Synthesis and X-ray Crystal Structure of *meso*-Octaalkyldithiaporphyrinogen

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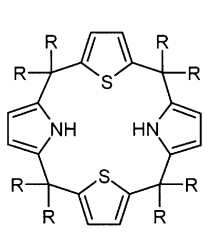
Porphyrinogens are macrocyclic species composed of four pyrrole rings linked in the 2 and 5 positions *via* sp^3 hybridized carbon atom. Although the porphyrinogen is well known as a precusor of porphyrin, its chemistry is almost unexplored, except for the spontaneous six-electron oxidation leading to the corresponding porphyrin.[1] This oxidation reaction is facile due to the presence of hydrogen atoms in the *meso*-positions. However, fully *meso*-substituted porphyrinogens, namely the *meso*-octaalkylporphyrinogen, are stable for oxidation. The first porphyrinogen, an octamethyl derivative, was prepared from the acid-catalyzed condensation between pyrrole and acetone in 1866 by Baeyer.[2] Surprisingly, the molecule and its homologues have been almost totally ignored by chemists over one hundred years. Recent studies revealed that the porphyrinogens act as receptors for anionic species[3,4] and for neutral species such as simple alcohols, amine, and amides.[5]

Replacement of the nitrogen atoms of *meso*-octaalkylporphyrinogen with other heteroatoms produces macrocycles with different complexing abilities. While the furan anologue of the *meso*-octaalkylporphyrinogen has been known recently,[6] the sulfur analogue has not been reported yet. Replacement of pyrrole with thiophene is of particular interest because of the multiple possibilities for metal-thiophene coordination. Herein, we report synthesis and X-ray crystal structure of *meso*-octaalkyldithiaporphyrinogen.

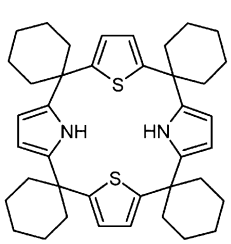
Experimental Section

Materials and Instrumentation. Thiophene (Aldrich), pyrrole (Aldrich), acetone (Oriental), cyclohexanone (Junsei), tetramethylethylenediamine (Aldrich) were distilled under N_2 just before use. $BF_3 \cdot OEt_2$ (Aldrich), 3-pentanone (Aldrich), 5-nonanone (Aldrich), and *n*-BuLi (10 M in hexane, Aldrich) was used as received.

^1H and ^{13}C NMR spectra were recorded on a Bruker AC-200F NMR spectrometer operating at 200 MHz and 50.32 MHz, respectively. TOF MALDI and high resolution FAB-MS spectra were obtained on a kratos kompact MALDI II and on a JSM-HX110A-HX110A, respectively.



R = methyl, **5**
ethyl, **6**
butyl, **7**



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General Procedure for the Preparation of 5,5,10,10,15,15,20,20-Octaalkyldithiaporphyrinogen. Tetramethylethylenediamine (0.1485 mol) and *n*-BuLi (10 M in hexane, 0.1485 mol) were injected into the hexane (100 mL) solution under Ar. Thiophene (0.059 mol) was added and the solution was refluxed for 1 hr. The 2,5-dilithiothiophene suspension was slowly transferred *via* a siphon to the THF (150 mL) solution of ketone (0.237 mol) at -10 °C. After the addition was completed the mixture was allowed to warm to room temperature and stirred for 20 min. Ice-cold NH_4Cl solution (100 mL) was added with stirring. The phases were separated and the water layer was extracted with ether (3 × 50 mL). The organic layers were combined, washed with water and dried with K_2CO_3. The solvent were evaporated and purified by chromatography over silica gel (230-400 mesh) with CH_2Cl_2/methanol (v/v – 95/5) as a eluant.

2,5-Bis(dialkylhydroxymethyl)thiophene (15.2 mmol) was added to a CH_2Cl_2 (150 mL) solution of pyrrole (15.2 mmol). $BF_3 \cdot OEt_2$ (9.12 mmol) was titrated to the solution and the reaction mixture was stirred at room temperature for 10 min. Solvents were removed and the residual solution was purified by silica gel chromatography with CH_2Cl_2/hexane (v/v – 60/40).

2,5-Bis(dimethylhydroxymethyl)thiophene 1: 25.5%; ^1H NMR ($CDCl_3$) δ 6.72 (s, 2H, thiophene β-H), 2.58 (s, 2H, -OH), 1.59(s, 12H, $-CH_3$). TOF MALDI $(M+H)^+$: *m/z* 201.1 (calcd for $C_{10}H_{16}O_2S+H^+$ 201.1007).

2,5-Bis(diethylhydroxymethyl)thiophene 2: 43%; ^1H NMR (C_6D_6) δ 6.62 (s, 2H, thiophene β-H), 1.75 (q, 8H, α-CH_2), 1.60 (s, 2H, -OH), 1.59 (s, 12H, β-CH_3). TOF-MALDI MS $(M+H)^+$: *m/z* 257.2 (calcd for $C_{14}H_{24}O_2S+H^+$ 257.1631).

2,5-Bis(dibutylhydroxymethyl)thiophene 3: 28.3%; ^1H NMR ($CDCl_3$) δ 6.66 (s, 2H, thiophene β-H), 1.93 (s, 2H, -OH), 1.81 (t, 8H, α-CH_2), 1.34 (m, 16H, β, γ-CH_2), 0.92 (s, 12H, δ-CH_3). TOF-MALDI MS $(M+H)^+$: *m/z* 369.3 (calcd for $C_{22}H_{40}O_2S \cdot H^+$ 369.2879).

2,5-Bis(cyclohexylhydroxymethyl)thiophene 4: 20%; ^1H NMR ($CDCl_3$) δ 6.70 (s, 2H, thiophene β-H), 1.75 (m, 22H, cyclohexyl, -OH)

5,5,10,10,15,15,20,20-Octamethyldithiaporphyrinogen 5: 35%; ^1H NMR (CD_2Cl_2) δ 7.23 (s, 2H, N-H), 6.73 (s, 4H, thiophene β-H), 5.90 (d, 4H, pyrrole β-H), 1.64 (s, 24H, $-CH_3$); ^{13}C NMR (CD_2Cl_2) 153.7 (s, 4C, thiophene α-C), 139.7 (s, 4C, thiophene β-C), 120.9 (d, 4C, pyrrole α-C),

102.3 (d, 4C, pyrrole β-C), 37.7 (s, 4C, *meso*-C), 30.7 (d, 8C, -CH_3). TOF-MALDI MS $(M-H)^+$: *m/z* 463.2 (calcd for $C_{28}H_{34}N_2S_2-H^+$ 463.2234)

5,5,10,10,15,15,20,20-Octaethyldithiaporphyrinogen 6: 21%; ^{1}H NMR ($CDCl_3$) δ 6.95 (s, 2H, N-H), 6.64 (s, 4H, thiophene β-H), 5.87 (d, 4H, pyrrole β-H), 1.92 (q, 16H, α-CH_2), 0.66 (t, 24H, β-CH_3); ^{13}C NMR ($CDCl_3$) 151.8 (s, 4C, thiophene α-C), 137.2 (s, 4C, thiophene β-C), 121.9 (d, 4C, pyrrole α-C), 104.3 (d, 4C, pyrrole β-C), 45.2 (s, 4C, *meso*-C), 30.0 (d, 8C, α-CH_2), 8.2 (d, 8C, β-CH_3). Anal. Calcd for $C_{36}H_{50}N_2S_2$: C, 75.08; H, 8.93; N, 4.87. Found: C, 74.99; H, 8.97; N, 4.91 HR FAB-MS $(M)^+$: *m/z* 574.34 (calcd for $C_{36}H_{50}N_2S_2$ 574.3404).

5,5,10,10,15,15,20,20-Octabutyldithiaporphyrinogen 7: 10%; ^{1}H NMR ($CDCl_3$) δ 6.99 (s, 2H, N-H), 6.93 (s, 4H, thiophene β-H), 5.85 (d, 4H, pyrrole β-H), 1.85 (s, 24H, α-CH_2), 1.23 (m, 32H, β, γ-CH_2), 1.01 (t, 24H, δ-CH_3); ^{13}C NMR ($CDCl_3$) 152.4 (s, 4C, thiophene α-C), 137.5 (s, 4C, thiophene β-C), 121.5 (d, 4C, pyrrole α-C), 103.9 (d, 4C, pyrrole β-C), 44.6 (s, 4C, *meso*-C), 38.0 (s, 8C, α-CH_2), 26.0 (s, 8C, β-CH_2), 23.0 (s, 8C, γ-CH_2), 13.9 (d, 8C, δ-CH_3). TOF-MALDI MS $(M+H)^+$: *m/z* 799.6 (calcd for $C_{52}H_{82}N_2S_2$ $+H^+$ 799.5978).

5,10,15,20-Tetracyclohexyldithiaporphyrinogen 8: 23%; ^{1}H NMR ($CDCl_3$) δ 7.03 (s, 2H, N-H), 6.66 (s, 4H, thiophene β-H), 5.83 (d, 4H, pyrrole β-H), 2.16 (m, 16H, α-CH_2), 1.53 (m, 24H, β, γ-CH_2); ^{13}C NMR ($CDCl_3$) 151.2 (s, 4C, thiophene α-C), 138.6 (s, 4C, thiophene β-C), 121.9 (d, 4C, pyrrole α-C), 102.1 (d, 4C, pyrrole β-C), 41.7 (s, 4C, *meso*-C), 38.1 (d, 8C, α-CH_2), 25.9 (s, 8C, β-CH_2), 22.6 (s, 4C, γ-CH_2).

X-ray Crystallography. A crystal having dimension 0.4 $\times$ 0.6 $\times$ 0.9 mm was mounted on a fiber. X-ray data were collected on Simens Smart CCD diffractometer equipped with graphite-monochromated Mo-K_α (λ = 0.71073 Å) radiation at room temperature. The unit cell was determined to be monoclinic, P21/*c* (No. 14) on the basis of 25 reflections. The data were collected by using the ω-2θ scan technique in the range $1.80 \leq \theta \leq 23.35°$. Lorentz and polarization corrections were applied to the intensity data, while no absorption correction was applied. The structure was solved by direct method and refined by full-matrix least-squares calculation with SHELXL-97.[7] Anisotropic thermal parameters were used for all non-hydrogen atoms. Crystal and intensity data are given in Table 1.

Table 1. Crystal Data and Structure Refinement for **6**

Empirical formula	$C_{36}H_{50}N_2S_2$
Formula weight	574.90
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	momoclinic, P21/*c*(No. 14)
Unit cell dimensions	a = 11.6169(2) A, α = 90°
	b = 21.784 , β = 110.1560(10)°
	c = 14.1176(2) A, γ = 90°
Volume	3353.78(7) Å^3
Z, Calculated density	4, 1.139 gcm^{-3}
Absorption coefficient	0.185 mm^{-1}
F(000)	1248
Crystal size	0.4×0.6×0.9 mm
θ range for data collection	1.80 to 23.35°
Index ranges	$-11 \leq h \leq 12$, $-24 \leq k \leq 21$, $-13 \leq l \leq 15$
Reflections collected /unique	14321/4859 [R(int) = 0.0874]
Data /restraints /parameters	4859/0/370
Goodness-of-fit on F^2	1.047
Final R indices [I>2sigma(I)]	R1 = 0.0495, wR2 = 0.1205
R indices (all data)	R1 = 0.0606, wR2 = 0.1279
Largest diff. peak and hole	0.342 and -0.283 e.A^{-3}

Results and Discussion

2,5-Dilithiothiophene was synthesized from refluxing hexane solution of thiophene with 2.0 equivalent of *n*-BuLi in the presence of tetramethylethylenediamine. 2,5-Dilithiothiophene was *in situ* reacted with dialkyl ketones such as acetone, 3-pentanone, 5-octanone, and cyclohexanone to produce the corresponding bis(dialkylhydroxymethyl)thiophene **1**, **2**, **3**, and bis(cyclohexylhydroxymethyl)thiophene **4** in moderate yields. Acid-catalyzed condensation of pyrrole with the compound **1**, **2**, **3** and **4** resulted in the formation of the corresponding 5,5,10,10,15,15,20,20-octaalkyldithiaporphyrinogen **5**, **6**, **7**, and 5,10,15,20-tetracyclohexyldithiaporphyrinogen **8**. The corresponding compound **5**, **6**, **7** and **8** were isolated as major products when 0.6 equivalent of $BF_3 \cdot OEt_2$ were used as the acid catalyst.

In the ^{1}H NMR spectra for the compound **5-8**, a broad N-*H* peak was observed around 6.9-7.3 ppm which is indicative for the formation of the porphyrinogen ligand. The resonance for the β-proton of thiophene and pyrrole was appeared in the range of 5.8-6.9 ppm. As illustrated in Figure 1, the ^{1}H NMR spectrum for the octamethyldithiaporphyrinogen shows only one singlet peak for the methyl groups at 1.64 ppm, thereby implying that the molecule in solution must be a dynamic molecule.

Single crystals of 5,5,10,10,15,15,20,20-octaethyldithiaporphyrinogen **6** suitable for an X-ray structure determination were obtained by slow evaporation of a toluene

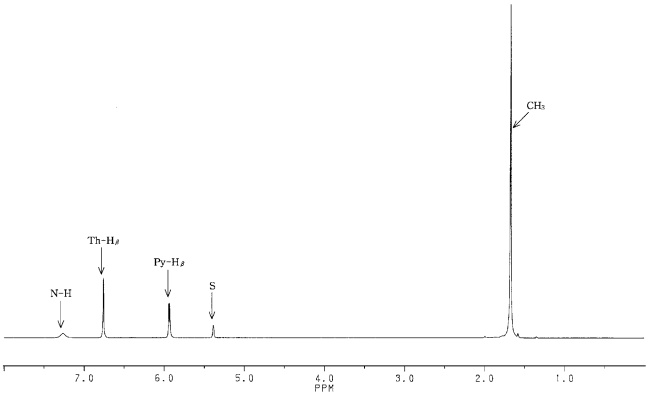

Figure 1. ^{1}H NMR spectrum of **5** in CD_2Cl_2: N-H = pyrrolic N-H. Th-H$_\beta$ β-proton of thiophene. Py-H$_\beta$ β-proton of pyrrole. S solvent $CDHCl_2$, CH_3 = methyl groups at the *meso* position.

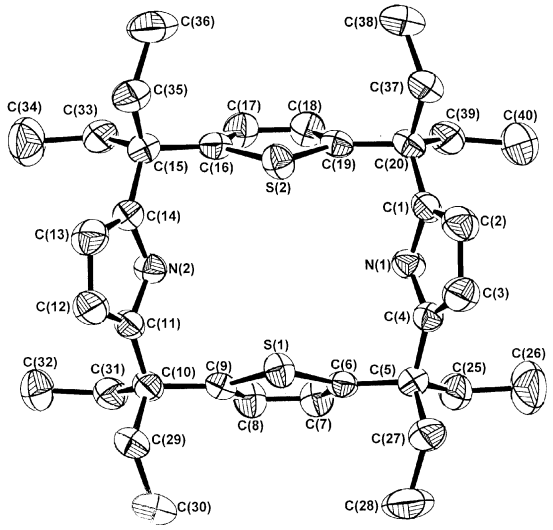

Figure 2. An ORTEP representation of **6** with atomic labeling scheme (50% probability ellipsoids). All hydrogens are omitted for clarity. Relevant dihedral angles (°): Pl.(C)-Pl.(S1) 107.40, Pl.(C)-Pl.(S2) 109.07, Pl.(C)-Pl.(N1) 116.70, and Pl.(C)-Pl.(N2) 121.42 Pl.(C) indicates the mean least-squares plane containing C(5), C(10), C(15), and C(20). Pl.(S1), Pl.(S2), Pl.(N1), and Pl.(N2) refer to the planes of the aromatic rings containing S(1), S(2), N(1), and N(2), respectively.

nate conformation in the solid state wherein adjacent rings are oriented in opposite directions just as the case of the previously reported octaethylporphyrinogen.[8] The thiophene rings are tilted towards the center of the cavity by 17.40 and 19.07°, respectively. In this conformation the shortest distance between sulfur atoms is 4.315 Å. There is no S-S bonding interaction from the S···S distance which is longer than the sum of van der waals radius, 3.76 Å. Also the pyrrole rings are tilted in the same way by 26.7 and 31.42°, respectively. The shortest distance between nitrogen atoms is 5.267 Å. An average distance between diagonal methylene carbons in the same side [C(25)···C(33), C(27)···C(35), C(29)···C(37) and C(31)···C(39)] is 9.2786 Å. The four *meso* sp^3-C atoms are nearly coplanar, the average deviation being 0.0943 Å.

Addition of 20.0 equivalent of tetamethylammonium fluoride to the CD_2Cl_2 solution of the compound **5** shifted a N-*H* resonance peak from 7.23 to 9.00 ppm in the ^1H NMR spectrum. Addition of 20.0 equivalent of tetramethylammonium chloride to the same solution caused a smaller shift of the N-*H* resonance peak to 7.26 ppm. This result indicates that hydrogen bonding occurs between N-*H* and the anion, even though the dithiaporphyrinogen is expected to be a weaker receptor to anions than the porphyrinogen because the dithiaporphyrinogen has only two N-H protons, while the previous known porphyrinogen has 4 N-H protons.

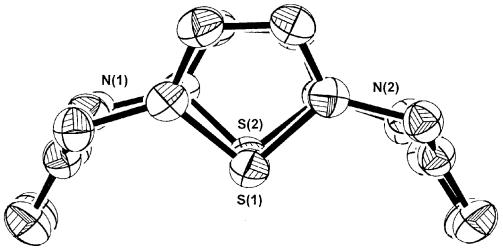

Figure 3. An ORTEP representation of **6** in a side view (50% probability ellipsoids). Octaethyl groups and all hydrogens are omitted for clarity.

Table 2. Selected Bond Lengths [Å] and Angles [°] for **6**

S(1)-C(6)	1.725(2)	C(2)-C(3)	1.412(3)
S(1)-C(9)	1.725(2)	C(3)-C(4)	1.354(3)
N(1)-C(4)	1.371(3)	C(4)-C(5)	1.509(3)
N(1)-C(1)	1.376(3)	C(5)-C(6)	1.512(3)
C(1)-C(2)	1.354(3)	C(6)-C(7)	1.350(3)
C(1)-C(20)	1.504(3)	C(9)-C(10)	1.521(3)
S(2)-C(16)	1.725(2)	C(10)-C(11)	1.507(3)
S(2)-C(19)	1.728(2)	C(14)-C(15)	1.515(3)
N(2)-C(14)	1.367(3)	C(15)-C(16)	1.519(3)
N(2)-C(11)	1.378(3)	C(19)-C(20)	1.521(3)
C(6)-S(1)-C(9)	92.99(11)	C(10)-C(9)-S(1)	120.13(15)
C(4)-N(1)-C(1)	110.96(18)	C(11)-C(10)-C(9)	109.46(17)
C(2)-C(1)-N(1)	106.3(2)	C(12)-C(11)-N(2)	106.3(2)
C(2)-C(1)-C(20)	133.5(2)	C(12)-C(11)-C(10)	133.6(2)
N(1)-C(1)-C(20)	120.25(19)	N(2)-C(11)-C(10)	120.01(19)
C(16)-S(2)-C(19)	93.04(11)	C(13)-C(14)-N(2)	106.7(2)
C(14)-N(2)-C(11)	110.69(18)	C(13)-C(14)-C(15)	132.6(2)
C(3)-C(4)-N(1)	106.1(2)	N(2)-C(14)-C(15)	120.56(19)
C(3)-C(4)-C(5)	134.1(2)	C(14)-C(15)-C(16)	108.99(19)
N(1)-C(4)-C(5)	119.77(19)	C(17)-C(16)-C(15)	130.6(2)
C(4)-C(5)-C(6)	109.03(19)	C(17)-C(16)-S(2)	109.27(19)
C(7)-C(6)-C(5)	130.2(2)	C(15)-C(16)-S(2)	120.01(16)
C(7)-C(6)-S(1)	109.31(18)	C(18)-C(19)-C(20)	131.2(2)
C(5)-C(6)-S(1)	120.47(16)	C(18)-C(19)-S(2)	109.42(18)
C(8)-C(9)-C(10)	129.9(2)	C(20)-C(19)-S(2)	119.34(16)
C(8)-C(9)-S(1)	109.92(18)	C(1)-C(20)-C(19)	109.43(17)

The porphyrinogen functions as a tetraanionic N_4 ligand suitable for stabilizing high oxidation state for transition metals,[9] while the dithiaporphyrinogen functions as a dianionic N_2S_2 ligand suitable for low oxidation state for transition metals.

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