Synthesis of Bronzaphyrin NS

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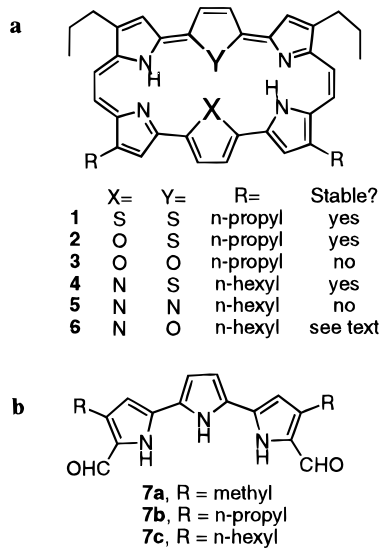
Introduction

The chemistry of porphyrin analogs and homologs has enjoyed a period of extended growth. Most of the isomers of porphyrin [1.1.1.1] have now been synthesized,[1] as well as a number of sapphyrin, corrin, and other macrocycles fitting the broad definition of "pentaplanar".[2] "Pentaplanar" is a term describing an aromatic macrocycle consisting of five-membered rings linked by sp^2-hybridized atoms.[3,4] This paper focuses on some members of the [2.0.0.2.0.0] family of annulenes (Figure 1a). This subset of the [2.0.0.2.0.0] family is known as the "bronzaphyrins" because of their color in solution.[5] Due to their heteroatoms' placement and the availability of labile protons on the interior perimeter, the bronzaphyrins as a family are potential "binucleating porphyrins" that may be able to hold two metal ions within a single aromatic macrocyclic ring. Those made so far are bronzaphyrin SS (**1**) and OS (**2**); bronzaphyrin OO (**3**) has not yet been isolated and may be too electrophilic to survive under ambient conditions. The final members of this series, bronzaphyrins NS (**4**), NN (**5**), and NO (**6**), have been synthetically unattainable because of the extreme insolubility of the precursor terpyrrole dialdehydes made thus far (Figure 1b): Both **7a**[6] and **7b**[7] are virtually insoluble in both THF and dioxane, the only acceptable solvents for the McMurry coupling of porphycene homologs. These observations prompted the synthesis of the much more soluble, ergo synthetically fecund, hexyl homolog **7c** reported herein, and subsequently **4**.

Results and Discussion

This approach to **7c** (Scheme 1) was rendered practical by a reported patent application for the synthesis of



	X=	Y=	R=	Stable?
1	S	S	n-propyl	yes
2	O	S	n-propyl	yes
3	O	O	n-propyl	no
4	N	S	n-hexyl	yes
5	N	N	n-hexyl	no
6	N	O	n-hexyl	see text

Figure 1.

β-keto esters.[8] Although an old class of compounds, their synthesis on a large scale has been either difficult or expensive to undertake due to the water- and oxygen-sensitivity of most methods.[9] By contrast, Meier's acyl-exchange method is run in air, tolerates minor amounts of water, is scalable, uses inexpensive reagents, and is adaptable to many functional groups. The calcium chelate of ethyl acetoacetate **8** is first prepared in dichloromethane suspension. This chelate readily undergoes acyl exchange with any acid chloride to give a chelated ester that is hydrolyzed, separated, and distilled. Ethyl 3-oxononanoate **9** has been routinely prepared in 80−100 g batches with yields as high as 70%, although yields around 40% are more typical.

Knorr synthesis using **9** gave a 40−45% yield of pyrrole **10**, which was treated with SO_2Cl_2 to give the aldehyde **11**. Stetter coupling of **11** gave the dipyrrolylbutanedione **12**, which gave terpyrrole ester **13** in 90% yield upon refluxing with $NH_4OAc/Ac_2O/HOAc$. Ester **13**, when treated with NaOH in refluxing ethylene glycol for 30 min, decarboxylated readily to give the highly air-sensitive, but thermally robust, terpyrrole **14**. Vilsmier−Clezy formylation of **14** with PhCOCl/DMF gave the dication **15**, which was isolated by filtration. Hydrolysis of **15** to give the desired aldehyde **7c** turned out to be nontrivial and was eventually achieved by use of $[Et_4N^+]_2[CO_3^{2-}]$ in DMF. Both **15** and **7c** are temperature sensitive, and care must be taken to keep the hydrolysis below 50 °C to achieve good purity and yield.

Macrocycle **4** was made by crossed McMurry coupling of **7c** with aldehyde **16**,[10] yielding a mixture of dihydro precursors **17**, **18**, and **19**. These precursors air oxidize to give only the two products **1** and **4**. Apparently **5** is

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(1) Sessler, J. L. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1348−1350.

(2) (a) Sessler, J. L.; Burrell, A. K. *Top. Curr. Chem.* **1991**, *161*, 177−273. (b) Vogel, E. *Pure Appl. Chem.* **1993**, *65*, 143−152. (c) Sapphyrin review: Sessler, J. L.; Cyr, M.; Burrell, A. K. *Tetrahedron* **1992**, *48*, 9661−9672.

(3) The term "expanded porphyrin" has been applied frequently to this class of compounds; however, there are examples of pentaplanar "contracted porphyrins", and the term "expanded porphyrin" has been used to describe a variety of macrocycles, many of which have saturated portions in the core of the ring and/or cannot bind metal ions. The term "pentaplanar" is suggested as a topographically and electronically precise term by the author. For those nonplanar, nonaromatic macrocycles that otherwise qualify as pentaplanar, the term "pentaform" may be preferable. For example, ref 4a−e describes several uncharged poly- and perthiophene "pentaform" annulenes with varying topologies ([2.0.0.2.0.0], [2.0.2.0], [2.0.0.2.0.0], and [2.1.2.1]). Of these, only tetrathia[22]annulene[2.1.2.1] is aromatic[4b] and, therefore, "pentaplanar".

(4) Thiophene-containing annulenes: (a) Kozaki, M.; Parakka, J. P.; Cava, M. P. *J. Org. Chem.* **1996**, *61*, 3657−3661. (b) Hu, Z.; Atwood, J. L.; Cava, M. P. *J. Org. Chem.* **1994**, *59*, 8071−8075. (c) Hu, Z. Y.; Cava, M. P. *Tetrahedron Lett.* **1994**, *35*, 3493−3496. (d) Hu, Z.; Scordilis-Kelley, C.; Cava, M. P. *Tetrahedron Lett.* **1993**, *34*, 1879−1882. (e) Elinger, F.; Gieren, A.; Hübner, Th.; Lex, J.; Merz, A.; Neidlein, R.; Salbeck, J. *Monatsh. Chem.* **1993**, *124*, 931−943.

(5) (a) Miller, D. C.; Johnson, M. R.; Ibers, J. A. *J. Org. Chem.* **1994**, *59*, 2877−2879. (b) Johnson, M. R.; Miller, D. C.; Bush, K.; Becker, J. J.; Ibers, J. A. *J. Org. Chem.* **1992**, *57*, 4414−4417.

(6) Merrill, B.; LeGoff, E. *J. Org. Chem.* **1990**, *112*, 2810−2813.

(7) Johnson, M. R. Unpublished data.

(8) Meier, J. *Chem. Abstr.* **1993**, *118*, 168706.

(9) (a) Benetti, S.; Romagnoli, R.; De Risi, C.; Spalluto, G.; Zanirato, V. *Chem. Rev.* **1995**, *95*, 1065−1114. (b) The reaction of Meldrum's acid with acid chlorides represents an additional possible route to large-scale synthesis of β-keto esters: Oikawa, Y.; Yoshioka, T.; Sugano, K.; Yonemitsu, O. *Organic Syntheses*; Wiley: New York, 1990; Collect. Vol. VI, pp 359−262. (c) Oikawa, Y.; Sugano, K.; Yonemitsu, O. *J. Org. Chem.* **1978**, *43*, 2087−2088.

(10) The use of solid $TiCl_4$·2THF in sealed preweighed bottles makes it possible to dispense with most of the rigors traditionally associated with handling liquid $TiCl_4$; with practice the Ti^0 reagent can be prepared from scratch in 2 h and in warm humid air if the solid $TiCl_4$·2THF is efficaciously handled.

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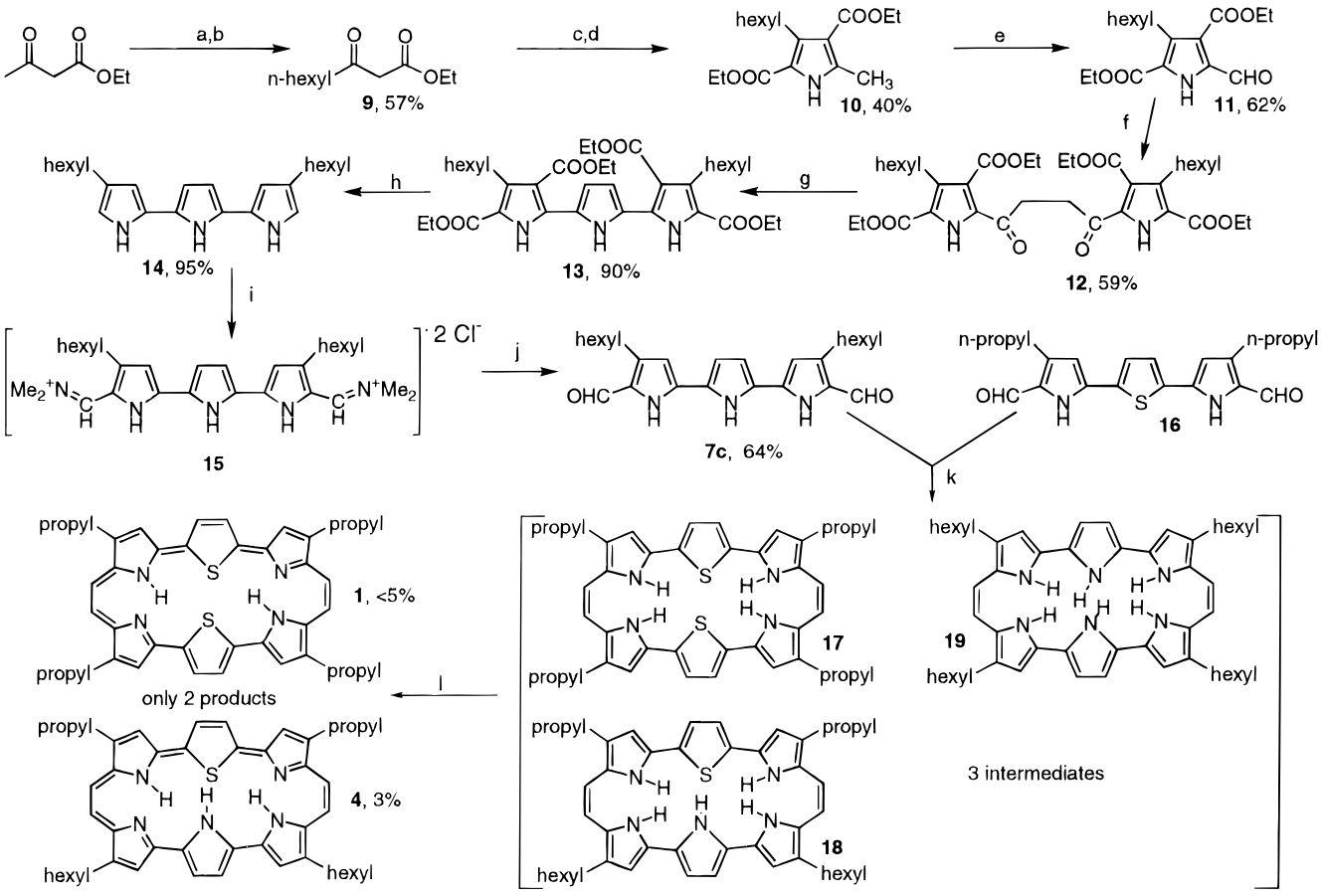
Scheme 1[a]



[a] Key: (a) $Ca(OH)_2/CH_2Cl_2$; (b) heptanoyl chloride; (c) $NaNO_2/H_2HOAc$; (d) Zn/HOAc/70−80 °C; (e) SO_2Cl_2/HOAc/70 °C; (f) divinyl sulfone/Et_3N/Stetter's thiazole/*p*-dioxane/70−75 °C/18 h; (g) NH_4OAc/Ac_2O/HOAc, reflux 18 h; (h) NaOH/$(CH_2OH)_2$/reflux; (i) PhCOCl/DMF/85 °C/11 h; (j) $[Et_4N^+]_2[CO_3^{2-}]$/DMF 55 → 45 °C; (k) $TiCl_4$·2THF/Zn^0/THF/reflux 18 h; (l) air oxidation.

unstable; a control reaction, in which **7c** was the only aldehyde present, gave only an insoluble black solid.[11] Products **1** and **4** have nearly identical chromatographic profiles, and their separation was enabled by the solubility of **4** in hot hexane. Remaining traces of **1** were removed by chromatography.

Compound **4**, like **1**, gives metallic green crystals that produce an orange solution when dissolved. A comparison of the three known bronzaphyrins' UV−vis spectra is given in Figure 2. They all display the same Q-Soret band structure, well accounted for by Platt's perimeter model,[12] with a split Soret region at 380−540 nm, multiple Q peaks at 700−900 nm, and an absorbance minimum at 600 nm that accounts for the orange color in solution. The proton NMR of **4** in $CDCl_3$ (Figure 3) is consistent with its structure; noteworthy is the concentration dependence of the resonances of the internal pyrrole resonances as well as certain external ring protons, attributable to aggregation effects. Under conditions of high dilution, the internal pyrrole resonances are very broad and centered at −0.9 (fwhm ≈ 0.5 ppm) and −5.3 (fwhm ≈ 0.18 ppm). At near saturation, they are sharper and further upfield (−2.3, fwhm 0.2 ppm; −6.8, fwhm 0.1 ppm). The three ring resonances in the region 10.08−10.11 also coalesce into a single peak and shift upfield as concentration increases. EI mass spectroscopy gives a strong parent peak at *m/e* = 711,

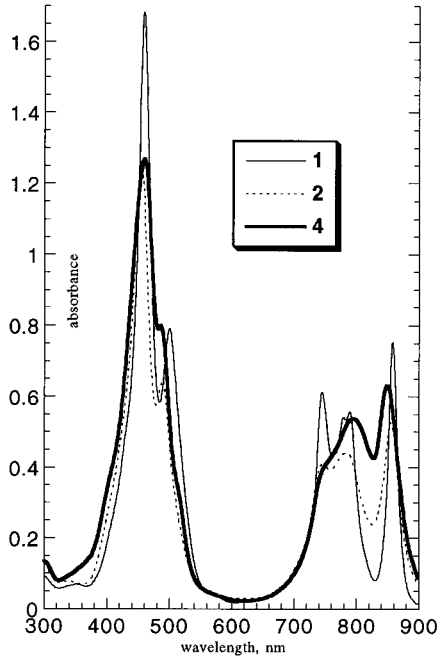


Figure 2. UV−vis spectra (THF, 10 μM) of bronzaphyrins **1**, **2**, and **4**.

(11) A prior experiment, conducted with D. C. Miller and J. A. Ibers, using **7b** and more rigorous anaerobic manipulation of the reaction and workup, gave a quenched solution that was colorless; upon exposure to air it slowly turned pale red and then brown. The colorless solution, when treated with methanolic $Cu^{II}(OAc)_2$, instantly gave a brilliant deep purple color that also quickly turned brown. No products were isolable from this reaction.

(12) Platt, J. R. *J. Chem. Phys.* **1949**, *17*, 484−495.

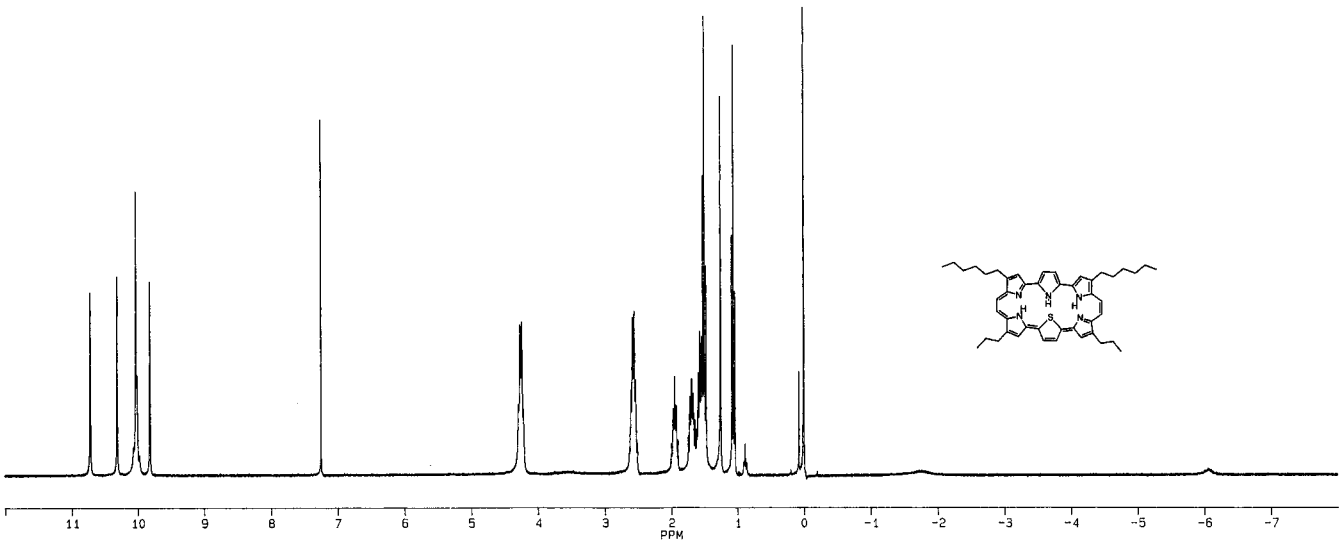


Figure 3. ^{1}H NMR (300 MHz, $CDCl_3$) of **4**.

suggesting a reduced chlorin-like analog of **4** formed instead of **4** itself; however, both proton and ^{13}C spectra of **4** are consistent with a fully aromatic structure and not a chlorin analog.[13]

The family of bronzaphyrins is potentially binucleating, with two centers for ion chelation, each site sharing the two central heteroatoms. Preliminary results indicate that, of the-first row transition metals, only Cu^{2+} shows affinity for **4** and causes rapid autoxidation of the ligand. The final member of the bronzaphyrin series, bronzaphyrin NO **6**, represents the current best hope for achieving wide-ranging binucleating ability in a single planar macrocycle. An experiment to this effect has given encouraging results and will be expanded upon in a further communication.

Experimental Section

Elemental analyses were performed by Atlantic Microlabs, Norcross, GA. Mass spectra were obtained from C. Lambert of the University of Maryland, College Park, MD. ^{1}H and ^{13}C NMR spectral data were collected on a Bruker AC-300 NMR spectrometer at 300 and 75 MHz, respectively, in $CDCl_3$ with TMS as reference. Compounds **1** and **2** were made by literature methods.[5] Anhydrous THF (Aldrich Chemical, Milwaukee, WI) was distilled over Na^0/benzophenone and degassed with argon for 30 min prior to use. Triethylamine (Fisher Scientific, Atlanta, GA) was distilled from CaH_2 prior to use. $TiCl_4$·2THF in 5 g wax-sealed bottles was obtained from Aldrich and opened within 10 s of addition. Divinyl sulfone, 3,4-dimethyl-5-(2-hydroxyethyl)thiazolium iodide, heptanoyl chloride, Et_4NOH, zinc dust, and anhydrous DMF were obtained from Aldrich and used as received. All other reagents and solvents were obtained from Fisher Scientific and used as received.

Ethyl 3-Oxononanoate (9). A three-necked round-bottomed flask was equipped with a reflux condenser, a high torque paddle stirrer, thermometer, and dropping funnel and was charged with powdered CaO (40.32 g, 0.72 mol) and CH_2Cl_2 (700 mL). To the stirred suspension was added ethyl acetoacetate (91 g, 0.70 moles) over a 1/2 h period, maintaining a temperature between 20 and 30 °C.[14] After the mixture was stirred for an additional 30 min, heptanoyl chloride (113 g, 0.76 mol) was added over 1.5 h at 25−35 °C (ice bath). The mixture was stirred for 12 h at room temperature. A solution of ammonium chloride (0.72 mol, 38.52 g) in water (280 mL) was added, followed by concd NH_4OH (150 mL). The mixture was then stirred for another 12 h and acidified to pH 0.5−1 with concd HCl. After 30 min of stirring, the organic layer was separated, washed with 5% Na_2CO_3 (250 mL) and water (2 × 250 mL), and then dried (Na_2SO_4), and volatiles were removed on a rotary evaporator. The liquid residue was cooled to ≤−10 °C[15] to precipitate heptanoyl amide, which was removed by cold vacuum filtration. The filtrate was fractionally distilled *in vacuo*, the fraction boiling at 71−91 °C/0.15 Torr collected (80 g, 0.4 mol, 57%). The distillates from several runs were combined and refractionated, the fraction boiling at 80 °C/0.01 Torr (lit.[16] bp 87 °C/0.8 Torr) used in the next step.

2,4-Dicarbethoxy-3-hexyl-5-methylpyrrole (10). A three-necked 5 L round-bottom flask was equipped with a stir paddle, thermometer, Claisen adapter, and dropping funnel and charged with ethyl 3-oxononanoate (300 g, 1.5 mol) in glacial acetic acid (1400 mL). Sodium nitrite ($NaNO_2$, 109.5 g, 1.58 mol) in water (300 mL) was added dropwise, maintaining a temperature of ≤15 °C with an ice bath. After the addition was complete (∼30 min), the clear yellow solution was stirred for an additional 2 h. A heating mantle was then placed under the flask and the flask fitted with a powder funnel. The dropping funnel was charged with ethyl acetoacetate (200 g, 1.54 mol). Powdered zinc (200 g, 3 mol) was slowly added portionwise; when the flask contents reached 65 °C, ethyl acetoacetate addition commenced, keeping the temperature between 80 and 90 °C. After all the reactants were added, the contents were stirred at 80−90 °C for an additional 1 h, cooled in an ice bath to 40 °C with vigorous stirring, and poured over crushed ice (∼5 Kg). The resulting ice-cold suspension was thoroughly admixed to fully precipitate the crude product. This product was collected by filtration, washed well with water, dissolved in 1400 mL of ethanol, and filtered to remove traces of zinc. The stirred solution was heated to boiling and neutralized with powdered $NaHCO_3$ until no more effervescence was observed at the boiling point. The solution was then filtered or decanted into a 2 L round-bottom flask and ethanol removed on the rotary evaporator. The residue was diluted with 1 L of hexane and dried ($MgSO_4$). Saponified pyrrole salts (if present) precipitated from the hexane solution in 10−30 min. The hexane solution was cooled to −20 °C and the precipitate collected by filtration, washed with cold hexane, and dried in air for 2 days to give the product pyrrole (134 g first crop, 186 g total, 0.6 mol, 40%), mp = 75−78 °C. Anal.

(13) The elemental compositions of dihydrobronzaphyrin and bronzaphyrin are within experimental error of each other and cannot be used to distinguish between the two.

(14) Constant attention must be paid to the stirring mixture. After 10 min, rapid solidification occurs and stirring must be increased at this point in order to avoid formation of a solid matrix. When properly monitored, the result is a viscous slurry. If a solid matrix forms, more CH_2Cl_2 must be added and the matrix broken up into small pieces and stirred until homogenous. The reaction outcome is unaffected by these extra steps.

(15) Dry ice added to the residue works well.

(16) Katzenellenbogen, J. A.; Utawanit, T. *J. Am. Chem. Soc.* **1974**, *96*, 6153−6158.

Calcd for $C_{17}H_{27}NO_4$: C, 66.0; H, 8.8; N, 4.5. Found: C, 65.95; H, 8.58; N, 4.51. ^{1}H NMR ($CDCl_3$) δ: 0.88 (t, 3 H, CH_2CH_2-$CH_2CH_2CH_2CH_2CH_3$); 1.29 (m, 2 H, $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 1.36, 1.37(2 × q, 8 H, 2 × OCH_2CH_3 + $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 1.50−1.63 (m, 4 H, $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 2.52 (s, 3 H, CH_3); 3.03 (t, 2 H, $CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 4.29, 4.33 (2 × q, 4 H, 2 × OCH_2CH_3); 9.1 (br s, 1 H, NH). ^{13}C NMR ($CDCl_3$) δ: 14.0, 14.3, 14.3, 22.6, 25.8, 29.6, 31.3, 31.7, 59.4, 60.2, 112.8, 117.5, 136.0, 139.1, 161.6, 165.2.

2,3-Dicarbethoxy-3-hexylpyrrole-5-carboxaldehyde (11). To a solution of hexylpyrrole **10** (154.5 g, 0.5 mole) in HOAc (1.5 L) maintained at 67−70 °C was added dropwise SO_2Cl_2 (140 g, 1.04 mol) over 10−15 min. A vigorous evolution of SO_2 ensued. The solution was stirred for an additional 30 min at 70−72 °C, followed by the addition of H_2O (200 mL). The reaction mixture was then divided into two halves. Each half was poured into a 2 L separatory funnel, diluted with an additional 700 mL of H_2O, and extracted three times with ligroin (500 mL, 2 × 250 mL). The ligroin extracts were combined, concentrated to 1−1.2 L, and washed with water (3 × 500 mL). The ligroin was completely removed on the rotary evaporator and the residue diluted to 1.2 L with EtOH. The ethanolic solution was brought to a boil with stirring and treated with $NaHCO_3$ (50−100 g) until no more effervescence was observed at the boiling point. The solution was cooled and filtered and the ethanol completely removed under high vacuum. The solid residue was dissolved in warm hexane (800 mL) and air cooled for 10−30 min to allow carboxyl salts to precipitate. These salts were filtered, and the clear solution was placed in a freezer. The precipitate was collected by filtration, washed with cold hexane, and dried to give the product **11** (100−101 g, 0.31 mol, 62%), mp 65−68 °C. ^{1}H NMR ($CDCl_3$) δ: 0.89 (t, 3 H, $CH_2CH_2CH_2CH_2CH_2CH_3$); 1.31 (m, 4 H, $CH_2CH_2CH_2CH_2CH_2CH_3$); 1.40 , 1.41 (2 × q, 8 H, 2 × OCH_2CH_3 + $CH_2CH_2CH_2CH_2CH_2CH_3$); 1.50−1.61 (m, 2 H, $CH_2CH_2CH_2CH_2CH_2CH_3$); 3.08 (t, 2 H, $CH_2CH_2CH_2CH_2CH_2CH_3$); 4.38, 4.39 (2 × q, 4 H, 2 × OCH_2CH_3); 9.89 (br s, 1 H, NH); 10.27 (s, 1 H, CHO). ^{13}C NMR ($CDCl_3$) δ: 14.1, 14.3, 22.6, 25.2, 29.5, 31.1, 31.7, 60.8, 61.2, 120.2, 123.5, 133.5, 136.2, 160.3, 163.5, 182.7. Anal. Calcd for $C_{17}H_{25}NO_5$: C, 63.1; H, 7.8; N, 4.3. Found: C, 63.20; H, 7.80; N, 4.38.

1,4-Bis[3,5-bis(ethoxycarbonyl)-4-*n*-hexyl-2-pyrrolyl]-1,4-butanedione (12). A mixture of aldehyde **11** (196 g, 0.606 mol), divinyl sulfone (35.8 g, 0.303 mol), 3,4-dimethyl-5-(2-hydroxyethyl)thiazolium iodide (25 g, 0.09 mol), and Et_3N (18.4 g, 0.18 mol) in dry dioxane (1200 mL) was stirred at 70−75 °C for 18 h. The dioxane was completely removed under high vacuum, the residue taken up in 1 L hot hexane, and filtered. The cooled filtrate was placed in a freezer for 12 h. The solid so obtained was collected by filtration and again recrystallized from hexane; cooling to room temperature gave a precipitate that was collected by filtration, washed with hexane, and dried to give product **12** (120 g, 0.18 mol, 59%), mp 85−85 °C. ^{1}H NMR ($CDCl_3$) δ: 0.89 (t, 6 H, $CH_2CH_2CH_2CH_2CH_2CH_3$); 1.31 (m, 8 H, $CH_2CH_2CH_2CH_2CH_2CH_3$); 1.37, 1.41 (2 × q, 16 H, 2 × OCH_2CH_3 + $CH_2CH_2CH_2CH_2CH_2CH_3$); 1.48−1.67 (m, 4 H, $CH_2CH_2CH_2$-$CH_2CH_2CH_3$); 2.91 (t, 4 H, $CH_2CH_2CH_2CH_2CH_2CH_3$); 3.36 (s, 4 H, C(=O))CH_2CH_2C(=O)); 4.35, 4.40 (2 × q, 8 H, 2 × OCH_2CH_3); 9.88 (br s, 2 H, NH). ^{13}C NMR ($CDCl_3$) δ: 13.8, 13.9, 14.0, 22.4, 25.2, 29.2, 31.0, 31.4, 60.8, 61.0, 119.5, 123.4, 133.5, 136.2, 160.3, 163.5, 190.4. Anal. Calcd for $C_{36}H_{52}N_2O_{10}$: C, 64.3; H, 7.8; N, 4.2. Found: C, 64.51; H, 7.84; N, 4.1.

3,5,3″,5″-Tetrakis(ethoxycarbonyl)-4,4″-di-*n*-hexyl-2,2′:5′,2″-terpyrrole (13). Butanedione **12** (67.3 g, 0.1 mol) was refluxed under N_2 for 18 h with ammonium acetate (200 g) and acetic anhydride (80 mL) in acetic acid (1 L). Most of the solvent was removed under reduced pressure. The residue was diluted with CH_2Cl_2 (500 mL) and water (500 mL) and transferred to a separatory funnel. The organic layer was separated and washed with water (500 mL) and saturated $NaHCO_3$ (500 mL). The organic layer was dried (Na_2SO_4) and concentrated on the rotary evaporator with addition of hexane. The evaporation was stopped when precipitate began to form. The precipitate was collected by filtration, washed with hexane, and dried in the dark to give the product **13** (58.6 g, 90 mmol, 90%) as a yellow microcrystalline powder, mp 127−128 °C. ^{1}H NMR ($CDCl_3$) δ: 0.9 (t, 6 H, $CH_2CH_2CH_2CH_2CH_2CH_3$); 1.31−1.41 (m, 24 H, 4 × OCH_2CH_3 + 2 × $CH_2CH_2CH_2CH_2CH_2CH_3$); 1.55 (m, 4 H, $CH_2CH_2CH_2CH_2CH_2CH_3$); 3.06 (t, 4 H, $CH_2CH_2CH_2CH_2CH_2CH_3$); 4.35, 4.36 (2 × q, 8 H, 4 × OCH_2CH_3); 6.61 (d, 4 H, pyrrole CH); 9.17 (br s, 2 H, NH); 12.64 (br s, 1 H, NH). ^{13}C NMR ($CDCl_3$) δ: 14.1, 14.2, 14.4, 22.7, 26.1, 29.7, 31.3, 31.8, 60.3, 60.4, 109.2, 111.7, 115.6, 118.7, 124.2, 132.1, 135.8, 161.2, 165.8, 169.1. Anal. Calcd for $C_{36}H_{51}N_3O_8$: C, 66.1; H, 6.4; N, 7.9. Found: C, 66.03; H, 6.40; N, 7.88.

4,4″-Di-*n*-hexyl-2,2′:5′,2″-terpyrrole (14). In a fume hood, a 2 L three-necked round-bottom flask was equipped with a magnetic stir egg, argon inlet, thermometer, and addition funnel, positioned over a strong magnetic stirrer (an Ikamag RCT was used), and a Bunsen burner clamped horizontally and pointing to the bottom edge of the flask. This setup was charged with ester **13** (13 g, 20 mmol), NaOH (20 g, 500 mmol), and ethylene glycol (200 mL). The addition funnel was replaced with an empty condenser topped with a still head, and the argon flow commenced, followed by stirring and flame heating of the flask contents. The contents dissolved after a few minutes and came to a boil. After 10 mL of liquid had distilled, the condenser water was turned on and reflux commenced. The flask contents were at a temperature of 185−200 °C. The still head was removed and replaced with a bubbler and the argon flow rate reduced. The flask contents were stirred for 30 min at reflux and allowed to cool to room temperature under argon. Degassed water (1 L) was added. The resultant precipitate was collected by filtration under an argon blanket, washed well with degassed water, and dried *in vacuo* for 2 days to give the product terpyrrole **14** (7 g, 19 mmol, 95%) as a light tan to dark green powder, used directly in the synthesis of **16** without further purification.

Tetraethylammonium Carbonate. A solution of tetraethylammonium hydroxide (35% w/v, 400 mL) in water was poured into a Dewar flask and diluted with an equal volume of ethanol. Dry ice (1 kg) was added and the flask covered and allowed to sit for 24 h. The solvents were removed under reduced pressure, and the solid product (optionally) was dried in air for 1 week. The product thus obtained (100% yield) was used in the step below without further purification.

2,5″-Diformyl-4,4″-di-*n*-hexyl-2,2′:5′,2″-terpyrrole (7c). The above terpyrrole **14** (7 g, 19 mmol) was dissolved in argon-purged DMF (50 mL) and cooled to −10 °C in a 100 mL two-necked round-bottom flask equipped with a stir bar and a thermometer. Benzoyl chloride (13.4 g, 95 mmol) was dropped in over 30 s, keeping the temperature at −10 °C with a cold bath. After the flask contents had solidified, the flask was placed in an oil bath, and the contents were held under N_2 at 85 °C for 11 h. The resulting hot solution was poured into a 100 mL beaker where it promptly solidified. The solid was allowed to cool to room temperature. DMF was removed by vacuum filtration with a rubber dam, leaving a copper-colored solid, salt **15**. The filtrate was cooled to −20 °C and gave an additional small amount of **15**. The solid **15** was suspended in fresh DMF (80 mL) in a 150 mL beaker, heated briefly to 70 °C until fully dissolved, and then cooled to 55 °C. Tetraethylammonium carbonate (17.6 g, 57 mmol) was added in chunks, resulting in gas evolution. The solution was stirred for 1−2 h and transferred to a 250 mL one-necked round-bottom flask. DMF was removed under reduced pressure (0.1 Torr); a Kügelrohr set to 50 °C helped to remove the last 10 mL of solvent. The residue, muddy with DMF, was diluted to 100 mL with ethanol and stirred vigorously until homogenous. The solid was collected by filtration, washed with hot ethanol, and dried to give the product aldehyde **7c** (5.36 g, 12.7 mmol, 64%) as a canary yellow powder, mp = 253−255 °C. ^{1}H NMR (DMSO-d_6) δ: 0.85 (t, 6 H, $CH_2CH_2CH_2CH_2CH_2CH_3$); 1.29 (br, 12 H, $CH_2CH_2CH_2CH_2CH_2CH_3$); 1.60 (m, 4 H, CH_2-$CH_2CH_2CH_2CH_2CH_3$); 2.70 (t, 4 H, $CH_2CH_2CH_2CH_2CH_2CH_3$); 6.46 (d, 2 H, pyrrole CH); 6.77 (s, 2 H, pyrrole CH); 9.51 (s, 2 H, CHO); 11.34 (br s, 1 H, NH); 11.74 (br s, 2 H, NH). ^{13}C NMR (DMSO-d_6, 39.5 ppm) δ: 13.6, 21.8, 24.6, 28.2, 30.7, 30.8, 107.0, 109.1, 125.0, 128.5, 132.2, 137.8, 175.6. Anal. Calcd for $C_{26}H_{35}$-N_3O_2: C 74.1; H, 8.4; N, 10.0. Found: C, 74.16; H, 8.33; N, 10.02.

Bronzaphyrin NS (4). A 1 L, three-necked round-bottom flask with a 34/45 center was equipped with a stir egg, inlet valve, and side stopper, charged with zinc dust (1.96 g, 30 mmol), and placed in an oven at 140 °C for 30 min alongside a condenser equipped with an inlet valve. The two pieces were removed from the oven, assembled, and evacuated while being cooled to room temperature. After backfilling with argon through the condenser, argon flow was established through the flask inlet and

the condenser removed, and $TiCl_4$·2THF (5 g, 15 mmol) was quickly added through the center hole. The condenser was reconnected and the condenser valve replaced with a rubber septum/bubbler. THF (100 mL) was added by cannula to the flask, and the contents were held at reflux for 30 min, establishing the characteristic black color of Ti^0. Aldehydes **7c** (316 mg, 0.75 mmol) and **16** (265 mg, 0.75 mmol) in THF (250 mL) were added by cannula to the flask over 5 min, and the contents were held at reflux for 18 h. The reaction was cooled to room temperature and quenched by the slow addition of 10% w/v Na_2CO_3 (50 mL). The THF was rotovapped off at 45 °C, the water decanted, and the residue taken up in $CHCl_3$ (150 mL) and dried (Na_2SO_4). The resulting black liquid was concentrated to 50 mL (45 °C) and passed through silica ($CHCl_3$ eluent). The overlapping orange bands were collected and concentrated to dryness (45 °C), leaving a green residue. This residue was extracted by 3 × 30 min reflux with hexane (3 × 150 mL). The hexane extracts were combined and concentrated to dryness, giving impure **4**. Traces of **1** that remained were removed by elution through a 2 × 30 cm silica column ($CHCl_3$ eluent), **1** running slightly faster than **4**. The main band of **4** was collected and recrystallized from hexane and then CH_2Cl_2/MeOH to give the product **4** (15 mg, 0.02 mmol, 3%) as metallic green flat needles. ^{1}H NMR (high dilution in $CDCl_3$) δ: −5.7 (br, 1 H, N*H*); −1.4 (v br, 2 H, N*H*); 1.03 (t, J = 7.2 Hz, 6 H, $CH_2CH_2CH_2CH_2CH_2CH_3$); 1.46−1.56 (m, 10H, $CH_2CH_2CH_3$ + $CH_2CH_2CH_2CH_2CH_2CH_3$); 1.67 (pent, J = 7.9 Hz, 4 H, $CH_2CH_2CH_2CH_2CH_2CH_3$); 1.94 (pent, J = 7.4 Hz, 4 H, $CH_2CH_2CH_2CH_2CH_2CH_3$); 2.57 (m, 8 H, $CH_2CH_2CH_3$ + $CH_2CH_2CH_2CH_2CH_2CH_3$); 4.29 (m, 8 H, $CH_2CH_2CH_3$ + $CH_2CH_2CH_2CH_2CH_2CH_3$); 9.95, 10.08, 10.09, 10.11, 10.41, 10.91 (5 × s, 5 × 2 H, ring C*H*). ^{13}C NMR ($CDCl_3$) δ: 14.3, 14.8, 22.9, 25.6, 29.2, 29.7, 30.0, 30.8, 32.1, 106.9, 107.4, 119.9, 122.8, 127.0, 128.4, 132.8, 133.2, 136.4, 140.7, 144.2, 145.0. MS *m*/*e*: 711 (100), 644 (15), 625 (4), 596 (4), 356 (7). HRMS: calcd for $C_{46}H_{55}N_5S$ 709.41785, found 709.41756. UV−vis (THF) λ (log ϵ): 460 (5.10), 486 sh (4.90), 795−96 (4.73), 850 (4.80).

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Supporting Information Available: ^{13}C NMR spectrum of **4**; ^{1}H and ^{13}C NMR spectra of **7c** and **10**-**13**; tabulated absorbance values (10 μM, THF) of **1**, **2**, and **4** (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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