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Improved Synthesis of Covalently Strapped Porphyrins. Application to Highly Deformed Porphyrin Synthesis[1]

Tilak P. Wijesekera, John B. Paine III, and David Dolphin*

Department of Chemistry, The University of British Columbia, Vancouver, British Columbia, Canada V6T 1Y6

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The synthesis of porphyrins carrying a hydrocarbon chain linked to diametrically opposite β-positions is described. The chain, in the form of the diacid chloride of an α,ω-dicarboxylic acid (**7**), was reacted at its termini, with 2 equiv of 2-(ethoxycarbonyl)-3,5-dimethylpyrrole (**6**), and the chain-linked bis[5-(ethoxycarbonyl)pyrrole] **8** so obtained was transformed into the pyrrole-2-carboxaldehyde **13** by using standard methodology. Protection of the formyl groups as the dicyanovinyl derivative and the activation of the 2-methyl substituents with sulfuryl chloride gave the bis[2-(chloromethyl)pyrrole] **16**, which on reaction with a 5-unsubstituted 2-pyrrolecarboxylate (**18**), in warm glacial acetic acid, afforded the chain-linked dipyrromethane dimer **20** in high yield. Regeneration of the formyl substituents and removal of the ester group (ethyl ester and benzyl ester variations are described) produced the chain-linked 5-formyl-5′-unsubstituted-dipyrromethane dimer **22**, which was cyclized intramolecularly, under high dilution, to give the strapped porphyrins **26** in good yield. This strategy of strap first, porphyrin last, enabled the successful synthesis of porphyrins carrying 11-, 10-, or 9-carbon bridges, which enforce a progressively increased distortion of the macrocycle, as evidenced by visible spectroscopy and X-ray crystallography.

Some of the more subtle protein-induced changes in heme chemistry are thought to involve a reversible deformation from planarity of the macrocyclic core,[2] attending the motion of the chelated metal normal to the macrocyclic-chelation plane. In particular, Perutz[3-5] has suggested such a motion as part of the mechanism for hemoglobin cooperativity.

As a potential model for studying the effect of porphyrin-core deformation on the stability, geometry, spectroscopy, and chemistry of metalloporphyrins and hemes, and the oxygen-binding behavior of the latter, we required a series of deformed porphyrinic molecules.

The simplest means of achieving maximal deformation seemed to be the application of as short a strap as possible to link two diametrically opposite β-positions (e.g., **2**, **12**). A variation in length and/or shape of such straps would allow a gradation of deformations to be studied.

A covalent strap should be as chemically inert as possible to avoid extraneous interactions with the chelated metal and to avoid rupture under the various reaction conditions one might wish to apply to the product. To achieve this, covalently linked straps consisting *solely* of *hydrocarbon* were desired. These are more difficult to apply, and require more synthetic effort, than the esters or amides used elsewhere,[6-14] but allow, far more easily, the attainment of tighter straps than heretofore reported. We present here the synthesis of highly deformed porphyrins following our improved synthetic route[15] to centrosymmetric porphyrins.

Inasmuch as a preformed porphyrin is unlikely to bend of its own volition to accommodate straps as short as would be required to permanently deform it, it seemed reasonable to approach the target by constructing the strap first and

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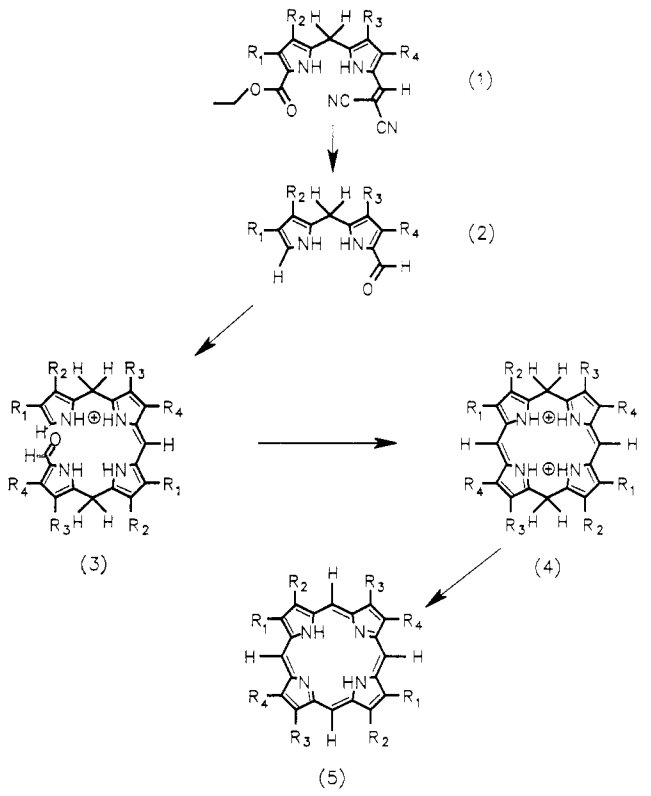
Scheme I



then building the porphyrin at both termini simultaneously. Even with those approaches that have involved ester or amide linkages, whereby strap completion followed porphyrin formation, the porphyrin was constructed with the bridge precursor (typically a 2-carboxyethyl function) in place. Furthermore, porphyrins frequently have awkward solubility characteristics that may frustrate many of the reactions one would like to attempt with them. When a strategy of strap first, porphyrin last, is employed, the first porphyrin encountered on the synthetic sequence is the desired product, potentially difficult separations of porphyrins thereby being avoided.

Considering the problem in the retrosynthetic direction, it must be noted that a 2,12-strapped porphyrin (given a symmetrical strap, and ignoring the other β-substituents) exhibits C_2 symmetry. Any disconnection that can make use of this rotational symmetry, so as to allow the various carbon–carbon bonds to be formed in pairwise fashion while building the porphyrin-core superstructure, will greatly reduce the synthetic effort. There are *four* possible pairwise disconnections of a *singly* strapped porphyrin into a *linked* pair of dipyrrolic synthons that retain this symmetry. These four disconnections differ significantly in accessibility from readily available precursors and correspond to those where the strap is at R_1, R_2, R_3, or R_4 (Scheme I) respectively. The two most convenient locations for the strap are at R_2 or R_3; chemistry relating to strapping at R_2 has been briefly reported elsewhere.[16] Here, and also as reported elsewhere,[17] we are concerned with methodology to provide a strap at R_3. In the synthetic direction, a "simultaneous" head-to-tail coupling of such linked dipyrroles will lead to the porphyrinic superstructure. Minor adjustments of the oxidation level will then produce the porphyrin, a highly favored process due to the large gain in aromatic stabilization.

This basic disconnection strategy was first applied by Diekmann, Chang, and Traylor[18] to the synthesis of a *p,p'*-biphenylenebis(tetramethylene)-strapped porphyrin, which they christened a "cyclophane porphyrin". They chose to employ dipyrrometh*enes* as the coupling dipyrrolic units, and the inherent reluctance of these to undergo the requisite electrophilic attack necessary for carbon–carbon bond formation was reflected in the yields obtained! It seemed to us that the dipyrrometh*ane* oxidation level would be more suitable for precursors of strapped porphyrins. The 5-formyl-5'-unsubstituted-2,2'-dipyrromethane **2** has been shown[15] to self-condense, under acid catalysis,[19,20] in a head-to-tail (centrosymmetric) fashion to yield a porphodimethene (**4**), which subsequently oxidizes to the porphyrin (Scheme I). A strapped bis(dipyrromethane) of this type was therefore expected to form a strapped porphodimethene, provided sufficiently high dilute conditions were imposed to ensure preferential intramolecular reaction. Furthermore, since the porphodimethene, so formed, consists of two diametrically opposed sp^3-hybridized methylene units, it could be expected to assume a folded "tent-like" geometry, thereby accommodating, *without strain*, a shorter bridging chain than an unstrained porphyrin could possibly tolerate.

The most conveniently available β-free pyrrole suitable for the synthesis of strapped bis(pyrroles) is 2-(ethoxycarbonyl)-3,5-dimethylpyrrole (**6**) (available in one step from 2,4-pentanedione and diethyl amino-[21] or oximinomalonate[22]). To initiate the synthesis of a strapped porphyrin, we reacted an α,ω-dicarboxylic acid with thionyl chloride to afford the diacid chloride **7**, which was condensed with 2 equiv of 2-(ethoxycarbonyl)-3,5-dimethylpyrrole (**6**). The optimal conditions for general acylation we have found employ anhydrous stannic chloride as catalyst (a slight excess over 1 equiv per acid chloride function being sufficient), added as rapidly as the exothermicity and effervescence permit, *to* a solution of the pyrrole and the acid chloride at room temperature in dichloromethane. The reaction was complete within 10–15 min after addition of catalyst, with negligible disruption of the ethyl ester function. Nitromethane (20–40 vol %) was employed as cosolvent, to maintain the homogeneity of the reaction mixture and prevent intermediates from oiling out (Scheme II).

Similar acylation conditions may be applied to 2-[(benzyloxy)carbonyl]-3,5-dimethylpyrrole, although considerable cleavage of the benzyl esters will ensue if the reaction is prolonged. As this material is also prepared by a transbenzylation step (from **6**), the introduction of benzyl esters was delayed until *after* the ketonic carbonyls of **8** had been reduced. This reduction was effected by diborane, a procedure developed by Whitlock and Hanauer[23] and by Jackson et al.[24,25] While the diborane reduction seemed to afford the best yields if the temperature was kept quite low, dimer pyrroles **8** frequently reduced sluggishly (owing to poor solubility) unless warmed to room temperature. The yields obtained of **9** fell in the

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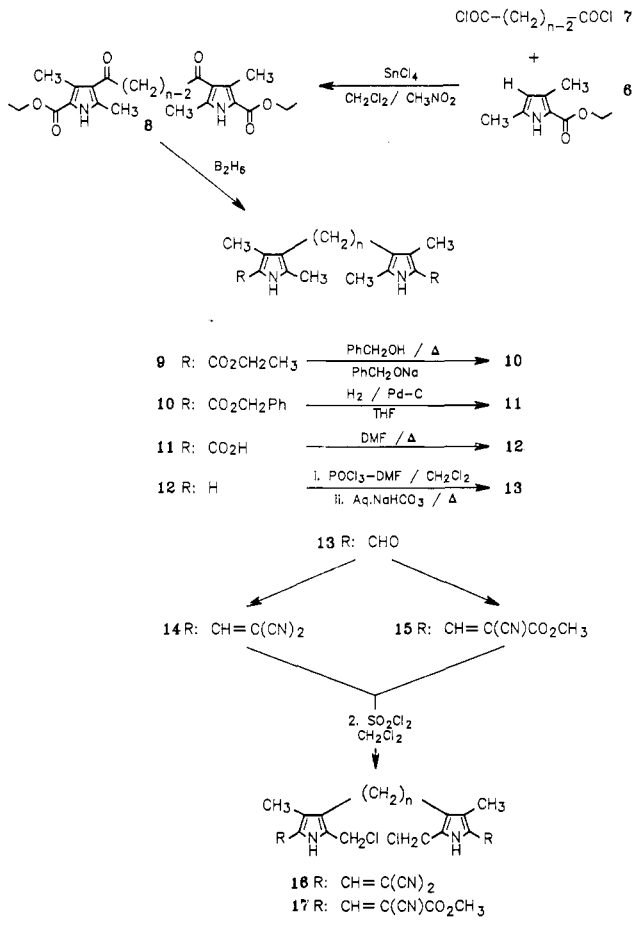
Scheme II[a]



[a] **a**, n = 11; **b**, n = 10; **c**, n = 9; **d**, n = 8.

75% to 85% range. Transbenzylation of **9** was effected[26] in refluxing benzyl alcohol by using a solution of sodium in benzyl alcohol as catalyst. When the hot reaction mixture was *cautiously* poured into aqueous methanol, the dibenzyl ester **10** crystallized out almost quantitatively.

At this point, our synthesis diverged from earlier work.[27] Catalytic hydrogenolysis over palladium on carbon in tetrahydrofuran quantitatively cleaved the benzyl esters of **10** to produce the labile dicarboxylic acid **11**. The alternative of saponifying the diethyl ester **9** directly suffers from the danger of partial decarboxylation of **11** during the saponification, or during the acidification step necessary to precipitate the product **11**, which furthermore may be tedious to filter.

The dicarboxylic acid **11** was refluxed (under inert atmosphere) in *N,N*-dimethylformamide[28] until the disappearance of the absorption at 280 nm signalled the completion of the decarboxylation. Vilsmeier formylation was then performed in situ directly upon the DMF solution of **12** so obtained. The intermediary iminium salt was hydrolyzed in weakly alkaline solution; sodium bicarbonate was added in excess in small portions (effervescence) until the solution was *permanently* neutral (*do not* use ammonia for this hydrolysis). A false (end point) neutrality was achieved, especially if the mixture was cool, as the dichloro phosphate anion present was only slowly hydrolyzed. Above 40 °C this decomposed rapidly. Only when $NaHCO_3$ was *permanently* in excess could the solution safely be heated (steam bath) to complete the hydrolysis. This procedure minimized the diversion of product into unwanted polymer. As the resulting dialdehyde **13** was exceedingly difficult to purify by crystallization or chromatography (too polar), it was reacted in crude form with the appropriate Knoevenagel reagent,[19,26] usually malononitrile. The resulting bis[(dicyanovinyl)pyrrole] **14**, purified by chromatography, was obtained in about 60–70% overall yield based on the dibenzyl ester **10**. It may be deprotected nearly quantitatively with aqueous alkali to give the parent dialdehyde **13** in analytical purity.

From this point the methodology followed that reported[15] for our model studies: the bis[(dicyanovinyl)pyrrole] **14** reacted with 2 equiv (one per methyl) of sulfuryl chloride in dichloromethane to afford, very selectively, the bis(chloromethyl) derivative **16** nearly quantitatively. This, in crude form, was suspended in glacial acetic acid and warmed with a slight excess of 2-(ethoxycarbonyl)-4-ethyl-3-methylpyrrole (**18**). Workup (crystallization) gave, in high yield (85% overall), the desired bis(dipyrromethane) **20**.

The deprotection step, by which both the carboxylic acid and formyl substituent are generated, was initially performed in aqueous ethanol with potassium hydroxide. The course of the reaction was monitored by UV spectroscopy and, due to the low temperatures enforced by the boiling point of the solvent, was unduly prolonged by the slow hydrolysis of the ester function. During this time some decomposition occurred, which resulted in the product exhibiting an anomalous NMR spectrum, suggestive of partial decarboxylation. Such preparations inevitably gave greatly reduced yields for the final cyclization step. By employing higher boiling 1-propanol as the organic cosolvent to solubilize the starting material **20**, we greatly reduced the time required to complete the deprotection, and product of far greater purity and reliability was obtained (negligible decarboxylation being observed).

Careful acidification (acetic acid) of the cooled hydrolysis solution afforded a gelatinous precipitate that filtered tediously, but that could be washed clean with water to afford a product (**21**) of acceptable analytical composition after drying in vacuo. This (**21**) was decarboxylated by reflux in *N,N*-dimethylformamide until the UV absorption at 280 nm had disappeared. Removal of solvent followed, and the resulting crude bis(5-formyldipyrromethane) **22** was added slowly, by syringe pump, to a solution of *p*-toluenesulfonic acid in dichloromethane–methanol, to effect the macrocyclization into the desired strapped porphyrin **26**. Chromatography gave the final product in good yield (25–40% overall from **21**, depending on chain length).

Inspection of space-filling models suggested that an 11-carbon strap might cause some strain in the macrocycle, so this was the first chain length examined as outlined above (series **a**), and the porphyrin was obtained in up to 40% yield for the final cyclization step. The benzyl ester variation,[15] (Scheme III) was also applied to this system (see the Experimental Section for details). Use of the resulting high-purity undecamethylenebis(5-formyldipyrromethane) **22a** afforded the porphyrin is even higher (50%) yield at the macrocyclization step.

When the undecamethylene-strapped porphyrin **26a** was examined spectroscopically, its UV–visible absorption was found to differ only slightly from that of its unstrained analogue, etioporphyrin II. This led us to synthesize (ethyl ester route only) the successively shorter straps derived from sebacic, azelaic, and suberic acids (series **b**, **c**, and

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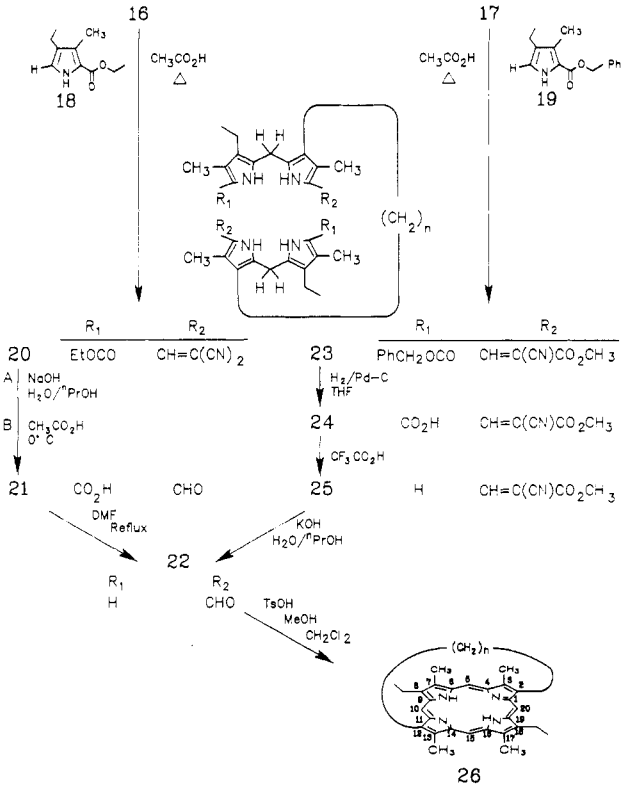
Scheme III[a]



[a] **a**, n = 11; **b**, n = 10; **c**, n = 9; **d**, n = 8.

d) respectively. (Experimental methods, yields, and the analytical data for all the intermediates in these series were entirely comparable and are provided as supplementary material.) Isolable product was obtained in the first two instances, although the yields on the final macrocyclization fell significantly as the chain was shortened. With the eight-carbon strap, the final macrocyclization gave only traces of a highly unstable substance, which we were unable to characterize. We can therefore state with some confidence that a *nine-carbon* chain is the shortest strap that can be accommodated by a porphyrin between two diametrically opposite β-positions without causing catastrophic loss of stability. Such porphyrins, however, were found to be of enhanced light sensitivity and should be handled accordingly. The presence of a strap on one face of the macrocycle helps reduce interporphyrinic attraction, so that such strapped porphyrins show increased solubility, compared to unstrapped analogues. Their light sensitivity as free bases may be further exacerbated by metalation. The zinc derivatives in particular were found to be very unstable to photochemical bleaching.

The proton magnetic resonance spectra of the strapped porphyrins (in deuteriochloroform) exhibit significant upfield shifts of the hydrocarbon chain proton resonances (Figure 1). The variation of the shielding effect of the aromatic ring current on the methylene protons results in the resonances being dispersed over a wide range of chemical shifts, from approximately +4 up to −6 ppm. Homonuclear decoupling experiments indicate that the two protons of the same methylene group are affected to different extents by the ring current and give rise to resonances well separated from each other. In the extreme case, the two protons on each of the two center carbons of the decamethylene chain of **26b** are separated by 3.64 ppm, clearly indicating the significance of the conformation at each carbon especially with respect to the diamagnetic ring current of the porphyrin. A detailed analysis of the NMR spectra is in progress, and the results will be published later.

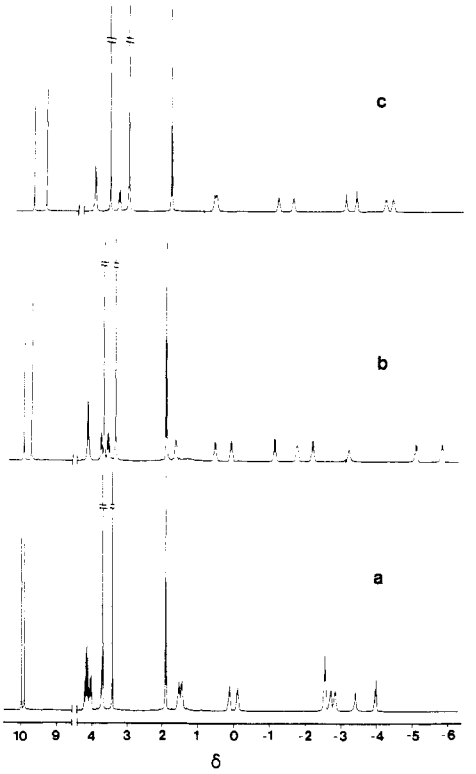


Figure 1. Proton NMR spectra (400 MHz, $CDCl_3$) of the porphyrins **26a** (n = 11), **26b** (n = 10), and **26c** (n = 9).

Experimental Section

Melting points were obtained by using a Thomas-Hoover Unimelt oilbath/capillary tube apparatus and are uncorrected. Silica gel (Woelm, 70–150 mesh) and alumina (Camag, basic) were used for column chromatography, and analytical TLC was performed on Analtech precoated silica gel plates (250 μm). Electronic absorption spectra were measured on a Cary 17 spectrophotometer, and proton NMR spectra were measured at 100 MHz on a Varian HA-100 or XL-100 or at 400 MHz on a Bruker WH-400 instrument. Carbon-13 NMR spectra were measured at 25.2 MHz on a Varian CFT-20 instrument (10-mm tube). Mass spectra were recorded on a Varian MAT CH 4-B or a Kratos/AES MS-902 spectrometer, while high-resolution measurements were obtained on a Kratos/AEI MS-50 spectrometer. Elemental analyses were performed by P. Borda at the University of British Columbia.

1,11-Bis[5-(ethoxycarbonyl)-2,4-dimethylpyrrol-3-yl]-1,11-undecanedione (8a). Undecanedioic acid[29] (21.4 g, 0.10 mol) and thionyl chloride (46.3 g, 0.390 mol) were refluxed (steambath) under moisture-exclusion conditions until the mixture was homogeneous and gas evolution had ceased (ca. 30 min). The excess thionyl chloride was removed by evaporation in vacuo and chased with carbon tetrachloride (4 × 30 mL). The resulting crude diacid chloride **7a** and 2-(ethoxycarbonyl)-3,5-dimethylpyrrole (**6**) (35 g, 0.21 mol) were dissolved in dichloromethane (300 mL)–nitromethane (200 mL). With continued exclusion of moisture (N_2 atmosphere), anhydrous stannic chloride (104.2 g, 0.40 mol) was added dropwise at room temperature over 3 h.

After 4 h more, the reaction mixture was poured into water (350 mL) acidified with concentrated HCl (10 mL) and stirred for 15 min to complete the hydrolysis of the tin complex. The resulting three-phase emulsion was suction filtered to recover the bulk of the product in solid form. The solids were washed (alternately) with water and dichloromethane, and finally with methanol (collected separately). After drying, the solids weighed 37.8 g (73.5% based on the diacid). Evaporation in vacuo of the

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organic phases from the filtrates afforded a second crop of 6.3 g (12.3%).

For analysis, a sample was recrystallized from tetrahydrofuran–methanol: mp 173.5–175.0 °C; ^{1}H NMR (10% TFA–$CDCl_3$) δ 1.33 [br, 10 H, 4,5,6,7,8-$(CH_2)_5$], 1.43 (t, J = 7 Hz, 6 H, ester), 1.69 [m, 4 H, 3,9-$(CH_2)_2$], 2.57 (s, 6 H, 4-CH_3), 2.59 (s, 6 H, 2-CH_3), 2.86 [t, J = 7.5 Hz, 4 H, 2,10-$(CH_2)_2$], 4.46 (q, J = 7 Hz, 4 H, ester), 10.15 (br, 2 H, NH); ^{13}C NMR (10% TFA–$CDCl_3$ at 77.18) δ 204.07 (2 C, ketonic C=O), 164.00 (2 C, ester C=O), 142.31 (2 C, 2), 132.26 (2 C, 4), 122.80 (2 C, 3), 118.49 (2 C, 5), 62.34 (2 C, CH_3CH_2O), 42.27 (2 C, methylene 2,10), 29.37 (5 C, methylene 4,5,6,7,8), 25.74 (2 C, methylene 3,9), 15.43 (2 C, 2-CH_3), 14.23 (2 C, CH_3CH_2O), 12.94 (2 C, 4-CH_3); CF_3CO_2H at 114.87, 159.92; MS, m/e 514 (23, M^+), 209 (72), 194 (100), 148 (87). Anal. Calcd for $C_{29}H_{42}N_2O_6$: C, 67.70; H, 8.17; N, 5.48. Found: C, 67.71; H, 8.21; N, 5.68.

1,11-Bis[5-(ethoxycarbonyl)-2,4-dimethylpyrrol-3-yl]undecane (9a). Diketone **8a** (32.0 g, 62.3 mmol) and sodium borohydride (5.0 g, 132.3 mmol) were stirred in anhydrous tetrahydrofuran (300 mL) under nitrogen, and the resulting suspension was treated dropwise (ice bath) with boron trifluoride etherate (30 mL, 238.1 mmol). The mixture was quenched by careful dropwise addition of glacial acetic acid (100 mL) followed by water (200 mL), causing separation of product. The mixture was extracted with dichloromethane, and the organic phase was isolated, filtered, diluted with methanol, and finally concentrated (rotary evaporator) until the product crystallized out in quantity. The solids were filtered off, washed with methanol, and dried. Yield: 25.1 g (82.9%). Evaporation of the filtrates gave a further 1.2 g (4.0%). For analysis, a sample was recrystallized from dichloromethane–methanol: mp 115.0–116.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.08–1.58 [m, 18 H, 2-10-$(CH_2)_9$], 1.31 (t, J = 7 Hz, 6 H, ester), 2.14 (s, 6 H, 2-CH_3), 2.22 (s, 6 H, 4-CH_3), 2.18–2.44 [m, 4 H, 1,11-$(CH_2)_2$], 4.25 (q, J = 7 Hz, 4 H, ester), 8.73 (br s, 2 H, NH); ^{13}C NMR ($CDCl_3$ at 77.17) δ 162.24 (2 C, C=O), 130.04 (2 C, 2), 126.99 (2 C, 4), 122.36 (2 C, 3), 116.76 (2 C, 5), 59.56 (2 C, CH_3CH_2O), 30.95 (2 C, methylene 2, 10), 29.69 (7 C, methylene 3–9), 24.10 (2 C, methylene 1,11), 14.64 (2 C, CH_3CH_2O), 11.41 (2 C, 2-CH_3), 10.73 (2 C, 4-CH_3); MS, m/e 486 (65, M^+), 440 (86), 180 (100), 134 (82). Anal. Calcd for $C_{29}H_{46}N_2O_4$: C, 71.60; H, 9.47; N, 5.76. Found: C, 71.60; H, 9.54; N, 5.85.

1,11-Bis[5-(benzyloxycarbonyl)-2,4-dimethylpyrrol-3-yl]undecane (10a). Diethyl ester **9a** (24 g, 49.4 mmol) and benzyl alcohol (125 mL) (redistilled from K_2CO_3 at 1 atm) were heated to boiling, under nitrogen, and a fresh solution of sodium in dry benzyl alcohol was added in (ca.) 1-mL portions until the evolution of ethanol began. Further portions were added every several minutes until the exchange was complete, and the boiling point had again risen above 200 °C.

The *hot* solution was quenched *at once* by pouring it *cautiously* into a magnetically stirred solution of acetic acid (20 mL) in methanol (500 mL). Water was added until crystallization began and then further after 5 min (400 mL in all) to complete crystallization.

The light pinkish solids (which darken steadily prior to filtration due to the presence of partially decarboxylated pyrrole) were filtered, washed with 50% aqueous methanol, and then dried. Yield: 28.4 g (94.3%).

A sample was recrystallized from tetrahydrofuran–methanol for analysis: mp 108.5–110.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.27 [br, 18 H, 2-10-$(CH_2)_9$], 2.18 (s, 6 H, 2-CH_3), 2.29 (s, 6 H, 4-CH_3), 2.20–2.52 (m, 4 H, 1,11-$(CH_2)_2$], 5.31 (s, 4 H, ArCH_2O), 7.22–7.56 (m, 10 H, Ar), 8.67 (br, 2 H, NH); ^{13}C NMR ($CDCl_3$ at 77.10) δ 161.68 (2 C, C=O), 136.77 (2 C, Ar-1), 130.37 (2 C, 2), 128.46 (4 C, Ar), 127.91 (6 C, Ar), 127.52 (2 C, 4), 122.50 (2 C, 3), 116.37 (2 C, 5), 65.30 (2 C, ArCH_2O), 30.85 (2 C, methylene 2,10), 29.61 (7 C, methylene 3–9), 24.02 (2 C, methylene 1,11), 11.37 (2 C, 2-CH_3), 10.84 (2 C, 4-CH_3); MS, m/e 610 (37, M^+), 502 (22), 242 (19), 108 (22), 91 (100). Anal. Calcd for $C_{39}H_{50}N_2O_4$: C, 76.69; H, 8.25; N, 4.59. Found: C, 76.61; H, 8.29; N, 4.69.

1,11-Bis(5-formyl-2,4-dimethylpyrrol-3-yl)undecane (13a).
(i) Debenzylation. Dibenzyl ester **10a** (17.5 g, 28.6 mmol) and 10% Pd–C (1.2 g) were stirred overnight under hydrogen (1 atm, room temperature), in tetrahydrofuran (125 mL) containing triethylamine (5 drops). When TLC examination showed absence of starting material, the catalyst was filtered, and the solvent was removed in vacuo below 40 °C, affording the crude bis(carboxypyrrolyl)undecane **11a** as a pale yellow solid.

(ii) Decarboxylation. The above dicarboxylic acid (**11a**) was dissolved in *N,N*-dimethylformamide (125 mL) and refluxed under nitrogen until the UV absorption maximum (one drop of the DMF solution was diluted with CH_2Cl_2) at 286 nm had been reduced to a minor shoulder (2–2.5 h).

The resulting solution was cooled (ice bath) and employed for the next step.

(iii) Formylation. Phosphorus oxychloride (30 mL) was added, dropwise, to an ice-cooled magnetically stirred solution of *N,N*-dimethylformamide (35 mL) in dichloromethane (120 mL). The decarboxylation mixture was then added dropwise to the ice-cooled solution of Vilsmeier reagent. After 30 min of further stirring, the dichloromethane was removed in vacuo and the remaining solution poured onto crushed ice (400 g).

Solid sodium bicarbonate was added cautiously (effervescence!) until the solution was weakly basic to universal indicator paper. The solution became acidic again when warming was begun on the steam bath, and further bicarbonate had to be added. A dark brown phase separated to the bottom, containing intermediary iminium salt, DMF, and unremoved dichloromethane. As the solution warmed further, the dichloromethane evaporated, and a clear brown single-phase solution resulted. (pH should remain around 8.)

The warm solution was suction filtered to remove minor insoluble tars. The volume of the filtrates was adjusted to 1200 mL with water, and heating was resumed on the steam bath. At 75 °C, the solution clouded and the product began to separate out as a gray solid. After a further 30–60 min of heating, the solid was filtered off and washed with water. After drying, the crude dialdehyde **13a** weighed 10.4 g (91% nominal yield, based on the dibenzyl ester **10a**).

The crude solid was reacted in its entirety with malononitrile to afford the bis[(dicyanovinyl)pyrrolyl]undecane **14a**. After purification by chromatography, a sample of this was *deprotected* with KOH in aqueous 1-propanol: mp 133.5–135.0 °C; ^{1}H NMR ($CDCl_3$) δ 1.26 [br, 18 H, 2-10-$(CH_2)_9$], 2.27 (s, 12 H, 2,4-CH_3), 2.27–2.49 [m, 4 H, 1,11-$(CH_2)_2$], 9.50 (s, 2 H, CHO), 9.84 (br, 2 H, NH); ^{13}C NMR ($CDCl_3$ at 77.12) δ 175.52 (2 C, CHO), 136.74 (2 C, 2), 132.71 (2 C, 4), 127.87 (2 C, 5), 123.44 (2 C, 3), 30.61 (2 C, methylene 2,10), 29.59 (7 C, methylene 3–9), 23.76 (2 C, methylene 1,11), 11.61 (2 C, 2-CH_3), 8.87 (2 C, 4-CH_3); MS, m/e 398 (22, M^+), 370 (23), 136 (100), 108 (76). Anal. Calcd for $C_{25}H_{38}N_2O_2$: C, 75.33; H, 9.61; N, 7.03. Found: C, 75.27; H, 9.88; N, 7.20.

1,11-Bis[5-(2,2-dicyanovinyl)-2,4-dimethylpyrrol-3-yl]undecane (14a). The crude bis(formylpyrrolyl)undecane **13a** (5.5 g) was dissolved in dichloromethane (100 mL)–methanol (20 mL) by warming (steam bath). The volume was reduced to ca. 50 mL by evaporation. Malononitrile (2.2 g), triethylamine (1 mL), and more methanol (250 mL) were added, and the mixture was warmed on the steam bath until TLC examination indicated completion of the reaction (subsequently, toluene was found to be a better solvent in that the intermediate monoaldehyde did not crystallize out at the reflux temperature).

The solution was boiled down to ca. 100 mL and then cooled to room temperature. The yellow-brown solids were filtered off and washed with methanol. Yield: 5.6 g. Concentration of the filtrates afforded an additional 0.6 g.

The combined crude solids (6.2 g) were chromatographed on silica gel (Akt I, 45 g) by using dichloromethane. The dark-colored impurities remained at the origin, and the pure product eluted out as a yellow solution. The product was crystallized from methanol, and the lemon-yellow solids thus obtained were analytically pure: yield, 5.2 g (69.5% overall from the dibenzyl ester **10a**); mp 153.0–154.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.24 [br, 18 H, 2-10-$(CH_2)_9$], 2.10 (s, 6 H, 4-CH_3), 2.27 (s, 6 H, 2-CH_3), 2.27–2.47 [m, 4 H, 1,11-$(CH_2)_2$], 7.27 (s, 2 H, vinyl), 9.35 (br s, 2 H, NH); ^{13}C NMR ($CDCl_3$ at 77.08) δ 141.37 (2 C, 2), 140.48 (2 C, CH=C), 136.44 (2 C, 4), 125.82 (2 C, 3), 124.14 (2 C, 5), 117.64 (2 C, CN), 116.26 (2 C, CN), 62.51 (2 C, CH=C), 30.25 (2 C, methylene 2,10), 29.59 (7 C, methylene 3–9), 23.92 (2 C, methylene 1,11), 12.56 (2 C, 2-CH_3), 9.64 (2 C, 4-CH_3); MS, m/e 495 (24), 494 (68, M^+), 184 (100). Anal. Calcd for $C_{31}H_{38}N_6$: C, 75.27; H, 7.74; N, 16.98. Found: C, 75.28; H, 7.46; N, 16.80.

1,11-Bis[5(*E*)-[2-cyano-2-(methoxycarbonyl)vinyl]-2,4-dimethylpyrrol-3-yl]undecane (15a). Dibenzyl ester **10a** (9.5 g, 15.6 mmol) was converted to the dialdehyde **13a** in the usual manner. The crude dialdehyde **13a** and methyl cyanoacetate (3.2 g, 36.8 mmol) were refluxed in toluene (260 mL)–cyclohexylamine (3 mL). The reaction was monitored by TLC and found to be complete in 2 h. The solvent was removed in vacuo, and the residue crystallized from dichloromethane–methanol in two crops. Chromatography of the crude product (7.6 g) over silica gel (Akt I, 100 g) with dichloromethane afforded, after crystallization from methanol, a yield of 6.6 g (75.9% overall for the dibenzyl ester **10a** of a bright lemon-yellow powder: mp 158.0–159.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.28 [br, 18 H, 2–10-$(CH_2)_9$], 2.19 (s, 6 H, 4-CH_3), 2.32 (s, 6 H, 2-CH_3), 2.26–2.50 [m, 4 H, 1,11-$(CH_2)_2$], 3.88 (s, 6 H, OCH_3), 7.95 (s, 2 H, vinyl), 9.51 (br, 2 H, NH); ^{13}C NMR ($CDCl_3$ at 77.17) δ 165.15 (2 C, C=O), 139.16 (2 C, 2), 137.89 (2 C, *C*H=C), 135.62 (2 C, 4), 125.01 (2 C, 3), 123.46 (2 C, 5), 120.29 (2 C, CN), 84.85 (2 C, CH=*C*), 52.38 (2 C, CH_3O), 30.41 (2 C, methylene 2,10), 29.54 (7 C, methylene 3–9), 24.01 (2 C, methylene 1,11), 12.38 (2 C, 2-CH_3), 9.66 (2 C, 4-CH_3); minor *Z* isomer at 167.49, 140.02, 136.79, 125.87, 125.31, 84.46, 28.47; MS, *m/e* 560 (39, M^+), 528 (11), 496 (16), 217 (89), 185 (100). Anal. Calcd for $C_{33}H_{44}N_4O_4$: C, 70.69; H, 7.91; N, 9.99. Found: C, 70.44; H, 8.06; N, 9.80.

1,11-Bis[5-(2,2-dicyanovinyl)-2-[[5-(ethoxycarbonyl)-3-ethyl-4-methylpyrrol-2-yl]methyl]-4-methylpyrrol-3-yl]undecane (20a). (i) Monochlorination of the α-Methyl Substituents. 1,11-Bis[5-(2,2-dicyanovinyl)-2,4-dimethylpyrrol-3-yl]undecane (**14a**) (2.05 g, 4.15 mmol) in anhydrous dichloromethane (80 mL) was stirred magnetically under nitrogen and treated dropwise, at room temperature, with a solution of sulfuryl chloride (1.13 g, 8.37 mmol; redistilled) in dichloromethane (50 mL). The pale yellow solution turned orange during the addition.

The solvent was carefully boiled away and displaced (gradually) with anhydrous diethyl ether, causing the product to crystallize.

The bis(chloromethyl) derivative **16a** was collected by filtration, washed with 10% dichloromethane in ether, and then with ether, and dried in air. The lemon yellow powdery solid was used in the following reaction without further purification.

(ii) Formation of the Bis(dipyrromethane). The above bis[(chloromethyl)pyrrolyl]undecane **16a** and 2-(ethoxycarbonyl)-4-ethyl-3-methylpyrrole[15] (**18**) (1.80 g, 9.94 mmol) were stirred in glacial acetic acid (150 mL) under nitrogen and warmed at 70 °C for 1 h. The yellow starting material dissolved with reaction, and the solution turned orange-red. Analysis by TLC showed a single yellow spot, colored violet by bromine vapor, in addition to a colorless spot due to the excess α-free pyrrole **18**.

The solution was cooled to room temperature and concentrated to ca. 25 mL under reduced pressure. Methanol (100 mL) was added and the mixture allowed to stand overnight under refrigeration.

The product crystallized as a dark yellow solid and was collected by filtration and washed with methanol. The yield of analytically pure material was 3.04 g (85.9% overall from the α-methyl precursor **14a**).

Four other preparations gave yields of 83.3%, 85.0%, 85.2%, and 92.6%. Second crops were not collected: mp 168.0–170.0 °C dec; ^{1}H NMR ($CDCl_3$) δ 1.03 (t, J = 7.5 Hz, 6 H, 3′-Et), 1.18–1.54 [br, 18 H, 2–10-$(CH_2)_9$], 1.34 (t, J = 7 Hz, 6 H, ester), 2.15 (s, 6 H, 4-CH_3), 2.30 (s, 6 H, 4′-CH_3), 2.21–2.58 [m, 4 H, 1,11-$(CH_2)_2$], 2.43 (q, J = 7 Hz, 4 H, 3′-Et), 3.98 (s, 4 H, *meso*-CH_2), 4.29 (q, J = 7 Hz, 4 H, ester), 7.34 (s, 2 H, vinyl), 8.90 (br, 2 H, 1′-NH), 9.24 (br, 2 H, 1-NH); ^{13}C NMR ($CDCl_3$ at 77.08) 162.13 (2 C, C=O), 140.73 (2 C, *C*H=C), 140.54 (2 C, 2), 136.25 (2 C, 4), 127.09 (2 C, 4′), 126.02 (2 C, 2′), 125.16 (4 C, 3,3′), 124.15 (2 C, 5), 118.91 (2 C, 5′), 116.84 (2 C, CN), 115.96 (2 C, CN), 64.24 (2 C, CH=*C*), 59.96 (2 C, CH_3CH_2O), 30.30 (2 C, methylene 2,10), 29.59 (7 C, methylene 3–9), 23.95 (4 C, methylene 1,11, 2 × *meso*-CH_2), 17.39 (2 C, 3′-CH_3CH_2), 15.38 (2 C, 3′-CH_3CH_2), 14.46 (2 C, CH_3CH_2O), 10.52 (2 C, 4′-CH_3), 9.62 (2 C, 4-CH_3); MS, *m/e* 852 (M^+), 806, 760. Anal. Calcd for $C_{51}H_{64}N_8O_4$: C, 71.80; H, 7.56; N, 13.13. Found: C, 72.04; H, 7.55; N, 13.35.

1,11-Bis[2-[(5-carboxy-3-ethyl-4-methylpyrrol-2-yl)-methyl]-5-formyl-4-methylpyrrol-3-yl]undecane (21a). In a 1-L Erlenmeyer flask, equipped with a Claisen adapter, a nitrogen inlet, and a reflux condenser, were placed the undecane-strapped dimeric dicyanovinyl dipyrromethane ester **20a** (1.88 g, 2.21 mmol), potassium hydroxide (23 g), and water (200 mL). The magnetically stirred suspension was warmed to reflux under nitrogen, and 1-propanol (70 mL) was added. The yellow solids dissolved promptly, giving a pale brown solution. Reflux was continued, and a sample was taken every half-hour, diluted with water, and inspected by UV–visible spectroscopy.

The starting material absorbed strongly at 407 nm and moderately at 275 nm with a shoulder around 315 nm. As the reaction progressed, the 407-nm absorption disappeared completely (after 90 min), and the product now absorbed strongly at 269 and 320 nm.

More water (300 mL) was added, and the solvent was permitted to boil off until the vapor temperature reached 100 °C. After cooling to room temperature under nitrogen, slimy product separated out in part. The solution was suction filtered (Whatman no. 541), and the separated solids washed through the filter with water. The final clear solution (1400 mL) was cooled on ice and acidified with glacial acetic acid.

The precipitated product was filtered off, washed with water, and dried in a vacuum desiccator over KOH for several days. The pale brown fluffy solid was analytically pure. Yield: quantitative. In every attempt, the yield exceeded 95%: mp 139.0–142.5 °C dec; ^{1}H NMR (DMSO-d_6) δ 0.84 (t, J = 7 Hz, 6 H, 3′-*Et*), 1.21 [br, 18 H, 2–10-$(CH_2)_9$], 2.15 (s, 6 H), 2.18 (s, 6 H), 2.16–2.46 [m, 8 H, 3′-Et, 1,11-$(CH_2)_2$], 3.82 (s, 4 H, *meso*-CH_2), 9.49 (s, 2 H, CHO), 11.00 (br, 2 H, 1-NH), 11.45 (br, 2 H, 1′-NH); CO_2H not observed; MS/*m/e* 700 (M^+, weak), 699, 698, 612. Anal. Calcd for $C_{41}H_{56}N_4O_6$: C, 70.26; H, 8.05; N, 7.99. Found: C, 70.45; H, 8.16; N, 8.20.

1,11-Bis[2-[[5-(benzyloxycarbonyl)-3-ethyl-4-methylpyrrol-2-yl]methyl]-5(*E*)-[2-cyano-2-(methoxycarbonyl)-vinyl]-4-methylpyrrol-3-yl]undecane (23a). (i) 1,11-Bis[5-(*E*)-[2-cyano-2-(methoxycarbonyl)vinyl]-2,4-dimethylpyrrol-3-yl]undecane (**15a**) (2.80 g, 5 mmol) in dichloromethane (80 mL) was treated, dropwise, at room temperature over 30 min, with a solution of sulfuryl chloride (1.45 g, 10.7 mmol) in dichloromethane (40 mL). After 10 min of additional stirring, the solution was concentrated under reduced pressure. The bis(chloromethyl) derivative **17a** crystallized out upon addition of hexane and was filtered off, washed with hexane, and employed in the next reaction without further purification.

(ii) The bis(chloromethyl) derivative **17a** and 2-(benzyloxycarbonyl)-4-ethyl-3-methylpyrrole[15] (**19**) (2.7 g, 11.1 mmol) were suspended in glacial acetic acid (150 mL) and warmed under nitrogen on a water bath. When the temperature reached 70 °C, the yellow solids dissolved, producing a clear dark red solution. Inspection of the reaction mixture by TLC showed a single dipyrromethane to be present. Concentration of the solution and addition of methanol caused the separation of an oil. The solvents were therefore removed completely in vacuo, and the residue was taken up in dichloromethane (100 mL) and washed with saturated aqueous sodium bicarbonate (2 × 40 mL) and then water (40 mL). The solvent was again removed in vacuo and the residue chromatographed over silica gel (Akt 1, 90 g). Dichloromethane eluted out the excess α-free pyrrole, and the product was eluted with 5% ethyl acetate in dichloromethane. Attempts to crystallize the product from dichloromethane–ethyl acetate, dichloromethane–methanol, or dichloromethane–diethyl ether all gave oils, so the product was eventually isolated as a yellow glass, 5.22 g (81.6%): mp 91.0–93.0 °C; ^{1}H NMR ($CDCl_3$) δ 1.03 (t, J = 7.5 Hz, 6 H, 3′-Et), 1.25 [br, 18 H, 2–10-$(CH_2)_9$], 2.14 (s, 6 H, 4-CH_3), 2.31 (s, 6 H, 4′-CH_3), 2.28–2.60 [m, 8 H, 3′-Et, 1,11-$(CH_2)_2$], 3.76 and 3.85 (2 s, 6 H, CH_3O isomers), 3.94 (s, 4 H, meso), 5.29 (s, 4 H, ArCH_2O), 7.25 (hook, vinyl isomer), 7.37 (m, 10 H, Ar), 7.90 (s, 2 H, vinyl), 8.84 (br, 2 H, 1′-NH), 9.40 (br, 2 H, 1-NH); ^{13}C NMR ($CDCl_3$ at 77.09) δ 165.16 (2 C, CO_2CH_3, isomer at 166.78), 161.54 (2 C, CO_2Bz), 138.45 (2 C, *C*H=C, isomer at 138.94), 137.71 (2 C, 2), 136.44 (2 C, Ar-1), 135.65 (2 C, 4), 128.42 (4 C, Ar), 127.94 (6 C, Ar), 127.71 (2 C, 2′), 126.98 (2 C, 4′), 125.23 (2 C, 3′), 124.39 (2 C, 3), 123.60 (2 C, 5), 119.48 (2 C, CN), 118.31 (2 C, 5′), 86.00 (2 C, CH=*C*), 65.56 (2 C, PhCH_2O), 52.45 (2 C, CH_3O), 30.37 (2 C, methylene 2,10), 29.59 (7 C, methylene 3–9), 23.84 (4 C, methylene 1,11, 2 *meso*-CH_2), 17.33 (2 C, 3′-CH_3CH_2), 15.39 (2 C, 3′-CH_3CH_2), 10.60 (2 C, 4′-CH_3), 9.36 (2 C, 4-CH_3); MS, *m/e* 1043 (M^+, v weak), 952, 934, 108, 91. Anal. Calcd for $C_{63}H_{74}N_6O_8$: C, 72.53; H, 7.15; N, 8.06. Found: C, 72.53; H, 7.05; N, 7.99.

1,11-Bis[2-[(5-carboxy-3-ethyl-4-methylpyrrol-2-yl)-methyl]-5(*E*)-[2-cyano-2-(methoxycarbonyl)vinyl]-4-methylpyrrol-3-yl]undecane (24a). Dibenzyl ester **23a** (2.11 g, 2.02 mmol) and 10% Pd–C (182 mg) were stirred in tetrahydrofuran (50 mL) under hydrogen (1 atm, room temperature). The uptake of hydrogen was rapid and linear with time and was complete in about 1 h. The catalyst was removed by filtration, and the filtrates were diluted with methanol and concentrated in vacuo. The product separated as a yellow powder and was kept overnight in a freezer to complete the precipitation. The solids were filtered and washed with methanol, to give 1.14 g (65.5%) of analytically pure material. Concentration of the filtrates gave a second crop: 0.34 g (19.5%).

Compound **24a**: mp 180.0–181.0 °C; ^{1}H NMR (DMSO-d_6) δ 0.87 (t, J = 7 Hz, 6 H, 3′-Et), 1.23 [br, 18 H, 2–10-$(CH_2)_9$, 2.16 (s, 6 H, 4-CH_3), 2.21 (s, 6 H, OCH_3), 4.07 (s, 4 H, *meso*-CH_2), 7.91 (s, 2 H, vinyl), 10.55 (br, 2 H, 1-NH), 11.12 (br, 2 H, 1′-NH), CO_2H not recorded; MS, m/e 774 (M − $2CO_2$), 742, 665. Anal. Calcd for $C_{49}H_{62}N_6O_8$: C, 68.19; H, 7.24; N, 9.74. Found: C, 68.18; H, 7.44; N, 9.66.

1,11-Bis[5(*E*)-[2-cyano-2-(methoxycarbonyl)vinyl]-2-[(3-ethyl-4-methylpyrrol-2-yl)methyl]-4-methylpyrrol-3-yl]undecane (25a). The undecanediylbis(carboxydipyrromethane) **24a** (1.39 g, 1.61 mmol) and redistilled trifluoroacetic acid (15 mL) were stirred under nitrogen at room temperature for 5 min. A sample was withdrawn into dichloromethane and inspected by TLC. A single yellow spot, colored red with bromine vapor, was obtained; no trace of yellow starting material remained at the origin.

Most of the acid was removed by evaporation under reduced pressure. The residue was taken into dichloromethane (75 mL), washed with saturated aqueous sodium bicarbonate (2 × 30 mL), and then concentrated in vacuo after addition of methanol. After a filtration and methanol wash, a yield of 1.02 g (81.8%) of an orange microcrystalline solid was obtained. The filtrates were concentrated and cooled in ice to afford an additional 0.13 g (10.4%): mp 132.0–134.0 °C; ^{1}H NMR ($CDCl_3$) δ 1.07 (t, J = 7.5 Hz, 6 H, 3′-Et), 1.28 [br, 18 H, 2–10-$(CH_2)_9$, 2.06 (s, 6 H, 4′-CH_3), 2.17 (s, 6 H, 4-CH_3), 2.24–2.62 [m, 8 H, 3′-Et, 1,11-$(CH_2)_2$], 3.84 (s, 6 H, OCH_3), 3.94 (s, 4 H, *meso*-CH_2), 6.51 (d, J = 2 Hz, 2 H, 5′-H), 7.56 (br, 2 H, 1′-NH), 7.91 (s, 2 H, vinyl), 9.41 (br, 2 H, 1-NH); ^{13}C NMR ($CDCl_3$ at 77.05) δ 165.22 (2 C, C=O), 140.43 (2 C, 2), 137.80 (2 C, *C*H=C), 135.68 (2 C, 4), 124.15 (2 C, 3), 123.45 (2 C, 5), 122.44 (2 C, 2′), 120.70 (2 C, 3′), 119.71 (2 C, CN), 118.49 (2 C, 4′), 115.11 (2 C, 5′), 85.62 (2 C, CH=*C*), 52.44 (2 C, OCH_3), 30.44 (2 C, methylene 2,10), 29.59 (7 C, methylene 3–9), 23.84 (4 C, methylene 1,11, 2 × *meso*-CH_2), 17.59 (2 C, 3′-*C*H_2CH_3), 15.65 (2 C, 3′-CH_2CH_3), 10.33 (2 C, 4′-CH_3), 9.56 (2 C, 4-CH_3); MS, m/e 774 (M^+), 742, 665. Anal. Calcd for $C_{47}H_{62}N_6O_4$: C, 72.84; H, 8.06; N, 10.84. Found: C, 73.00; H, 7.90; N, 10.73.

1,11-Bis[2-[(3-ethyl-4-methylpyrrol-2-yl)methyl]-5-formyl-4-methylpyrrol-3-yl]undecane (22a). The preceding dimeric cyanoacrylate **25a** (903 mg, 1.17 mmol) and potassium hydroxide (4 g) were heated to reflux in water (75 mL) under nitrogen. 1-Propanol (35 mL) was added to solubilize the starting material, and the reaction was monitored by UV–visible spectroscopy. The cyanoacrylate absorption maximum at 407 nm was gradually replaced by the formylpyrrole maximum at 320 nm. The reaction was complete after approximately 2.5 h of reflux. When the alcohol was boiled off, the product separated as a mixture of brown lumps and finely crystallized solid. This was filtered off, washed with water, and dried in a vacuum desiccator over KOH: yield, 682 mg (95.6%); mp 157.0–158.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.08 (t, J = 7.5 Hz, 6 H, 3′-Et), 1.29 [br, 18 H, 2–10-$(CH_2)_9$], 2.05 (s, 6 H, 4′-CH_3), 2.27 (s, 6 H, 4-CH_3), 6.44 (d, J = 2 Hz, 2 H, 5′-H), 8.07 (br, 2 H, 1′-NH), 9.41 (br, 2 H, 1-NH), 9.47 (s, 2 H, CHO); ^{13}C NMR ($CDCl_3$ at 77.03) δ 175.93 (2 C, C=O), 138.10 (2 C, 2), 133.20 (2 C, 4), 128.27 (2 C, 5), 123.34 (2 C, 3), 122.35 (2 C, 2′), 121.39 (2 C, 3′), 117.76 (2 C, 4′), 114.78 (2 C, 5′), 30.77 (2 C, methylene 2,10), 29.63 (7 C, methylene 3–9), 23.81 (2 C, methylene 1,11), 22.97 (2 C, *meso*-CH_2), 17.68 (2 C, 3′-*C*H_2CH_3), 15.82 (2 C, 3′-CH_2CH_3), 10.35 (2 C, 4′-CH_3), 8.92 (2 C, 4-CH_3); MS, m/e 612 (M^+), 583, 122, 121, 94. Anal. Calcd for $C_{39}H_{56}N_4O_2$: C, 76.43; H, 9.21; N, 9.14. Found: C, 75.61; H, 9.06; N, 9.35.

8,18-Diethyl-3,7,13,17-tetramethyl-2,12-undecamethyleneporphine (26a). Method A. (i) Decarboxylation. 1,11-Bis[2-[(5-carboxy-3-ethyl-4-methylpyrrol-2-yl)methyl]-5-formyl-4-methylpyrrol-3-yl]undecane (**21a**) (715 mg, 1.02 mmol) was stirred at reflux in *N*,*N*-dimethylformamide (160 mL) under nitrogen for 2 h. The reaction was monitored by UV–visible spectroscopy: the absorption maximum at 280 nm decayed relative to the 320-nm maximum and was eventually reduced to a shoulder.

The solution was cooled to room temperature under nitrogen, concentrated in vacuo to approximately 50 mL, and then added to dichloromethane (200 mL).

This was washed with water (3 × 60 mL) to remove most of the remaining DMF, dried over sodium sulfate, filtered, and diluted to 500 mL with dichloromethane in preparation for the next step.

(ii) Intramolecular 2 + 2 Coupling. The cyclization was carried out in two 2-L Erlenmeyer flasks (covered with aluminum foil to exclude light), each containing *p*-toluenesulfonic acid (4.0 g) in methanol (25 mL)–dichloromethane (600 mL), stirred magnetically at room temperature. The dichloromethane solution resulting from the decarboxylation step was added very slowly to the catalyst solution by means of a syringe pump; the entire addition was complete in 6 days.

The reddish violet solution was concentrated in vacuo to approximately 150 mL and then extracted with saturated aqueous sodium bicarbonate (3 × 50 mL) to remove the acid catalyst. The solution was then taken to dryness in vacuo.

The residue was taken up in minimal dichloromethane and chromatographed as described below.

(iii) Chromatographic Purification of Porphyrin. The crude porphyrin was first chromatographed on silica gel (Akt I, 80 g) with dichloromethane as the eluting solvent. The porphyrin was completely adsorbed on the column, and most of the brown impurities eluted out. The solvent was changed to 2% methanol in dichloromethane, to elute the porphyrin as a dark purple solution, containing some brown impurities.

The partially purified porphyrin was rechromatographed on activity IV silica gel (40 g) by using dichloromethane. The porphyrin and some of the impurities were adsorbed at the origin. The first band eluting out was brown and nonfluorescent. This was followed by a fluorescent band (very dilute and exhibiting an etio-type spectrum), which was also discarded. The solvent was then changed to 1% methanol in dichloromethane to get the product moving on the column. A trace of brown impurity moved almost behind the porphyrin and was collected since it could not be separated without sacrificing a considerable amount of porphyrin.

The final purification was effected with basic alumina (20 g; 3% water added), with dichloromethane eluant. All of the impurities remained at the origin, and only the porphyrin product moved.

The clean reddish-violet solution eluting out was concentrated, and the porphyrin crystallized from nitromethane and dried on a vacuum line, to give a yield of 232 mg (39.6%).

The overall yields for this decarboxylation–cyclization procedure varied between 22.0% and 39.6% and appeared to depend to a large extent on the particular sample of the starting material. (All of the recorded yields are for first crops only.)

Compound **26a**: mp 297.0–298.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 2 H, 5-H, 15-H), 9.80 (s, 2 H, 10-H, 20-H), 4.12 (m, 4 H, C*H*$_2$CH$_3$), 4.02 (m, 2 H, one proton each of chain 1,11), 3.65 (m, 2 H, one proton each of chain 1,11), 3.64 (s, 6 H, CH_3), 3.37 (s, 6 H, CH_3), 1.84 (t, 6 H, CH_2CH_3), 1.43 (m, 4 H, chain), 0.12 (m, 2 H, chain), −0.12 (m, 2 H, chain), −2.58 (m, 4 H, chain), −2.82 (m, 4 H, chain), −3.46 (br, 2 H, NH), −4.03 (m, 2 H, chain); ^{13}C NMR (10% TFA–$CDCl_3$ at 77.13) δ 146.73, 145.12, 143.67, 141.41, 140.56, 140.25, 140.05, 139.20 (each 2 C, porphyrin core α- and β-carbons), 100.89, 99.94 (each 2 C, meso), 28.86, 28.67 (3 C), 27.00, 25.98, 25.38 (11 C, chain carbons), 20.20 (2 C, *C*H_2CH_3), 16.61 (2 C, CH_2CH_3), 12.21, 11.75 (each 2 × CH_3); CF_3CO_2H at 114.75, 159.31; visible spectrum (CH_2Cl_2) λ_{max} (nm) (log ϵ), 400.7 (5.24), 503.1 (4.05), 539.8 (4.05), 571.9 (3.80), 625.8 (3.59). Anal. Calcd for $C_{39}H_{50}N_4$: C, 81.49; H, 8.77; N, 9.75. Found: C, 81.22; H, 8.73; N, 9.77. M_r 574.4040; $^{12}C_{39}{}^1H_{50}{}^{14}N_4$ requires 574.4036.

Method B. High-purity undecanediyl-bis(5-formyldipyrromethane) **22a** derived from the cyanoacrylate–benzyl ester route (317 mg, 0.52 mmol) in dichloromethane (200 mL) was cyclized by syringe-pump addition to a solution of *p*-toluenesulfonic acid

(4 g) in methanol (25 mL)–dichloromethane (600 mL). Workup as before afforded a first crop of 153 mg (51.5%) of purified porphyrin, identical in all respects with that material obtained by method A. A mixed melting point showed no depression.

8,18-Diethyl-3,7,13,17-tetramethyl-2,12-decamethyleneporphine (26b): prepared from the appropriate precursor **21b** by method A. In five preparations, overall yields (from **21b**) of 29.1%, 31.3%, 33.2%, 34.7%, and 37.3% were obtained. The product was crystallized from the dichloromethane chromatographic eluates by adding nitromethane and concentrating in vacuo: mp 269.0–270.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.89 (s, 2 H, 5-H, 15-H), 9.67 (s, 2 H, 10-H, 20-H), 4.06 (m, 4 H, CH_2CH_3), 3.67 (m, 2 H, chain 1,10), 3.60 (s, 6 H, CH_3), 3.46 (m, 2 H, chain 1,10), 3.27 (s, 6 H, CH_3), 1.81 (t, J = 7 Hz, 6 H, CH_2CH_3), 1.51 (m, 2 H, chain 2,9), 0.46 (m, 2 H, chain 2,9), 0.03 (m, 2 H, chain 3,8), −1.17 (m, 2 H, chain 3,8), −1.79 (m, 2 H, chain 4,7), −2.23 (m, 2 H, chain 5,6), −3.27 (br, 2 H, NH), −5.13 (m, 2 H, chain 4,7), −5.87 (m, 2 H, chain 5,6); ^{13}C NMR (10%, TFA–$CDCl_3$ at 77.14) δ 146.87, 145.61, 143.61, 141.22, 140.44, 140.29, 138.95, 138.23 (2 C each, porphyrin core α- and β-carbons), 101.24, 100.05 (2 C each, meso), 28.47, 27.94, 26.96, 26.46, 25.96 (2 C each, chain), 20.20 (2 C, CH_2CH_3), 16.62 (2 C, CH_2CH_3), 11.77 (4 C, CH_3); CF_3CO_2H at 114.71, 159.37; visible spectrum (CH_2Cl_2) λ_{max} (nm) (log ϵ), 402.0 (5.21), 507.5 (3.96), 544.4 (4.03), 572.7 (3.78), 626.2 (3.37). Anal. Calcd for $C_{38}H_{48}N_4$: C, 81.38; H, 8.63; N, 9.99. Found: C, 81.04; H, 8.62; N, 9.93. M_r 560.3873; $^{12}C_{38}{}^1H_{48}{}^{14}N_4$ requires 560.3879.

8,18-Diethyl-3,7,13,17-tetramethyl-2,12-nonamethyleneporphine (26c). This was prepared similarly to its undecane homologue **26a** via method A. This porphyrin was found to be adsorbed onto silica gel far more strongly than its undeca- and decamethylene analogues. On activity I silica gel, 5% methanol–dichloromethane was required to make the product move, but not without some impurities. Activity IV silica gel required 2% methanol–dichloromethane for elution of product, again contaminated with impurities. On basic alumina (3% water), this homologue did *not* move with dichloromethane alone (unlike the C_{10} or C_{11} analogues); however, 10% ethyl acetate–dichloromethane eluted the porphyrin out pure, leaving all the impurities at the origin.

The maximum yield obtained for the purified porphyrin was 26.8%. Four other preparations gave yields of 20.0%, 21.8%, 25.1%, and 25.0%. In all instances, the porphyrin was crystallized from nitromethane. It was observed later that this porphyrin was *less* soluble in methanol than in nitromethane, unlike its two homologues: mp >330 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (s, 2 H, 5-H, 15-H), 9.36 (s, 2 H, 10-H, 20-H), 3.97 (m, 4 H, CH_2CH_3), 3.57 (s, 6 H, CH_3), 3.29 (m, 2 H, chain 1,9), 3.03 (m, 2 H, chain 1,9), 3.00 (s, 6 H, CH_3), 1.79 (t, 6 H, CH_2CH_3), 0.56 (m, 4 H, chain 2,2,8,8), −1.14 (m, 2 H, chain 3,7), −1.56 (m, 2 H, chain 3,7), −3.06 (br, 2 H, NH), −3.33 (m, 2 H, chain 5,5), −4.15 (m, 2 H, chain 4,6), −4.35 (m, 2 H, chain 4,6). ^{13}C NMR (10% TFA–$CDCl_3$ at 77.13) δ 146.60 (4 C), 144.65, 141.21, 140.42, 139.59, 139.07, 134.27 (2 C each, porphyrin core, α and β), 101.48, 99.72 (2 C each, meso), 28.72 (4 C), 28.22 (1 C), 25.84 (2 C), 24.97 (2 C) (chain), 20.12 (2 C, CH_2CH_3), 16.47 (2 C, CH_2CH_3), 11.66 (4 C, CH_3); CF_3CO_2H at 114.89, 159.30; visible spectrum (CH_2Cl_2) λ_{max} (nm) (log ϵ) 405.3 (5.23), 513.5 (3.91), 551.7 (4.08), 579.1 (3.82), 633.0 (3.43). Anal. Calcd for $C_{37}H_{46}N_4$: C, 81.27; H, 8.48; N, 10.25. Found: C, 81.33; H, 8.57; N, 10.24. M_r 546.3737; $^{12}C_{37}{}^1H_{46}{}^{14}N_4$ requires 546.3723.

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Registry No. **6**, 2199-44-2; **7a**, 45165-01-3; **7a** (diacid), 1852-04-6; **7b** (diacid), 111-20-6; **7c** (diacid), 123-99-9; **7d** (diacid), 505-48-6; **8a**, 87281-00-3; **8b**, 87280-99-7; **8c**, 87280-98-6; **9a**, 87280-88-4; **9b**, 87280-87-3; **9c**, 87280-86-2; **10a**, 87280-91-9; **10b**, 87280-90-8; **10c**, 87280-89-5; **11a**, 87280-83-9; **12a**, 87280-94-2; **13a**, 87280-97-5; **13b**, 87280-96-4; **13c**, 87280-95-3; **13d**, 113088-82-7; **14a**, 87280-79-3; **14b**, 87280-78-2; **14c**, 87280-77-1; **14d**, 113109-07-2; (*E*,*E*)-**15a**, 113088-76-9; (*Z*,*Z*)-**15a**, 113088-77-0; **16a**, 87280-74-8; (*E*,*E*)-**17a**, 113088-78-1; **18**, 4391-98-4; **19**, 51089-83-9; **20a**, 87280-73-7; **20b**, 87280-72-6; **20c**, 87280-71-5; **20d**, 113088-83-8; **21a**, 87280-70-4; **21b**, 87280-69-1; **21c**, 87280-68-0; **21d**, 113088-84-9; **22a**, 87280-67-9; (*E*,*E*)-**23a**, 113088-79-2; (*E*,*E*)-**24a**, 113088-80-5; (*E*,*E*)-**25a**, 113088-81-6; **26a**, 87280-61-3; **26b**, 87280-60-2; **26c**, 87280-58-8; $CH_2(CN)_2$, 109-77-3; $CH_2(CN)CO_2CH_3$, 105-34-0.

Supplementary Material Available: Experimental details for compounds **8b,c**, **9b,c**, **10b,c**, **13b–d**, **14b–d**, **20b–d**, and **21b–d** (11 pages). Ordering information is given on any current masthead page.