Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron 62 (2006) 11908–11915
Tetrahedron

A convenient preparation of thioether functionalized porphyrins

Michael M. Pollard and John C. Vederas*

Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada T6G 2G2

Received 21 August 2006; revised 20 September 2006; accepted 22 September 2006
Available online 27 October 2006

Abstract—This paper describes a convenient and high yielding three-step approach for the synthesis of *trans*-tetraphenylporphyrins possessing two thioethers in the *ortho* positions, which will facilitate the synthesis of more elaborate and complex porphyrin architectures. Their synthesis is realized by a double nucleophilic aromatic substitution of 2 equiv of a thiolate on 2,6-dichlorobenzaldehyde to generate a bis-thioether substituted benzaldehyde. This aldehyde is then condensed with 2 equiv of pyrrole to give a dipyrromethane, which in the final step reacts with an aromatic aldehyde to give a series of thioether-substituted *trans*-tetraphenylporphyrins.

1. Introduction

Porphyrins are a core structural motif that is central to the research of a wide variety of fields including material science,[1] supramolecular chemistry,[2] catalysis,[3] biomimetic chemistry,[3d,4] and small molecule sensing.[5] Among porphyrins, *trans*-substituted *meso*-tetraphenylporphyrins (TPPs) are especially attractive because they reduce the symmetry of the molecule and provide an opportunity for selective functionalization. The resulting linear substitution pattern can be conveniently harnessed for the construction of large, derivatized porphyrinic scaffolds and complex architectures.

Functionalization at the *ortho* positions (R groups, Fig. 1) of the *meso*-aryl group of TPPs is crucial to the successful development of many of these systems.[3,5] This substitution pattern is advantageous because it places the functionality over the porphyrin core, thus enabling the chemists to alter the photophysical or catalytic property of the system by proximity and steric effects.

The low yields universal to the preparation of porphyrins make elaborate multistep synthesis of their precursors unattractive. Nevertheless, the utility of porphyrins decorated with the desired 2,6-disubstituted phenyl groups on the *meso* positions is highlighted by the numerous, often lengthy, and expensive approaches taken by various researchers to prepare these molecules. Recent examples include the work of Jux[6] who described a useful approach to *trans*-TPPs bearing *meso*-2,6-bis(bromomethyl)phenyl groups via 2,6-bis-(methoxymethyl)benzaldehyde (five steps to the aldehyde and nine steps to the functionalized porphyrin). Higuchi et al.[7] described the preparation of 2,6-diamidophenyl *meso* substituted porphyrins, requiring 10 chemical transformations. Starting with 2,6-dimethoxybenzaldehyde, Lindsey et al.[8] reported the preparation of TPPs possessing alkoxy ethers at both *ortho* positions of the *meso*-phenyl groups. Foxon et al.[9] prepared similarly substituted porphyrins substituted by chiral ethers starting from resorcinol (three steps). Additionally, Rose et al.[10] reported a carefully optimized synthesis of the air sensitive *meso*-tetrakis(2,6-diamino-4-*tert*-butylphenyl)porphyrin (five steps), which required 3 weeks for a good yield in its final step.

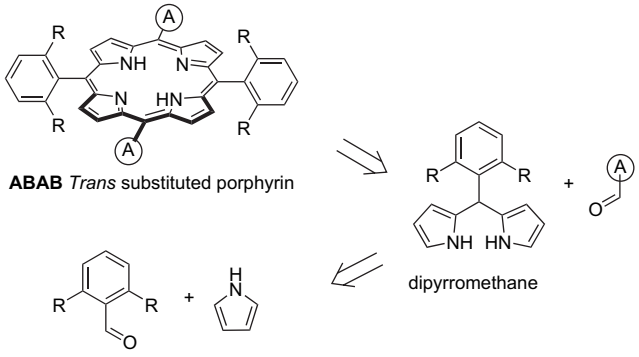


Figure 1. Retrosynthesis for C_2-symmetric **ABAB** *trans*-porphyrins.

Here, we report a conceptually simple, convenient, and efficient method for the preparation of 2,6-dithioether substituted benzaldehydes. These aldehydes are readily converted to dipyrromethanes upon treatment with a Lewis acid, which are then applied in a scrambling free synthesis of C_2-symmetric *trans*-TPPs. We envision that this approach will

Keywords: *trans*-Porphyrins; Thioethers; Synthesis; Dipyrromethanes; 2,6-Disubstituted aldehydes.
* Corresponding author. Tel.: +1 780 492 5475; fax: +1 780 492 2134; e-mail: john.vederas@ualberta.ca

0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.09.091

facilitate the synthesis of complex porphyrin architectures, which are useful for broad range of applications in the field of porphyrin chemistry including catalysis, biomimetic chemistry, and material science.

2. Results and discussion

2.1. 2,6-Disubstituted benzaldehydes

We anticipated that starting from the inexpensive 2,6-dichlorobenzaldehyde, a variety of thiols could be introduced at the *ortho* positions via thioethers using nucleophilic aromatic substitution. This was inspired by one example in the literature where Gairns et al.[11] prepared 2,6-bis(phenylsulfanyl)benzaldehyde **2a** from 2,6-dichlorobenzaldehyde and potassium thiophenolate in HMPA over 2 days. We sought to employ mild conditions while avoiding the use of the known carcinogen HMPA.

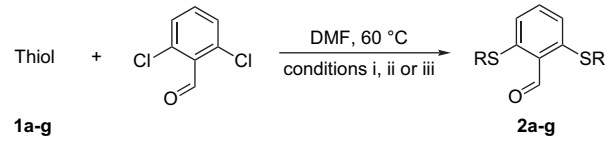
We found that when heated to 60 °C for 30 min, 2,6-dichlorobenzaldehyde reacted smoothly with potassium thiophenolate to give the double substitution product in 93% yield without chromatography (Table 1).

This method also succeeded with aliphatic thiols (Table 1, entries **1b**–**1g**). At 60 °C, over 3 h, 2,6-dichlorobenzaldehyde reacts with 2.2 equiv of KSMe to give dithioether **2b** in excellent yield. The application of similar conditions to other substrates shows how this nucleophilic aromatic substitution is general for many aliphatic thiols. Treatment of dichlorobenzaldehyde with 2.2 equiv of thiols **1c**–**1e** and **1g** and K_2CO_3 in DMF furnished the corresponding dithioether products **2c**–**2e** and **2g** in good to excellent yields, typically without the need for chromatography.

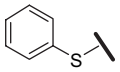
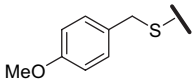
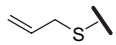
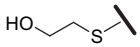
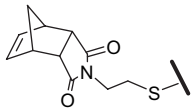
Notably, *tert*-butyl mercaptan (**1f**) was unreactive when the above conditions were employed (Table 1, i and ii), probably due to the lower acidity of this thiol. This transformation proceeded efficiently when the deprotonation of the thiol was performed with NaH in DMF prior to the addition of the aldehyde, affording the product in 88% yield.

The use of only 1 equiv of thiol **1h** in the procedure leads to the selective formation of the monosubstituted product **2h** in 82% isolated yield after recrystallization of the crude reaction product (Fig. 2). ^{1}H NMR analysis of the crude reaction mixture showed 90% conversion to the desired **2h** as well as 6% of the disubstituted product **2e** and 4% starting aldehyde.[12]

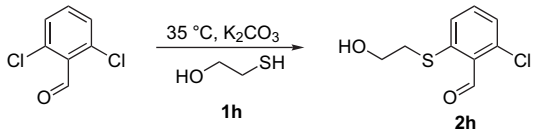
Table 1. Synthesis of 2,6-dithioether aldehydes



1a-g **2a-g**

Thiol	R—	Conditions	Product	Yield (%)
1a		ii	**2a**	93
1b		i	**2b**	93
1c		i	**2c**	89
1d		i	**2d**	71
1e		i	**2e**	83
1f		iii	**2f**	88
1g		i	**2g**	89

Conditions: (i) 2.0 or 2.2 equiv of both thiol and K_2CO_3; (ii) commercially available potassium thiomethoxide was used, and the reaction was done in a glove box; (iii) thiol **1f** was premixed with NaH in DMF before the slow addition of the aldehyde.



1h **2h**

Figure 2. Selective monosubstitution of the dichlorobenzaldehyde.

2.2. Dipyrromethanes

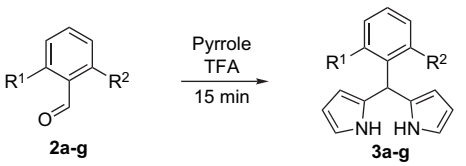
With the series of 2,6-disubstituted aldehydes available, we attempted to prepare the corresponding dipyrromethanes using the conditions developed by Lindsey et al.[13] Treatment of aldehyde **2a** with TFA in excess pyrrole gives dipyrromethane **3a** in 53% yield (Table 2). Application of this procedure to aldehydes **2b**–**2f** followed by flash chromatography gave the desired dipyrromethanes **3b**–**3f**, respectively, in moderate yields ranging from 31–51% with no observed scrambling. These results are typical for dipyrromethanes, which cannot be distilled or selectively precipitated.[13,14] The successful application of the method to aldehyde **2h** bearing an unprotected alcohol highlights the convenience of this method for the rapid access of porphyrin precursors under mild conditions without the need for elaborate protecting group strategy.

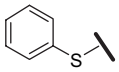
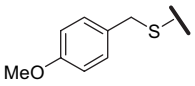
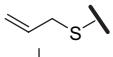
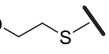
2.3. Porphyrins

Initially, we explored the use of dipyrromethane **2a** in the synthesis of **ABAB** C_2-symmetric *trans*-TPPs. Since standard conditions[15] for the synthesis of *trans*-TPPs typically give significant amounts of scrambling of the *meso* substituents, we employed conditions developed by Lindsey et al. to minimize this for the preparation of porphyrins from 5-(2,6-dichlorophenyl)dipyrromethane and 5-mesityldipyrromethanes.[13]

Treating 1 equiv of **3a** and 1 equiv of *p*-tolualdehyde with 1.78 equiv of TFA in DCM,[13] followed by oxidation with DDQ furnished the **ABAB** *trans*-porphyrin **4a** in 25% yield (Table 3, entry 1). Although the yields initially may seem modest, they are quite reasonable for this type of porphyrin formation.[1a]

Table 2. Preparation of difunctionalized dipyrromethanes



Aldehyde	R^1—	R^2—	Product	Yield (%)
2a	$R^1=R^2=$		**3a**	53
2b	$R^1=R^2=$		**3b**	31
2c	$R^1=R^2=$		**3c**	48
2d	$R^1=R^2=$		**3d**	51
2f	$R^1=R^2=$		**3f**	46
2h	R^1=Cl	R^2 = 	**3h**	40

This procedure was successfully applied to the synthesis of a series of porphyrins. Employing Lindsey's conditions,[13] porphyrins **4b**–**4i** were prepared in moderate to good yields (19–51%). The use of dipyrromethane **3h** in the synthesis gave porphyrin **4h** as a mixture of rotamers, which were separated by careful flash chromatography to give 17% of the α,α-isomer and 16% of the α,β-isomer.

In conclusion, we have developed a quick, convenient, and inexpensive way to prepare *trans*-TPPs bearing thioethers in the 2 and 6 positions of the *meso*-phenyl groups. Considering the mild conditions used, this method should be compatible with a wide range of functionality, making it an attractive approach for the preparation of elaborate porphyrin architectures. Moreover, since these systems also bear multiple thioether functions, it offers the possibility of using these thioether porphyrins for applications requiring their self-assembly on gold surfaces.

3. Experimental

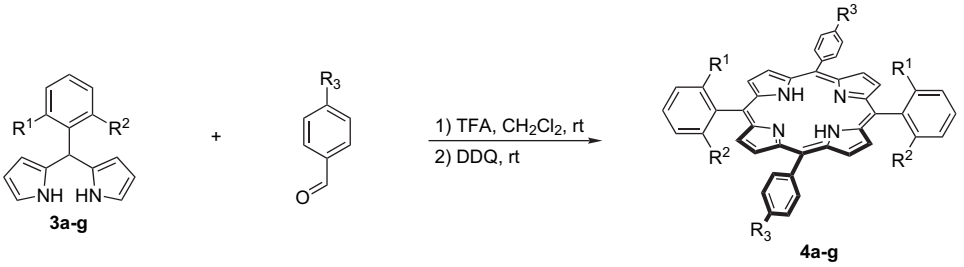
3.1. General remarks

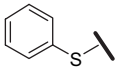
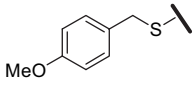
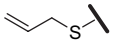
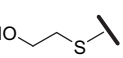
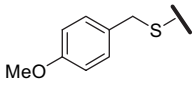
All reagents and solvents used were of ACS grade and were used without further purification unless otherwise mentioned. All processes involving air or moisture sensitive reactants and/or requiring anhydrous conditions were performed under a positive pressure of pre-purified argon using flame-dried glassware. Unless otherwise specified, solutions of Na_2CO_3 and NaOH refer to saturated aqueous solutions.

Compound visualization during TLC analysis was achieved by UV fluorescence, and simply heating on a hot plate for 30 s (this is particularly effective for dipyrromethanes, which develop a green color, which is different from the reaction byproducts).

Infrared spectra (IR) were recorded on a Nicolet Magna 750 FT-IR spectrometer as either a cast or microscope (μscope).

Table 3. Synthesis of C_2-symmetric *trans*-porphyrins



Dipyrromethane	R^1—	R^2—	R^3—	Product	Yield (%)
3a	$R^1=R^2=$		TMS—≡—	**4a**	25
3b	$R^1=R^2=$			**4b**	19
3c	$R^1=R^2=$			**4c**	51
3d	$R^1=R^2=$			**4d**	21
3h	R^1 = 	R^1=Cl		**4h**	33[a] (α,α=17%, α,β=16%)
3c	$R^1=R^2=$			**4i**	21

[a] Due to the hindered rotation around the porphyrin-*meso*-aryl bond, the α,α- and the α,β-isomer could be separated.

Cast refers to the evaporation of a solution on a NaCl plate. Mass spectra (MS) were recorded on a Kratos AEIMS-50 high-resolution mass spectrometer (HRMS), using electron impact ionization (EI), Applied Biosystems (sinapinic acid as the matrix), and Micromass ZabSpec Hybrid Sector-TOF using positive mode electrospray (ES). Microanalyses were obtained on Perkin–Elmer 240 or Carlo Erba 1180 elemental analyzer. Nuclear magnetic resonance (NMR) spectra were obtained on Inova Varian 400 and 500 MHz instruments. ^{1}H NMR chemical shifts are reported in parts per million (ppm) downfield relative to tetramethylsilane (TMS) using the residual solvent resonance as the reference: $CDCl_3$, δ 7.24; CD_3OD, δ 3.30. The coupling constants reported are within an error range of 0.2–0.4 Hz. ^{13}C NMR shifts are reported relative to: $CDCl_3$, δ 77.0; CD_3OD, δ 49.0. Porphyrin α-carbon signals are typically not reported because of signal broadening due to NH tautomerization.[16] Signals are reported within 0.1 ppm except where close peaks necessitate an additional significant figure.

3.1.1. 5-(3,5-Dioxo-4-aza-tricyclo[5.2.1^{2,6}]dec-8-en-4-yl)ethanethiol (1g). Norborn-5-ene-2,3-*endo*-dicarboxylic anhydride[17] (1.64 g, 10.0 mmol), triethylamine (2.02 g, 20.0 mmol), and 2-thioethanolamine hydrochloride (1.13 g, 10.0 mmol) were dissolved in DMF (10 mL) and placed in a sealed tube. The solution was purged with argon (20 min), the reaction vessel was sealed, and then heated at 140 °C for 14 h. The tube was then cooled, the reaction mixture was diluted with water (50 mL), extracted with EtOAc (50 mL), and the organic layer was washed with water (3×50 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification by flash chromatography eluting with Hex/EtOAc (4/1) afforded a white solid (290 mg, 11%): mp 111–114 °C; IR ($CHCl_3$, cast) 3062, 2989, 2944, 2871, 2559, 1766, 1701, 1395, 1336, 1159, 724 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.33 (t, 1H), 1.50 (dt, 1H, J=9.0, 1.5 Hz), 1.69 (dt, 2H, J=8.5, 1.5 Hz), 2.53 (m, 2H), 3.22 (dd, 2H, J=1.5, 3.0 Hz), 3.35 (m, 2H), 3.47 (m, 2H), 6.07 (t, 2H, J=2.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 22.0, 41.3, 45.0, 45.8, 52.3, 134.4, 177.2; HRMS (EI) calcd for $C_{13}H_{15}O_2NS$: 265.0772, found: 265.0774 [M$^+$] (21.3%).

3.1.2. 2,6-Bis(phenylsulfanyl)benzaldehyde (2a). Thiophenol (2.05 mL, 22.0 mmol) was added to a nitrogen flushed (20 min) stirred mixture of 2,6-dichlorobenzaldehyde (1.75 g, 10.0 mmol), K_2CO_3 (3.04 g, 2.20 mmol), and DMF (5.0 mL). The mixture was stirred for 5 min, and then heated to 60 °C until the reaction was complete as judged by TLC (Hex/EtOAc 6/1) (ca. 30 min). The mixture was diluted with water (15 mL), the product was filtered, rinsed with water (6×10 mL), and dried in vacuo at 55 °C for 3 h to give the aldehyde **2a** (3.11 g, 93%). All spectroscopic data were consistent with the reported data.[11]

3.1.3. 2,6-Bis(methylsulfanyl)benzaldehyde (2b). Under inert atmosphere (glove box), NaSMe (1.46 g, 21.0 mmol) was added portionwise to a stirred solution of 2,6-dichlorobenzaldehyde (1.75 g, 10.0 mmol) in DMF (10 mL) (caution, exothermic!). The mixture was stirred for 20 min, then heated to 60 °C, and stirred for 1 h. The mixture was cooled to rt, diluted with EtOAc (25 mL), and washed with water (3×15 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude residue by recrystallization (MeOH) gave **2b** as a white solid (1.85 g, 93%): mp 95–97 °C; IR ($CHCl_3$, cast) 2981, 2921, 2861, 2767, 1670, 1550, 1437, 1416, 1200, 949, 756 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.42 (s, 6H), 7.05 (d, 2H, J=8.0 Hz), 7.36 (t, 1H, J=8.0 Hz), 10.64 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 16.2, 121.9, 129.4, 132.9, 145.7, 189.9; HRMS (EI) calcd for $C_9H_{10}OS_2$: 198.0173, found: 198.0175 [M$^+$] (100.0%). Anal. Calcd for $C_9H_{10}OS_2$: C, 54.51; H, 5.08. Found: C, 54.25; H, 5.06.

3.1.4. 2,6-Bis(4-methoxybenzylsulfanyl)benzaldehyde (2c). 4-Methoxybenzylmercaptan (900 μL, 6.00 mmol) was added to an argon flushed (20 min) stirred mixture of 2,6-dichlorobenzaldehyde (525 mg, 3.00 mmol), K_2CO_3 (996 mg, 7.00 mmol), and DMF (3 mL). The mixture was stirred for 5 min, and then heated to 60 °C for 2 h until a light yellow solid precipitated. Water (15 mL) and EtOAc (25 mL) were then added to the reaction mixture, which was then filtered, the solid was washed with cold EtOAc (3×5 mL), and dried in vacuo to give analytically pure **2c** (290 mg). The filtered organic layer was separated, washed with water (5×15 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of this crude residue by recrystallization from Hex/EtOAc (4/1) gave a further 810 mg (total 1.11 g, 90%): mp 142–143 °C; IR (CH_2Cl_2, cast) 2953, 2930, 2833, 2755, 1664, 1609, 1557, 1304, 1257, 1177, 1031, 772 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.82 (s, 6H), 4.11 (s, 4H), 6.86 (AA′BB′, 4H), 7.26 (m, 6H), 7.26 (t, 1H, J=8.0 Hz), 10.67 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 38.3, 55.3, 114.1, 126.0, 127.8, 130.1, 131.9, 132.7, 143.6, 159.6, 191.3; HRMS (EI) calcd for $C_{23}H_{22}O_3S_2$: 410.1010, found: 410.1010 [M$^+$] (14.6%). Anal. Calcd for $C_{23}H_{22}O_3S_2$: C, 67.29; H, 5.40; S, 15.62. Found: C, 66.96; H, 5.58; S, 15.40.

3.1.5. 2,6-Bis(allylsulfanyl)benzaldehyde (2d). Allyl mercaptan (5.0 mL, 70% purity; stench!) was added to an argon flushed stirred suspension of 2,6-dichlorobenzaldehyde (1.75 g, 10.0 mmol) and K_2CO_3 (4.14 g, 30.0 mmol) in DMF (10 mL). The mixture was heated to 65 °C for 10 h, cooled, diluted with EtOAc (20 mL), and water (10 mL), and then separated. The organic layer was washed with Na_2CO_3 (2×20 mL), water (4×20 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude residue by flash chromatography (Hex/EtOAc, 7/1) gave **2d** as an oil (1.77 g, 71%); IR (neat film) 3081, 2978, 2858, 1670, 1636, 1561, 1552, 1435, 1406, 1202, 988, 922, 772 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.56 (dt, 4H, J=1.2, 6.8 Hz), 5.13 (dq, 2H, J=1.1, 10.0 Hz), 5.21 (dq, 2H, J=1.4, 17.2 Hz), 5.86 (ddt, 2H, J=17.0, 10.2, 6.8 Hz), 7.23 (AB_2, 2H), 7.36 (AB_2, 1H), 10.73 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 36.9, 118.8, 125.9, 132.0, 132.4, 132.5, 143.1, 191.4; HRMS (EI) calcd for $C_{13}H_{14}OS_2$: 250.0486, found: 250.0479 [M$^+$] (14.5%).

3.1.6. 2,6-Bis(2-hydroxyethylsulfanyl)benzaldehyde (2e). 2-Mercaptoethanol (1.72 g, 1.50 mL, 22.0 mmol) was added to a stirred degassed suspension of K_2CO_3 (3.00 g, 22.0 mmol) and 2,6-dichlorobenzaldehyde (1.75 g, 10.0 mmol) in DMF (5 mL). This mixture was heated to 65 °C for 8 h, cooled to rt, filtered, and recrystallized from $CHCl_3$/Hex to give 2.14 g (83%) of a light yellow solid: mp 130–131 °C; IR (μscope) 3231 (br), 2928, 2872, 1670,

1200 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.14 (t, 4H, J=6.3 Hz), 3.83 (t, 4H, J=6.0 Hz), 7.31–7.32 (A_2B, 1H), 7.38–7.41 (A_2B, 2H), 10.76 (s, 1H); ^{13}C NMR (CD_3OD, 125 MHz) δ 36.9, 61.1, 126.5, 133.4, 134.1, 144.5, 192.5; HRMS (EI) M^+ $C_{11}H_{914}O_3S_2$ calcd: 258.0385, found: 258.0384.

3.1.7. 2,6-Bis(*tert*-butylsulfanyl)benzaldehyde (2f). *tert*-Butyl mercaptan (2.45 mL, 22.0 mmol) was added dropwise to a stirred degassed suspension of NaH (50% in mineral oil, 0.96 g, 20.0 mmol) in DMF (5 mL). After the hydrogen evolution ceased, 2,6-dichlorobenzaldehyde (1.75 g, 10.0 mmol) was added portionwise (caution, exothermic!). This mixture was stirred for 2 h at 60 °C, cooled to rt, diluted with water (ca. 80 mL), and extracted with EtOAc (3×40 mL). The combined organic extracts were washed with water (4×20 ml), and concentrated in vacuo to give an amber oil. This material was heated to 100 °C in vacuo for 20 min, and then cooled to give a yellow solid. This was recrystallized from MeOH to give the title compound as a yellow crystalline solid (2.03 g, 72%). The mother liquor from the recrystallization was concentrated in vacuo, and the solid was again recrystallized to give an additional 452 mg (total yield, 88%): mp 58.0–59.5 °C; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.12 (s, 18H), 7.31–7.32 (A_2B, 1H), 7.38–7.41 (A_2B, 2H), 10.76 (s, 1H); ^{13}C NMR (CD_3OD, 125 MHz) δ 11.4, 41.1, 126.5, 133.4, 134.2, 146.5, 192.2; HRMS (EI) M^+ $C_{15}H_{22}OS_2$ calcd: 282.1112, found: 282.1115.

3.1.8. 2,6-Bis(2-(3,5-dioxo-4-aza-tricyclo[5.2.1^{2,6}]dec-8-en-4-yl)ethanethio)benzaldehyde (2g). A solution of thiol **1g** (223 mg, 0.842 mmol) and 2,6-dichlorobenzaldehyde (85 mg, 0.49 mmol) in dry DMF (2 mL) was degassed with a stream of argon for 30 min. K_2CO_3 (138 mg, 1.00 mmol) was added under an argon blanket and the mixture was maintained at this temperature for a further 5 min under argon. The mixture was heated to 60 °C and stirred for 4 h. The mixture was cooled, diluted with H_2O (10 mL), and extracted with EtOAc (3×15 mL). The combined organic layers were washed with water (3×20 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude residue by flash chromatography eluting with Hex/EtOAc (2/1 to 1/2) afforded the aldehyde **2g** as a yellow solid (239 mg, 89%): R_f=0.2 (Hex/EtOAc, 4/3), mp 117–119 °C; IR ($CHCl_3$, cast) 2989, 2860, 1764, 1698, 1670, 1562, 1396, 1335, 1203, 1126, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.50 (d, 2H, J=8.5 Hz), 1.69 (dt, 2H, J=8.5, 1.5 Hz), 2.93 (m, 4H), 3.21 (dd, 4H, J=1.5, 3.0 Hz), 3.34 (m, 4H), 3.54 (m, 4H), 6.07 (t, 2H, J=1.8 Hz), 7.36 (AB_2, 2H), 7.45 (AB_2, 1H), 10.61 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 29.9, 40.0, 44.9, 45.8, 52.2, 124.9, 131.7, 133.2, 134.5, 142.2, 177.2, 190.6; HRMS (EI) calcd for $C_{29}H_{28}O_5S_2N_2$: 548.14398, found: 548.14340 [M^+] (1.20%).

3.1.9. 2-Chloro-6-(2-hydroxyethylsulfanyl)benzaldehyde (2h). 2-Mercaptoethanol (780 mg, 700 μL, 10.0 mmol) was added to a stirred degassed suspension of K_2CO_3 (1.40 g, 10.0 mmol) and 2,6-dichlorobenzaldehyde (1.75 g, 10.0 mmol) in DMF (5 mL) at 0 °C. This mixture was heated to 40 °C for 3 h, cooled to rt, diluted with water (ca. 70 mL), and filtered. This material was recrystallized from EtOAc/Hex to give a light yellow solid: mp 114–115 °C; IR (CH_2Cl_2, cast) 3253 (br), 2924, 2880, 2767, 1667, 1415 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.13 (br s, 1H), 3.15 (t, 2H, J=6.0 Hz), 3.88 (t, 2H, J=6.0 Hz), 7.21 (dd, 1H, J=8.0, 1.0 Hz), 7.31 (d, 1H, J=8.5 Hz), 7.37 (t, 1H, J=8.0 Hz), 10.58 (d, 1H, J=0.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz), δ 35.1, 60.2, 124.7, 126.5, 129.5, 133.5, 139.9, 143.9, 190.5; HRMS (EI) M^+ $C_9H_9O_2S^{37}Cl$ calcd: 217.9982, found: 217.9971.

3.1.10. 5-(2,6-Bis(phenylsulfanyl)phenyl)dipyrromethane (3a). TFA (30 μL, 0.40 mmol) was added to a degassed stirred solution of aldehyde **2a** (1.29 g, 4.00 mmol) in pyrrole (10.7 g). The solution was stirred for 15 min, and then the reaction was quenched by the addition of 0.1 M NaOH (4 mL). EtOAc (20 mL) was added and the layers were separated. The organic layer was washed with water (3×10 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification by flash chromatography (Hex/EtOAc=8/1) gave an amber solid (928 mg, 53%); IR (CH_2Cl_2, cast) 3390, 3056, 1674, 1552, 1476, 1438, 749 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.13 (m, 2H), 6.21 (q, 2H, J=3.0 Hz), 6.70 (dd, 2H, J=2.7, 1.5 Hz), 6.78 (s, 1H), 7.18 (t, 1H, J=7.8 Hz), 7.16 (d, 2H, J=7.8 Hz), 7.20–7.35 (m, 10H), 8.63 (br s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.9, 107.8, 108.6, 116.9, 127.2, 127.9, 129.3, 130.9, 131.3 (br), 132.9, 136.5, 137.7 (br), 143.5; HRMS (EI) calcd for $C_{27}H_{22}S_2N_2$: 438.1224, found: 438.1225 [M^+], (100%).

3.1.11. 5-(2,6-Dithiomethoxyphenyl)dipyrromethane (3b). TFA (129 μL, 1.66 mmol) was added to a degassed stirred solution of aldehyde **2b** (990 mg, 5.0 mmol) in pyrrole (20 mL). After the solution was stirred for 25 min, the reaction was quenched by the addition of 0.1 M NaOH (20 mL). The mixture was diluted with EtOAc (30 mL) and separated. The organic layer was washed with water (2×20 mL), dried (Na_2SO_4), concentrated in vacuo, and purified by flash chromatography (Hex/EtOAc=5/1) to give a colorless foam (509 mg, 31%): mp 102–104 °C; IR ($CHCl_3$, cast) 3373, 2917, 1557, 1433, 1027, 715 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.42 (s, 6H), 6.08 (m, 2H), 6.19 (m, 2H), 6.52 (s, 1H), 6.72 (m, 2H), 7.13 (d, 2H, J=8.0 Hz), 7.21 (t, 1H, J=7.6 Hz), 8.67 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 17.7, 39.9, 107.7, 108.3, 116.6, 124.8, 127.6, 130.6, 138.4, 139.1; HRMS (EI) calcd for $C_{17}H_{18}S_2N_2$: 314.0912, found: 314.0907 [M^+] (100.0%). Anal. Calcd for $C_{17}H_{18}S_2N_2C$: 64.97; H, 5.73; N, 8.92. Found: C, 65.12; H, 5.44; N, 8.89.

3.1.12. 5-(2,6-Bis(4-methoxybenzylsulfanyl)phenyl)dipyrromethane (3c). TFA (710 mg μL, 6.23 mmol) was added to a degassed stirred solution of aldehyde **2c** (1.44 g, 3.50 mmol) in pyrrole (35 mL) and CH_2Cl_2 (ca. 5 mL added to dissolve the aldehyde). After the solution was stirred for 15 min, the reaction was quenched by the addition of 0.1 M NaOH (20 mL). EtOAc (50 mL) was added, the layers were separated, and the organic layer was washed with water (2×40 mL), dried (Na_2SO_4), concentrated in vacuo, and purified by flash chromatography (Hex/EtOAc, 4/1) to give a light yellow foam (880 mg, 48%): R_f=0.2 (Hex/EtOAc=4/1), mp 65–70 °C (dec); IR (CH_2Cl_2, cast) 3387, 2932, 2834, 1609, 1554, 1511, 1249 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.70 (s, 6H), 4.02 (s, 4H), 6.02 (m, 2H), 6.13 (q, 2H, J=3.0 Hz), 6.58 (dt, 2H, J=1.5, 2.7 Hz),

6.72 (s, 1H), 6.82 (AA′BB′, 4H), 7.08–7.18 (m, 6H), 7.89 (br s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 40.1 (br), 40.7, 55.6, 107.8, 108.6, 114.3, 116.9, 127.6, 129.6, 130.3, 131.0, 131.4, 137.6, 143.7, 159.2; HRMS (EI) calcd for $C_{31}H_{30}O_2N_2S_2$: 526.1749, found: 526.1753 [M^+] (61.3%).

3.1.13. 5-(2,6-Bis(allylsulfanyl)phenyl)dipyrromethane (3d). TFA (30 μL, 0.40 mmol) was added to a degassed stirred solution of aldehyde **2d** (1.00 g, 4.00 mmol) in pyrrole (10.7 g). After the solution was stirred for 15 min, the reaction was quenched by the addition of 0.1 M NaOH (4 mL). The mixture was diluted with EtOAc (20 mL) and separated. The organic layer was washed with water (3×10 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification by flash chromatography (Hex/EtOAc=8/1) gave an amber solid (760 mg, 51%); IR (CH_2Cl_2, cast) 3380, 3080, 2976, 1665, 1634, 1555, 1427, 1027, 922, 749 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.49, (d, 4H, J=7.2 Hz), 5.10 (m, 4H), 5.82 (m, 2H), 6.07 (m, 2H), 6.20 (m, 2H), 6.72 (m, 2H), 6.78 (s, 1H), 7.18 (t, 1H, J=8.0 Hz), 7.33 (d, 2H, J=8.0 Hz), 8.65 (br s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 38.4, 40.4, 107.5, 108.5, 116.5, 118.1, 127.2, 130.1, 131.1, 133.3, 137.0, 143.1; HRMS (EI) calcd for $C_{21}H_{22}S_2N_4$: 366.1224, found: 366.1221 [M^+] (100%).

3.1.14. 5-(2,6-Bis(*tert*-butylsulfanyl)phenyl)dipyrromethane (3f). TFA (23 μL, 0.30 mmol) was added to a degassed stirred solution of aldehyde **2f** (846 mg, 3.0 mmol) in pyrrole (15 mL) and CH_2Cl_2 (ca. 5 mL added to dissolve the aldehyde). After the solution was stirred for 15 min, the reaction was quenched by the addition of 0.1 M NaOH (30 mL). The mixture was diluted with EtOAc (100 mL) and separated. The organic layer was washed with water (2×40 mL), dried (Na_2SO_4), concentrated in vacuo, and purified by flash chromatography (Hex/EtOAc) to give **3f** as a light yellow foam (549 mg, 46%); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.18 (s, 18H), 5.94–5.96 (m, 2H), 6.12 (q, 2H, J=3.0 Hz), 6.65 (dd, 2H, J=1.5, 3.0 Hz), 7.09 (s, 1H), 7.15 (t, 1H, J=8.0 Hz), 7.61 (d, 2H, J=8.0 Hz), 8.52 (br s, 2H, N*H*); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 31.5, 41.4, 48.0, 107.2, 108.2, 115.7, 125.9, 131.8, 137.3 (br, 2 overlapping C, supported with the HMBC spectrum), 149.6 (1C not observed); HRMS (EI) calcd for $C_{23}H_{30}N_2S_2$: 398.1850, found: 398.1841 [M^+], (51%).

3.1.15. 5-(2-Chloro-6-(2-hydroxyethylsulfanyl)phenyl)-dipyrromethane (3h). TFA (710 mg μL, 6.23 mmol) was added to a degassed stirred solution of aldehyde **2h** (756 mg, 3.50 mmol) in pyrrole (35 mL) and CH_2Cl_2 (ca. 5 mL added to dissolve the aldehyde prior to the addition of pyrrole). After the solution was stirred for 15 min, the reaction was quenched by the addition of 0.1 M NaOH (20 mL). The mixture was diluted with EtOAc (50 mL) and separated. The organic was washed with water (2× 40 mL), dried (Na_2SO_4), concentrated in vacuo, and purified by flash chromatography (Hex/EtOAc, 4/1 to 2/1) to give a light yellow foam (480 mg, 1.45 mmol, 40%); IR ($CHCl_3$, cast) 3358, 1667, 1556, 720 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.83 (br s, 1H), 3.00 (t, 2H, J=5.5 Hz), 3.61 (t, 2H, J=5.5 Hz), 6.01–6.05 (m, 2H), 6.17 (q, 2H, J=3.0 Hz), 6.50–6.67 (br s, 1H), 6.68–6.70 (m, 2H), 7.12 (t, 1H, J=8.0 Hz), 7.26 (d, 1H, J=8.0 Hz), 7.33 (br s, 1H), 8.60–8.80 (br s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 38.4, 40.3, 59.8, 107.4, 108.6, 117.0, 128.1, 130.2, 135.7, 137.7; HRMS (EI) calcd for $C_{17}H_{17}ON_2S^{35}Cl$: 332.0750, found: 332.0750 [M^+] (100%).

3.1.16. 5,15-Bis(2,6-diphenylsulfanylphenyl)-10,20-bis(*p*-tolyl)porphyrin (4a). TFA (144 μL, 1.78 mmol) was added to a degassed solution of **3a** (438 mg, 1.00 mmol) and *p*-tolualdehyde (120 mg, 1.00 mmol) in CH_2Cl_2 (100 mL). After the solution was stirred for 30 min, DDQ (340 mg, 1.50 mmol) was added. After an additional 1 h, the reaction mixture was filtered through a Florisil column (2 cm× 10 cm), and eluted with CH_2Cl_2. The purple fractions were combined, and concentrated in vacuo to give a purple solid. This solid was purified further by flash chromatography (Hex/EtOAc) to give the title compound (154 mg, 25%); IR (CH_2Cl_2, cast) 3316, 3072, 2956, 2156, 1549, 1248, 797 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ −2.38 (s, 2H), 0.40 (s, 18H), 7.1–7.2 (s, 20H), 7.23 (d, 4H, J=8.0 Hz), 7.45 (t, 2H, J=8.0 Hz), 7.88 (AA′MM′, 4H), 8.22 (AA′MM′, 4H), 8.77 (s, 8H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 0.09, 95.4, 105.2, 115.8, 119.0, 122.4, 126.2, 127.9, 129.1, 129.4, 130.0 (br), 130.3, 131.4 (br), 133.5, 134.2, 134.5, 139.5, 142.4, 143.1; MS (ES) 1239.4 [MH^+]; UV 432, 524, 559, 598, 660 nm.

3.1.17. 5,15-Bis(2,6-thiomethoxyphenyl)-10,20-bis(*p*-tolyl)porphyrin (4b). TFA (69 μL, 0.89 mmol) was added to a solution of dipyrromethane **3b** (157 mg, 0.500 mmol) and *p*-tolualdehyde (60 mg, 0.50 mmol) in freshly distilled CH_2Cl_2 (50 mL). After the solution was stirred for 30 min, DDQ (170 mg, 0.75 mmol) was added and the mixture was stirred for further 45 min. The crude mixture was filtered through a Florisil column (2.5×15 cm) and eluting with CH_2Cl_2. Concentration in vacuo gave a purple solid (40 mg, 19%); IR (CH_2Cl_2, cast) 3319, 2916, 1555, 1428, 965, 786 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ −2.43 (s, 2H), 2.20 (s, 12H), 2.66 (s, 6H), 7.40 (AA′BB′, 4H), 7.47 (d, 4H, J=8.0 Hz), 7.75 (t, 2H, J=8.3 Hz), 8.06 (AA′BB′, 4H), 8.56 (d, 4H, J=4.5 Hz), 8.82 (d, 4H, J=4.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 16.2, 21.6, 114.7, 119.7, 120.5, 127.3, 129.5, 129.8 (br), 131.8 (br), 134.5, 137.2, 137.4, 139.0, 143.4; HRMS (ES) calcd for $C_{50}H_{43}N_4S_4$: 827.2371, found: 827.2371 [MH^+].

3.1.18. 5,15-Bis(2,6-bis(4-methoxybenzylsulfanyl)-phenyl)-10,20-bis(*p*-tolyl)porphyrin (4c). TFA (137 μL, 1.78 mmol) was added to a solution of dipyrromethane **3c** (526 mg, 1.00 mmol) and *p*-tolualdehyde (120 mg, 1.00 mmol) in freshly distilled CH_2Cl_2 (100 mL). After the solution was stirred for 30 min, DDQ (340 mg, 1.5 mmol) was added and the mixture was stirred for further 45 min. The crude mixture was filtered through an alumina column (2.5×15 cm) and eluted with CH_2Cl_2. Concentration of the purple eluent gave a purple solid (322 mg, 51%); IR (CH_2Cl_2, cast) 3350, 3317, 2924, 2933, 1609, 1582, 1511, 1249, 798 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ −2.36 (s, 2H), 2.75 (s, 6H), 3.64 (s, 12H), 3.82 (s, 8H), 6.57 (AA′BB′, 8H), 6.86 (AA′BB′, 8H), 7.61 (m, 6H), 7.52 (AA′BB′, 4H), 8.05 (AA′BB′, 4H), 8.56 (d, 4H, J=4.5 Hz), 8.82 (d, 4H, J=4.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.7, 37.9, 55.2, 113.6, 115.5, 124.6, 128.6, 129.0, 129.6, 131.3 (br), 134.6, 137.1, 139.2, 140.6, 141.5, 158.4; MS (ES) 1251.4 [MH^+]; λ_{abs} 430, 523, 555, 602, 660 nm.

3.1.19. 5,15-Bis(2,6-diallylsulfanylphenyl)-10,20-bis(*p*-tolyl)porphyrin (4d). TFA (144 μL, 1.78 mmol) was added to a degassed solution of **3d** (467 mg, 1.00 mmol) and 4-(trimethylsilylethynyl)benzaldehyde (202 mg, 1.00 mmol) in CH_2Cl_2 (100 mL). After the solution was stirred for 30 min, DDQ (340 mg, 1.50 mmol) was added. After an additional 1 h, the reaction mixture was filtered through a Florisil column (2 cm×10 cm) and eluted with CH_2Cl_2. The purple fractions were combined, and concentrated in vacuo to give a purple solid. This solid was purified further by flash chromatography (Hex/EtOAc, 6/1) to give the title compound (98 mg, 21%): R_f=0.5 (Hex/EtOAc, 3/1); IR (CH_2Cl_2, cast) 3318, 3021, 2918, 1636, 1553, 1347, 982 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ −2.40 (s, 2H, NH), 2.67 (s, 6H), 3.49 (dt, 8H, *J*=5.5, 1.3 Hz), 4.92 (dq, 4H, *J*=10.0, 1.3 Hz), 5.02 (dq, 4H, *J*=17.0, 1.5 Hz), 5.51 (ddt, 4H, *J*=17.5, 10.0, 6.8 Hz), 7.51 (AA′BB′, 8H), 7.67 (t, 2H, *J*=7.5 Hz), 8.10 (AA′BB′, 4H), 8.59 (d, 4H, *J*=5.0 Hz), 8.78 (d, 4H, *J*=4.8 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.6, 36.5, 115.4, 117.8, 124.2, 127.4, 128.9, 129.8 (br), 131.5 (br), 133.2, 134.6, 137.2, 139.2, 140.6, 141.3; HRMS (ES) calcd for $C_{58}H_{51}S_4N_4$: 931.2997, found: 931.3004 [MH^+].

3.1.20. 5,15-Bis(2,6-diphenylsulfanylphenyl)-10,20-bis(*p*-tolyl)porphyrin (4i). TFA (144 μL, 1.78 mmol) was added to a degassed solution of **3c** (366 mg, 1.00 mmol) and *p*-tolualdehyde (120 mg, 1.00 mmol) in CH_2Cl_2 (100 mL). After the solution was stirred for 30 min, DDQ (340 mg, 1.50 mmol) was added. After an additional 1 h, the reaction mixture was filtered through a Florisil column (2 cm× 10 cm) and eluted with CH_2Cl_2. The purple fractions were combined, and concentrated in vacuo to give a purple solid. This solid was purified further by flash chromatography (Hex/EtOAc, 6/1) to give the title compound as a purple solid (155 mg, 21%): R_f=0.5 (Hex/EtOAc, 3/1); IR (CH_2Cl_2, cast) 3316, 2930, 1682, 1609, 1511, 1301, 1249, 800 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ −2.52 (s, 2H, NH), 3.60 (s, 12H), 3.78 (s, 8H), 6.50 (AA′MM′, 8H), 6.78 (AA′MM′, 8H), 7.47 (d, *J*=7.5 Hz, 4H), 7.59 (t, *J*=7.5 Hz, 2H), 7.97 (AA′MM′, 4H), 8.07 (AA′MM′, 4H), 8.49 (d, *J*=5.5 Hz, 4H), 8.67 (d, *J*=5.5 Hz, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 37.8, 55.1, 93.9, 113.5, 116.0, 118.1, 124.5, 128.5, 129.1, 129.6, 130 (br), 131 (br), 135.8, 136.3, 140.2, 141.5, 141.7, 158.5, (two carbon signals not observed); MS (ES) 1475.1 [MH^+].

3.1.21. 5,15-Bis(2-chloro-6-(2-hydroxyethylsulfanyl)-phenyl-10,20-bis(4-butoxyphenyl)porphyrin (4h). TFA (144 μL, 1.78 mmol) was added to a solution of **3h** (332 mg, 1.00 mmol) and 4-butoxybenzaldehyde[18] (192 mg, 1.00 mmol) in CH_2Cl_2 (100 mL). After the solution was stirred 30 min, DDQ (340 mg, 1.50 mmol) was added and the mixture was stirred for further 45 min. The crude mixture was filtered through a Florisil column (2.5×15 cm) and eluted with CH_2Cl_2→2% MeOH in CH_2Cl_2 until no further porphyrin was eluted. The eluent was concentrated in vacuo and purified by flash chromatography to give the α,α-isomer (82 mg, 17%) and the α,β-isomer (77 mg, 16%). Data for the α,α-isomer: IR (CH_2Cl_2, cast) 3600–3150, 3316, 2955, 2924, 2854, 1505, 1466, 1245 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ −2.46 (s, 2H), 1.11 (t, 6H, *J*=7.4 Hz), 1.60 (br s, 2H), 1.67 (Hex, 4H, *J*=7.4 Hz), 1.98 (quin, 4H, *J*=7.0 Hz), 2.72 (t, 4H, *J*=6.0 Hz), 3.39 (t, 4H, *J*=5.8 Hz), 4.24 (t, 4H, *J*=6.4 Hz), 7.25 (d, 4H, *J*=7.8 Hz), 7.58 (dd, 2H, *J*=1.6, 7.8 Hz), 7.66 (t, 2H, *J*=8.0 Hz), 7.69 (dd, 2H, *J*=1.6, 8.0 Hz), 8.09 (dd, 2H, *J*=2.8, 0.4 Hz), 8.15 (dd, 2H, *J*=2.8, 0.4 Hz), 8.63 (d, 4H, *J*=4.8 Hz), 8.89 (d, 4H, *J*=4.8 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.0, 19.4, 31.5, 36.7, 59.7, 68.0, 112.8, 114.6, 120.1, 125.3, 126.5, 129 (br), 130.0, 132 (br), 133.8, 135.59, 135.63, 138.0, 140.4, 142.0, 144–148 (br), 159.0; HRMS (ES) calcd for $C_{56}H_{53}N_4O_4S_2Cl_2$: 979.2885, found: 979.2884. Data for α,β-isomer: IR (CH_2Cl_2, cast) 3600–3200, 3317, 2956, 2925, 1505, 1472, 1429, 1245, 1174 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ −2.42 (s, 2H), 1.27 (t, 6H, *J*=7.4 Hz), 1.39 (br s, 2H), 1.68 (Hex, 4H, *J*=7.4 Hz), 1.98 (quin, 4H, *J*=7.0 Hz), 2.70 (t, 4H, *J*=5.8 Hz), 3.37 (t, 4H, *J*=5.8 Hz), 4.24 (t, 4H, *J*=6.6 Hz), 7.25 (AA′BB′, 4H), 7.53 (d, 2H, *J*=7.8 Hz), 7.61 (t, 2H, *J*=7.9 Hz), 7.67 (d, 2H, *J*=8.0 Hz), 8.14 (AA′BB′, 2H), 8.65 (d, 4H, *J*=4.8 Hz), 8.92 (d, 4H, *J*=4.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0, 19.4, 31.5, 38.7, 59.7, 68.0, 112.8, 114.6, 120.1, 125.3, 126.5, 129.2 (br), 130.0, 132.0 (br), 133.8, 135.6, 140.0, 142.0, 159.0; HRMS (ES) calcd for $C_{56}H_{53}N_4O_4S_2Cl_2$: 979.2885, found: 979.2886.

Acknowledgements

We gratefully acknowledge the financial support from the Natural Sciences and Engineering Research Council of Canada (NSERC) and the Canada Research Chair in Bioorganic and Medicinal Chemistry.

References and notes

1. (a) Holten, D.; Bocian, D. F.; Lindsey, J. S. *Acc. Chem. Res.* **2002**, *35*, 57–69; (b) Boyd, P. D. W.; Reed, C. A. *Acc. Chem. Res.* **2005**, *38*, 235–242; (c) Anderson, H. L. *Chem. Commun.* **1999**, 2323–2330.
2. Kieran, A. L.; Bond, A. D.; Belenguer, A. M.; Sanders, J. K. M. *Chem. Commun.* **2003**, 2674–2675.
3. (a) Collman, J. P.; Kaplun, M.; Sunderland, C. J.; Boulatov, R. *J. Am. Chem. Soc.* **2004**, *126*, 11166–11167; (b) Collman, J. P.; Yan, Y.-L.; Lei, J.; Dinolfo, P. H. *Org. Lett.* **2006**, *8*, 923–926; (c) Gao, G.-Y.; Harden, J. D.; Zhang, X. P. *Org. Lett.* **2005**, *7*, 3191–3193; (d) Collman, J. P.; Boulatov, R.; Sunderland, C. J.; Fu, L. *Chem. Rev.* **2004**, *104*, 561–588.
4. Balaban, T. S. *Acc. Chem. Res.* **2005**, *38*, 612–623.
5. (a) Sen, A.; Suslick, K. S. *J. Am. Chem. Soc.* **2000**, *122*, 11565–11566; (b) Ogoshi, H.; Mizutani, T. *Acc. Chem. Res.* **1998**, *31*, 81–89.
6. Jux, N. *Org. Lett.* **2000**, *2*, 2129–2132.
7. Nakagawa, H.; Nagano, T.; Higuchi, T. *Org. Lett.* **2001**, *3*, 1805–1807.
8. (a) Wagner, R. W.; Ruffing, J.; Breakwell, B. V.; Lindsey, J. S. *Tetrahedron Lett.* **1991**, *32*, 1703–1706; (b) Wagner, R. W.; Lindsey, J. S.; Turowska-Tyrk, I.; Scheidt, W. R. *Tetrahedron* **1994**, *50*, 11097–11112.
9. Foxon, S. P.; Lindsay Smith, J. R.; O'Brien, P.; Reginato, G. *J. Chem. Soc., Perkin Trans. 2* **2001**, 1145–1153.
10. Rose, E.; Kossanyi, A.; Quelquejeu, M.; Soleilhavoup, M.; Duwavran, F.; Bernard, N.; Lecas, A. *J. Am. Chem. Soc.* **1996**, *118*, 1567–1568.

11. Gairns, R. S.; Grant, R. D.; Moody, C. J.; Rees, C. W.; Tsoi, S. C. *J. Chem. Soc., Perkin Trans. 1* **1986**, 491–495.
12. As judged by the relative integrations of the formyl signals of the three compounds.
13. Littler, B. J.; Miller, M. A.; Hung, C.-H.; Wagner, R. W.; O'Shea, D. F.; Boyle, P. D.; Lindsey, J. S. *J. Org. Chem.* **1999**, *4*, 1391–1396.
14. Attempts to distill **3a** employing a Kugelrohr apparatus resulted only in the degradation of the material.
15. Lindsey, J. S.; Wagner, R. W. *J. Org. Chem.* **1989**, *54*, 828–836.
16. Medforth, C. J. *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic: Boston, 2000; Vol. 5, p 30.
17. Ray, F. E.; Sawicki, E.; Borum, O. H. *J. Am. Chem. Soc.* **1952**, *74*, 1247–1249.
18. Li, R.-L. D.; Diedrich, S. W.; Hansch, C. *J. Med. Chem.* **1981**, *24*, 538–544.