsed with hexane, MeOH and ether to give **5** (182 mg, 74%).

White powder; mp 224.4–225.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51–7.35 (m, 8H, H-1',4',5',8'), 7.01–6.99 (m, 8H, H-2',3',6',7'), 6.60 (d, 2H, *J* = 3.4 Hz, H-5), 5.37 (s, 1H, H-9'), 5.33 (s, 1H, H-10'); IR

(KBr disk) ν_{max} 3412 cm^{-1}; MS (EI) *m*/*z* (rel intensity) 484 (M$^+$, 55); Anal. Calcd for $C_{36}H_{24}N_2 \cdot 1/4CHCl_3$: C, 84.63; H, 4.75; N, 5.45. Found: C, 84.97; H, 4.77; N, 5.36.

Cyclo[8]pyrrole 6

Entry 1: 1 M H_2SO_4 (10 mL) and a solution of $FeCl_3 \cdot 6H_2O$ (0.29 g) in H_2O (10 mL) were added dropwise slowly to a stirred solution of **5** (48 mg, 0.099 mmol) in $CHCl_3$ (100 mL) at 0 °C. The mixture was stirred at room temperature for 24 h. After an addition of water, the organic layer was washed successively with water and brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with $CHCl_3$ followed by recrystallization from $CHCl_3$/MeOH and rinsing with hexane, water and EtOH to give **6** (31 mg, 61%).

Entry 2: Conc. H_2SO_4 (0.1 mL) and a solution of $NaNO_2$ (14 mg) in H_2O (2 mL) were added dropwise to a stirred solution of **5** (97 mg, 0.20 mmol) in $CHCl_3$ (200 mL) at 0 °C. The mixture was stirred at room temperature for 24 h. After concentration under reduced pressure, the residue was purified by column chromatography on silica gel with $CHCl_3$ followed by recrystallization from $CHCl_3$/MeOH to give **6** (60 mg, 59%).

Entry 3: Conc. H_2SO_4 (0.05 mL) and a solution of $Ce(SO_4)_2$ (60 mg) in H_2O (1 mL) were added dropwise to a stirred mixture of **5** (49 mg, 0.10 mmol), $TBAHSO_4$ (0.6 mg) and Na_2SO_4 (133 mg) in $CHCl_3$ (100 mL) at 0 °C. The mixture was stirred at room temperature for 24 h. After an addition of water, the organic layer was washed successively with water and brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with $CHCl_3$ followed by recrystallization from $CHCl_3$/MeOH and rinsing with hexane to give **6** (33 mg, 65%).

Yellow powder; mp >300 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (m, 32H, H-1',4',5',8'), 8.18 (s, 16H, H-9',10'), 7.28 (m, 32H, H-2',3',6',7'), −2.45 (brs, 8H, NH); UV–vis–NIR ($CHCl_3$) λ_{max}, nm (log ε) 467 (5.23), 1087 (5.52); MS (MALDI–TOF) *m*/*z* 2026 [M+H]$^+$; Anal. Calcd for $C_{144}H_{88}N_8SO_4 \cdot H_2O$: C, 84.60; H, 4.44; N, 5.48. Found: C, 84.39; H, 4.56; N, 5.35.

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REFERENCES AND NOTES

1. D. Seidel, V. Lynch, and J. L. Sessler, *Angew. Chem. Int. Ed.*, 2002, **41**, 1422.

2. J. L. Sessler, E. Karnas, S. K. Kim, Z. Ou, M. Zhanf, K. M. Kadish, K. Ohkubo, and S. Fukuzumi, *J. Am. Chem. Soc.*, 2008, **130**, 15256; L. R. Eller, M. Stępień, C. J. Fowler, J. T. Lee, J. L. Sessler, and B. A. Moyer, *J. Am. Chem. Soc.*, 2007, **129**, 11020; M. Stępień, B. Donnio, and J. L. Sessler, *Angew. Chem. Int. Ed.*, 2007, **46**, 1431; A. Gorski, T. Köhler, D. Seidel, J. T. Lee, G. Orzanowska, J. L. Sessler, and J. Waluk, *Chem. Eur. J.*, 2005, **11**, 4179.
3. T. Okujima, G. Jin, N. Matsumoto, J. Mack, S. Mori, K. Ohara, D. Kuzuhara, C. Ando, N. Ono, H. Yamada, H. Uno, and N. Kobayashi, *Angew. Chem. Int. Ed.*, 2011, **50**, 5699.
4. V. V. Roznyatovskiy, J. M. Lim, V. M. Lynch, B. S. Lee, D. Kim, and J. L. Sessler, *Org. Lett.*, 2011, **13**, 5620; T. Sarma and P. K. Panda, *Chem. Eur. J.*, 2011, **17**, 13987.
5. T. Okujima, C. Ando, J. Mack, S. Mori, I. Hisaki, T. Nakae, H. Yamada, K. Ohara, N. Kobayashi, and H. Uno, *Chem. Eur. J.*, 2013, *in press*.
6. S. Ito, T. Murashima, and N. Ono, *J. Chem. Soc.*, *Perkin Trans. 1*, 1997, 3161.
7. The diffraction data were corrected for Lorentz, polarization, and absorption effects. The structures were solved with SIR2004[8] and refined with SHELXL-97.[9] All calculations were performed by using the Crystal Structure crystallographic software package.[10] CCDC-946058 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data center via www.ccdc.cam.ac.uk/data_request/cif.
8. SIR2004: an improved tool for crystal structure determination and refinement, M. C. Burla, R. Caliandro, M. Camalli, B. Carrozzini, G. L. Cascarano, L. De Caro, C. Giacovazzo, G. Polidori, and R. Spagna, *J. Appl. Cryst.*, 2005, **38**, 381.
9. SHELXL-97: Program for solution and refinement of crystal structures from diffraction data, University of Göttingen, Göttingen, Germany; *"A short history of SHELX"*. G. M. Sheldrick, *Acta Cryst.*, 2008, **A64**, 112.
10. Rigaku (2010) Crystal Structure. Version 3.8.2 or 4.0.1. Rigaku Corporation, Tokyo, Japan.
11. H. Uno, H. Watanabe, Y. Yamashita, and N. Ono, *Org. Biomol. Chem.*, 2005, **3**, 448.