Simple Methodology for Syntheses of Porphyrins Possessing Multiple Peripheral Substituents with an Element of Symmetry

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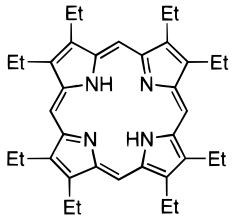
New methodology was developed for synthesis of regiochemically pure porphyrins with D_{2h} symmetry (e.g. **9**) via tetramerization reactions involving two different pyrroles. The two pyrrole components were a 2,5-diunsubstituted pyrrole (e.g. **11**) and a 2,5-bis[(*N*,*N*-dimethylamino)methyl]pyrrole (e.g. **10**), the latter being formed from a 2,5-di-unsubstituted pyrrole by treatment with excess Eschenmoser's reagent (*N*,*N*-dimethylmethyleneammonium iodide). A bis-butanoporphyrin **16** was transformed into the corresponding *opp*-bis-benzoporphyrin **17** by treatment with DDQ. The synthetic method was further extended to allow the synthesis of more unsymmetrical porphyrins, with C_{2v} symmetry (e.g. **32**), by reacting a tripyrrane (e.g. **27**) with a 2,5-bis[(*N*,*N*-dimethylamino)-methyl]pyrrole (e.g. **18**). The structures and substituent arrays in both type of porphyrins were confirmed by single-crystal X-ray crystallography.

Introduction

Over the past 50 years, numerous advances in porphyrin synthetic methodology have been realized. These developments have advanced systematically through monopyrrole tetramerization,[1−3] dipyrromethene self-condensation in organic acid melts,[4] "2 + 2" MacDonald dipyrromethane syntheses,[5,6] "3 + 1" synthesis using a tripyrrane and a diformylpyrrole,[7] and then on to the truly general approaches through *b*-bilenes and *a*,*c*-biladienes.[8−10] However, it still remains a fact that if the target porphyrin is totally symmetrical [e.g. octaethylporphyrin (**1**) or tetraphenylporphyrin (**2**)], a one-pot monopyrrole "tetramerization" approach is the only efficient method, but if asymmetry is required in the product porphyrin substituent array, and if extensive chromatographic purification is to be avoided, a more elaborate route via dipyrroles, tripyrroles, or open-chain tetrapyrroles must be employed.[9]



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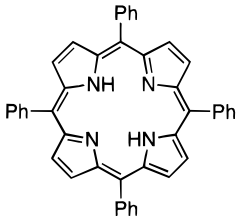

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Most porphyrin cyclization procedures proceed by way of acid catalysis and if porphyrinogens are intermediates at any point, acid-catalyzed redistribution of the pyrrole subunits to give a complex mixture of porphyrin products is likely (unless the product porphyrin is substituted throughout with only one kind of substituent, e.g. **1** or **2**, which renders the redistribution invisible). Not all porphyrin syntheses proceed through porphyrinogen intermediates, but those which do, and which have more than one type of 3,4-substituent on the monopyrrole (e.g. **3**), are usually subject to mixture problems. For example (Scheme 1), it might be thought possible to obtain a "type-I"[11] porphyrin **4** by acid-catalyzed self-condensation of pyrrole **3**, bearing a 2-substituent with a good leaving group at the benzylic carbon. Though such an expectation[12,13] is occasionally close to reality,[14] it has to be recognized that contamination with other porphyrin so-called type-isomers is often the case.[15,16] As shown in Scheme 1, under acidic conditions, the intermediate is actually a mixture of porphyrinogens **5**−**8** due to acid-catalyzed "scrambling" of the pyrrole subunits either at the macrocyclic porphyrinogen stage or at some earlier open-chain methylene-linked oligopyrrole stage.[17] The product from such a reaction (Scheme 1) is usually a mixture of various proportions of all four porphyrin type isomers.[15,16]

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‡ Dedicated to Professor Dr. Horst Senger on the occasion of his 65th birthday.

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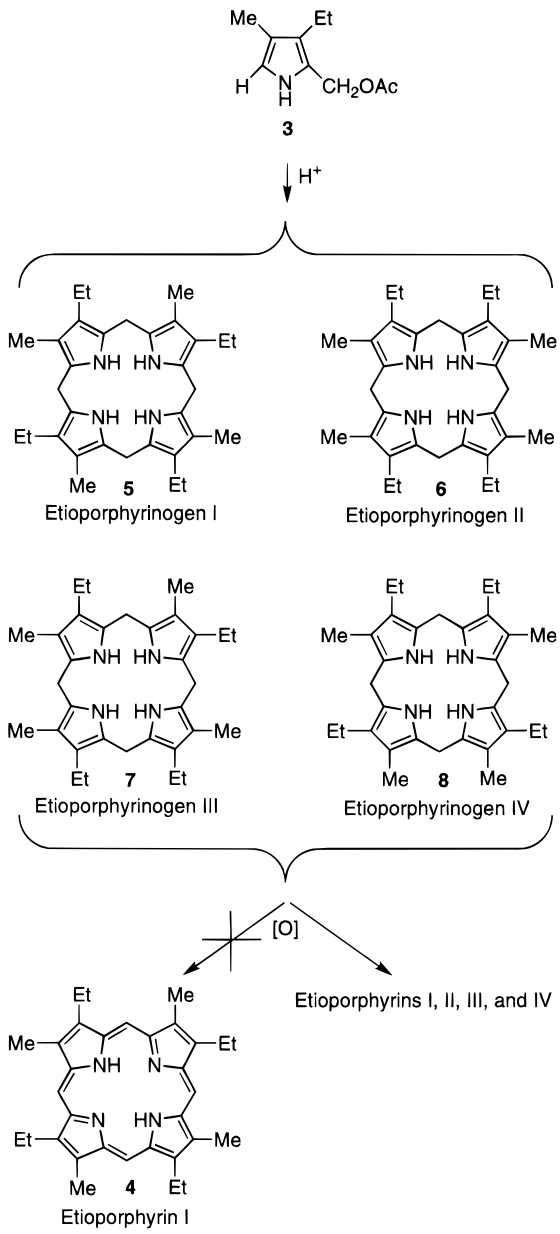
0022-3263/96/1961-0998$12.00/0

Scheme 1



It occurred to us that it might be possible to avoid the troublesome redistribution of the pyrrole subunits which leads to the formation of mixtures in such reaction if, (i) the reaction is carried out under nonacidic conditions and (ii) the intermediate porphyrinogen is rapidly oxidized *in situ* to porphyrin. In this paper,[18] we report a new method for synthesis of porphyrins with like pyrrole rings opposite to each other, and an extension of this methodology to a "3 + 1" synthesis of porphyrins, utilizing a tripyrrane and a 2,5-bis[(*N*,*N*-dimethylamino)methyl]-pyrrole.

Results and Discussion

Porphyrins with D_{2h} Symmetry from One-Pot Reactions of Two Different Pyrroles. One of our proposed criteria for avoiding the pyrrole unit "scrambling" of an intermediate porphyrinogen is to carry out the reaction under nonacidic conditions. But, tetramerization reactions using pyrroles such as **3** require acid in order to protonate the acetoxy leaving group to facilitate its displacement by the nucleophilic 2-position of another pyrrole. In order avoid acid catalysis, the leaving group on the benzylic carbon at the 2-position of the pyrrole needs to be very reactive so that it can be displaced without acid catalysis. An ideal 2-substituent, capable of fulfilling the above requirement, is the (dimethylamino)methyl group, which through quaternization for example with an alkyl halide, can be readily displaced from the benzylic carbon under neutral conditions as a trialkylamine. It also occurred to us that it should be possible, in principle, to obtain a regiochemically pure porphyrin product (with like pyrrole rings opposite each other)[19] (e.g. **9**) if one were to react two pyrroles together under neutral conditions, provided that one of these pyrroles (e.g. **10**) possessed all of the future *meso*-carbons of the porphyrin product, and the other pyrrole (e.g. **11**) contained none of them. The positioning of the benzylic carbons would, in effect, determine which of the two constituent pyrroles in the mixture could react with it next.

Pyrrole Mannich bases [2-[(*N*,*N*-dimethylamino)methyl]pyrroles] have previously been used in porphyrin syntheses.[20] In our strategy, *2,5*-bis[(*N*,*N*-dimethylamino)methyl]pyrroles e.g. **10** and **12**, were the key intermediates in the approach, and these were readily formed in 83-86% yields by treatment of the corresponding 2,5-diunsubstituted pyrroles **13** or **14** in nitromethane with an excess of Eschenmoser's reagent.[21] It was first necessary to ascertain whether or not the use of a 2,5-bis[(*N*,*N*-dimethylamino)methyl]pyrrole under standard acidic polymerization conditions would indeed give a mixture of porphyrins! Thus, pyrrole **10** with 3,4-dimethylpyrrole[22] (**11**) was treated in acetic acid at reflux in the presence of oxygen. A mixture of porphyrin products was obtained [^{1}H NMR (300 MHz, in $CDCl_3$), *meso* proton signals at 10.03, 10.07, and 10.10 ppm]; this is presumably the anticipated outcome of acid-catalyzed scrambling of the initially formed porphyrinogen or partially oxidized porphomethene species prior to aerobic oxidation to porphyrin. Similar results were obtained when **10** and **11** were heated together in acetic acid containing potassium ferricyanide as oxidant.[23] We did not immediately proceed to the use of methyl iodide for quaternization of **10** since we wanted to investigate the stability of this pyrrole in neutral solvents in the presence of nucleophilic pyrroles. Reaction of pyrroles **10** and **11** in methanol in the presence of $K_3Fe(CN)_6$ gave, after workup, chromatography, and recrystallization, a 19% yield of isomerically pure porphyrin **9**.[24] This was evident from the fact that the proton NMR spectrum showed only one *meso*

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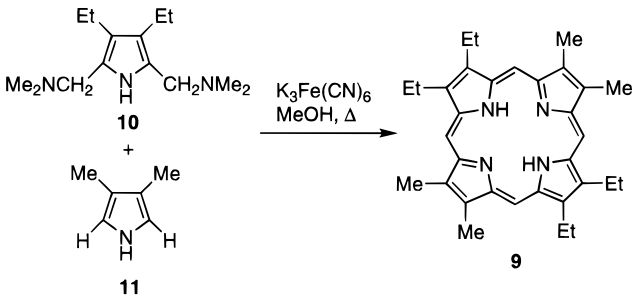
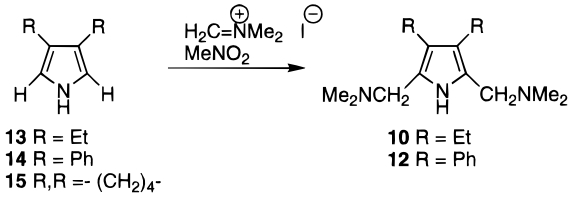
(24) A single crystal X-ray structure of the bis-perchlorate salt of porphyrin **9**, which fully confirms the substituent regiochemistry, has been published elsewhere: Senge, M. O.; Forsyth, T. P.; Nguyen, L. T.; Smith, K. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2485.



proton signal at 10.07 ppm which accounted for four protons. Thus, even in the absence of a quaternization agent, the [(dimethylamino)methyl]pyrrole **10** was sufficiently reactive to suffer benzylic displacement by a reasonably electron-rich monopyrrole. Similar results were obtained using **10** and 3,4-butanopyrrole[22] (**15**) to afford porphyrin **16**. Porphyrin **16** when treated with DDQ in refluxing toluene afforded the dibenzoporphyrin **17** in which both of the cyclohexane rings in the precursor were aromatized.[19] This was evident, from ^{1}H NMR spectroscopy, by the disappearance of peaks at 2.54 and 4.16 ppm and the appearance of aromatic signals at 8.54 and 9.64 ppm. The structural composition of **17** was further confirmed by HRMS.

However, when 2,5-bis[(*N*,*N*-dimethylamino)methyl]-pyrrole (**10**) was treated with 3,4-diphenylpyrrole[25] (**14**) under the same conditions, only decomposition products and a trace amount of porphyrin mixture were observed. Presumably pyrrole **14** is not as electron-rich as dialkylpyrroles **11**, **13**, or **15**, or possibly, steric effects due to the bulky phenyl substituents on **14** inhibited its reaction with pyrrole **10**. We therefore proceeded to switch the functional groups on the starting pyrroles so that the bridging carbon units were built into the less reactive 3,4-diphenylpyrrrole (**14**); treatment with excess Eschenmoser's reagent gave **12**. Although the subsequent macrocyclization reaction with **13** took place, it required a longer time to complete and a mixture of porphyrins was obtained [^{1}H NMR (300 MHz, in $CDCl_3$), *meso* proton signals at 10.13, 10.17, and 10.21 ppm].



It seemed clear that the reactivity of the leaving groups in **12** needed to be enhanced, and so we fell back upon our original synthetic design involving quaternization of the (dialkylamino)methyl function. Pyrrole **12** was readily bis-quaternized by use of excess iodomethane in benzene. The quaternized pyrrole **18** (not characterized) reacted smoothly with pyrrole **13** to afford pure porphyrin **19** in 18% yield. Spectrophotometry showed the onset of porphyrin formation after about 5 min, and the proton NMR spectrum of the product showed it was the desired porphyrin as indicated by the observation of only one *meso* proton signal at 10.21 ppm (4 H). Unambiguous proof of the substituent regiochemistry of porphyrin **19** was obtained by X-ray crystallography; Figure 1 shows the structure.

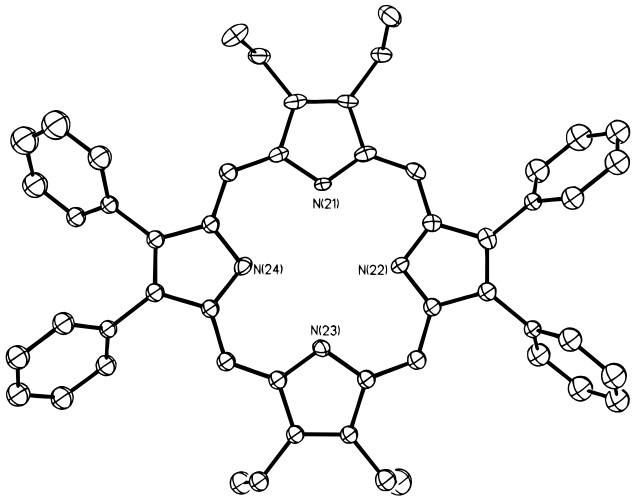
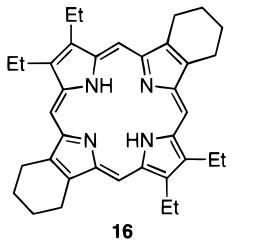
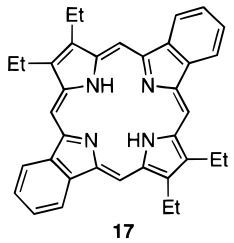
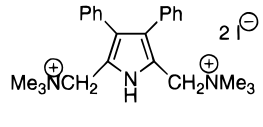
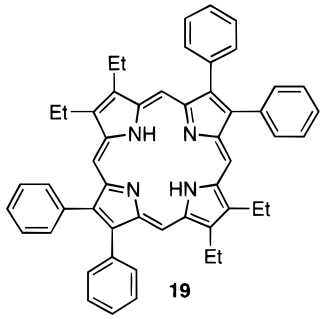


Figure 1. View of the molecular structure of porphyrin **19**. Hydrogens have been omitted for clarity.









Porphyrins with C_{2v} Symmetry from a "3 + 1" Approach. After the above methodology was successfully developed and tested, we further expanded it to synthesize porphyrins with less symmetry. This approach is much more versatile than that described above since it provides access to porphyrin with three different pyrrole subunits in a predestined array. Boudif and Momenteau have recently published[7] a similar "3 + 1" approach to porphyrin synthesis involving a tripyrrane and a 2,5-diformylpyrrole. Our tripyrranes **20**−**24** were synthesized (Scheme 2) in 59−84% yields by condensation of 2,5-diunsubstituted pyrroles (**11**, **13**−**15**) and (acetoxymethyl)pyrroles **25** and **26**[26] in methanol with a catalytic amount of TsOH.

Catalytic debenzylation of the tripyrrane esters **20**−**24** afforded the tripyrrane dicarboxylic acids **27**−**31** in quantitative yields. These were then dissolved in methanol and heated at reflux for 15 min before 2,5-bis[(*N*,*N*-dimethylamino)methyl]pyrrole (**10**) or the quaternized

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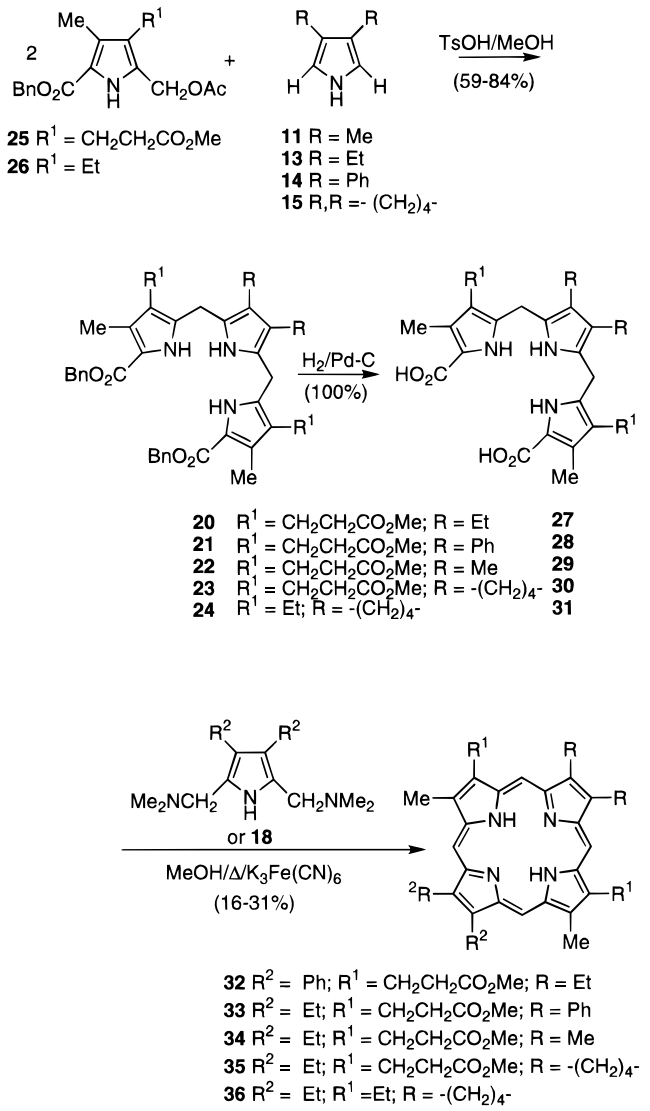
(26) Smith, K. M. In *Porphyrins and Metalloporphyrins*; Smith, K. M., Ed.; Elsevier: Amsterdam, 1975; p 763.

Scheme 2



25 $R^1 = CH_2CH_2CO_2Me$
26 $R^1 = Et$

11 R = Me
13 R = Et
14 R = Ph
15 R,R = -$(CH_2)_4$-

20 $R^1 = CH_2CH_2CO_2Me$; R = Et **27**
21 $R^1 = CH_2CH_2CO_2Me$; R = Ph **28**
22 $R^1 = CH_2CH_2CO_2Me$; R = Me **29**
23 $R^1 = CH_2CH_2CO_2Me$; R = -$(CH_2)_4$- **30**
24 R^1 = Et; R = -$(CH_2)_4$- **31**

32 R^2 = Ph; $R^1 = CH_2CH_2CO_2Me$; R = Et
33 R^2 = Et; $R^1 = CH_2CH_2CO_2Me$; R = Ph
34 R^2 = Et; $R^1 = CH_2CH_2CO_2Me$; R = Me
35 R^2 = Et; $R^1 = CH_2CH_2CO_2Me$; R = -$(CH_2)_4$-
36 R^2 = Et; R^1 =Et; R = -$(CH_2)_4$-

pyrrole **18** and $K_3Fe(CN)_6$ were added. The desired porphyrins **32**−**36** were isolated in 16−31% yields (unoptimized) after simple chromatographic separation to remove trace amounts of other isomers and recrystallization. Because of symmetry, the proton NMR spectra of all these porphyrins showed two *meso* proton signals of approximately equal intensity. X-ray crystallography (Figure 2) was used to definitively identify the substituent array in porphyrin **35**, concomitantly validating the new methodology.

Conclusion

A new synthetic method has been developed which allows the synthesis of regiochemically pure porphyrins (such as **9**, **16**, and **19**), in reasonable overall yield, by a simple one-pot monopyrrole tetramerization involving two different pyrroles; the methodology employs 2,5-bis-[(*N*,*N*-dimethylamino)methyl]pyrroles (e.g. **10**), which are usually sufficiently electrophilic under neutral conditions to undergo rapid reaction with 2,5-unsubstituted pyrroles to provide a single pure porphyrinic product by way of a porphyrinogen intermediate; addition of $K_3Fe(CN)_6$ aids by rapidly oxidizing the porphyrinogen in methanolic solution. When such macrocyclization reactions are demonstrated to be slow, mixtures of porphyrins tend to

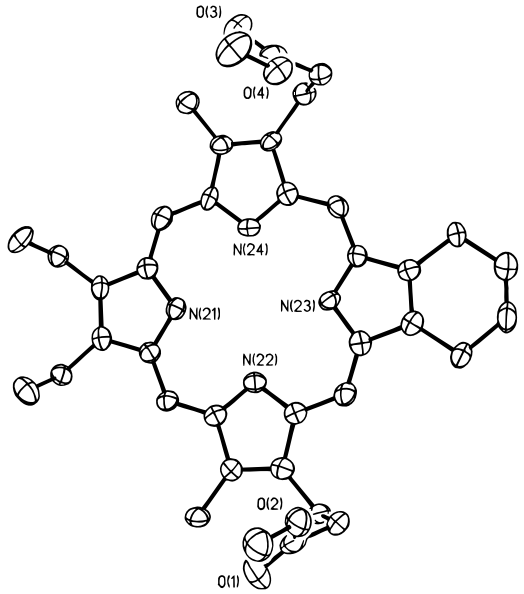


Figure 2. View of the molecular structure of porphyrin **35**. Hydrogens have been omitted for clarity.

be obtained; under such circumstances, quaternization of the bis[(dimethylamino)methyl]pyrrole with methyl iodide, to give e.g. **18**, increases the reaction rate and can provide isomerically pure porphyrin product. The method was elevated to the next level of complexity by employing a "3 + 1" approach, in which a tripyrrane is reacted with a 2,5-bis[(*N*,*N*-dimethylamino)methyl]pyrrole in methanol containing $K_3Fe(CN)_6$. Porphyrins **32**−**36**, each containing three different pyrrole subunits, were synthesized in this manner. This methodology enables the synthesis a number of porphyrins which might otherwise require laborious routes such as dipyrromethane condensation or *b*-bilene/*a*,*c*-biladiene cyclization. Finally, the bis-butanoporphyrin **16** was transformed into the corresponding *opp*-bis-benzoporphyrin **17** by treatment with DDQ.

Experimental Section

General experimental techniques and analytical measurements were applied as previously described.[6] Eschenmoser's reagent (*N*,*N*-dimethylmethyleneammonium iodide) was purchased from Aldrich and used as received.

2,5-Bis[(*N*,*N*-dimethylamino)methyl]-3,4-diethylpyrrole (10). 3,4-Diethylpyrrole[22] (**13**) (2.22 g, 18.02 mmol) and Eschenmoser's reagent[21] (4.48 g, 46.90 mmol) were dissolved in 200 mL of dry $MeNO_2$ and stirred at rt under N_2 for 12 h before the solvent was removed. The residue was redissolved in CH_2Cl_2 and washed with saturated Na_2CO_3 (3×) and dried over anhydrous Na_2SO_4, and the solvent was evaporated to afford a crude dark brown solid (3.67 g, 86%), pure enough (NMR) for subsequent reactions without further purification: ^{1}H-NMR ($CDCl_3$) δ 1.08 (t, J = 7.5 Hz, 6 H), 2.19 (s, 12 H), 2.39 (q, J = 7.5 Hz, 4 H), 3.32 (s, 4 H), 8.13 (br s, 1 H).

2,5-Bis[(*N*,*N*-dimethylamino)methyl]-3,4-diphenylpyrrole (12). 3,4-Diphenylpyrrole[25] (**14**) (2.60 g, 11.90 mmol) and Eschenmoser's reagent (6.61 g, 35.62 mmol) were dissolved in 250 mL of dry $MeNO_2$ and stirred at rt under N_2 for 12 h. Another 1.52 g of the Eschenmoser's reagent was added and the reaction was heated at reflux for 15 min before the solvent was evaporated. Workup as described above to give the crude title compound (3.97 g, 83%): ^{1}H-NMR ($CDCl_3$) δ 2.22 (s, 12 H), 3.46 (s, 4 H), 7.19 (m, 10 H), 8.92 (br s, 1 H).

2,3,12,13-Tetraethyl-7,8,17,18-tetramethylporphyrin (9). Pyrrole **10** (0.84 g, 3.55 mmol) and 3,4-dimethylpyrrole[22] (**11**) (0.34 g, 3.56 mmol) were added to a solution of $K_3Fe(CN)_6$ (3.80 g, 11.54 mmol) in MeOH (75 mL). The mixture was heated

under reflux for 4 h before the solvent was removed. The residue was dissolved in CH_2Cl_2 and washed with H_2O, 5% ammonium hydroxide (2×), H_2O, and brine, and then dried over anhydrous Na_2SO_4. The solvent was evaporated, and the crude product was chromatographed on silica gel eluting with 10% petroleum ether/CH_2Cl_2. Recrystallization from CH_2Cl_2/cyclohexane afforded the title compound in 19.5% yield (162 mg): mp > 300 °C; vis λ_{max} (CH_2Cl_2) 397 nm (ϵ 150000), 498 (13100), 530 (9700), 566 (6400), 618 (4900); ^{1}H-NMR ($CDCl_3$) δ −3.79 (br s, 2 H), 1.91 (t, J = 7.5 Hz, 12 H), 3.61 (s, 12 H), 4.10 (q, J = 7.5 Hz, 8 H), 10.07 (s, 4 H). Anal. Calcd for $C_{32}H_{38}N_4$: C, 80.29; H, 8.00; N, 11.70. Found: C, 80.19; H, 7.98; N, 11.65%.

7,8:17,18-Dibutano-2,3,12,13-tetraethylporphyrin (16). The title compound was prepared from the corresponding pyrrole **10** (0.50 g, 2.10 mmol) and 3:4-butanopyrrole[22] (**15**) (0.25 g, 2.06 mmol) as described above, in a yield of 12% (62 mg): mp > 300 °C; vis λ_{max} (CH_2Cl_2) 398 nm (ϵ 147000), 498 (12000), 532 (10000), 566 (6100), 618 (4800); ^{1}H-NMR ($CDCl_3$) δ −3.78 (br s, 2 H), 1.91 (t, J = 7.5 Hz, 12 H), 2.54 (s, 8 H), 4.08 (q, J = 7.5 Hz, 8 H), 4.16 (s, 8 H), 10.00 (s, 4 H). Anal. Calcd for $C_{36}H_{42}N_4$: C, 81.47; H, 7.98; N, 10.56. Found: C, 81.07; H, 7.80; N, 10.48%.

7,8:17,18-Dibenzo-2,3,12,13-tetraethylporphyrin (17). Porphyrin **16** (0.10 g. 0.19 mmol) and DDQ (0.22 g, 0.95 mmol) were dissolved in toluene (50 mL). The mixture was heated at reflux for 12 h before the solvent was evaporated. The dark residue was chromatographed on silica gel eluting with CH_2Cl_2. Recrystallization from CH_2Cl_2/cyclohexane afforded the title compound as a dull purple crystalline solid (75 mg, 75%): mp > 300 °C; vis λ_{max} (CH_2Cl_2) 387 nm (ϵ 74500), 406 (188000), 480 (5000), 514 (10000), 546 (38900), 584 (6800), 642 (25300); ^{1}H-NMR ($CDCl_3$ + TFA) δ −2.65 (br s, 2 H), 1.81 (t, J = 7.5 Hz, 12 H), 4.17 (q, J = 7.5 Hz, 8 H), 8.50 (m, 4 H), 9.60 (m, 4 H), 10.91 (s, 4 H); HRMS calcd for $C_{36}H_{34}N_4$ 522.2783, found 522.2780.

2,3,12,13-Tetraethyl-7,8,17,18-tetraphenylporphyrin (19). Pyrrole **12** (0.26 g, 0.78 mmol) was dissolved in benzene (25 mL), and MeI (3 mL) was added dropwise. The mixture was stirred at rt for 10 min before it was stored at 0 °C for several h. The product was collected by filtration and washed with cold benzene to afford pyrrole **18**, as a yellow-brown powder, in quantitative yield. Pyrrole **18** (0.48 g, 0.78 mmol) and 3,4-diethylpyrrole (**13**) (0.10 g, 0.80 mmol) were immediately reacted in the same manner as described above for porphyrin **9** to provide the title compound in 18% yield (45 mg): mp > 300 °C; vis λ_{max} (CH_2Cl_2) 410 nm (ϵ 211000), 508 (11000), 548 (23000), 568 (14000), 624 (6500); ^{1}H-NMR ($CDCl_3$) δ −3.65 (br s, 2 H), 1.86 (t, J = 7.5 Hz, 12 H), 4.05 (q, J = 7.5 Hz, 8 H), 7.70 (m, 12 H), 8.04 (m, 8 H), 10.21 (s, 4 H). Anal. Calcd for $C_{52}H_{46}N_4$: C, 85.92; H, 6.38; N, 7.71. Found: C, 85.61; H, 6.30; N, 7.56%.

2,5-Bis[(5-(benzyloxycarbonyl)-3-[2-(methoxycarbonyl)ethyl]-4-methylpyrrol-2-yl]methyl]-3,4-diethylpyrrole (20). 3,4-Diethylpyrrole[22] (**13**) (0.37 g, 3.00 mmol) and benzyl 5-(acetoxymethyl)-4-[2-(methoxycarbonyl)ethyl]-3-methylpyrrole-2-carboxylate[25] (**25**) (2.02 g, 5.41 mmol) were dissolved in MeOH (35 mL) and TsOH (0.10 g) was added. The mixture was heated at 60 °C under N_2 for 12 h before the volume was reduced to about 20 mL. The resulting suspension was stored at 0 °C for several hours, and the solid was filtered and washed with cold MeOH to afford an off-white powder (1.72 g, 84%): mp 163−164 °C; ^{1}H-NMR ($CDCl_3$) δ 1.16 (t, J = 7.5 Hz, 6 H), 2.24 (s, 6 H), 2.33, 2.65 (each t, J = 7.8 Hz, 4 H), 2.50 (q, J = 7.5 Hz, 4 H), 3.61 (s, 10 H), 4.46 (br s, 4 H), 7.01 (m, 4 H), 7.25 (m, 6 H), 8.72 (br s, 1 H), 10.86 (br s, 2 H). Anal. Calcd for $C_{44}H_{51}N_3O_8$: C, 70.47; H, 6.85; N, 5.60. Found: C, 70.43; H, 6.81; N, 5.51%.

Tripyrranes 21−24 were prepared from the appropriate 2,5-diunsubstituted pyrroles (**11**, **13**, **14**, **16**) and 2-(acetoxymethyl)pyrroles (**25**, **26**)[26] using the procedure described for tripyrrane **20**:

2,5-Bis[[5-(benzyloxycarbonyl)-3-[2-(methoxycarbonyl)ethyl]-4-methylpyrrol-2-yl]methyl]-3,4-diphenylpyrrole (21). Obtained as an off-white powder in 79% yield: mp 153−155 °C; ^{1}H-NMR ($CDCl_3$) δ 2.11, 2.34 (each t, J = 7.8 Hz, 4 H), 2.20 (s, 6 H), 3.52 (s, 6 H), 3.82 (s, 4 H), 4.55 (br s, 4 H), 7.08−7.29 (m, 20 H), 9.51 (br s, 1 H), 11.15 (br s, 2 H). Anal. Calcd for $C_{52}H_{51}N_3O_8$: C, 73.83; H, 6.08; N, 4.97. Found: C, 73.90; H, 6.09; N, 5.05%.

2,5-Bis[[5-(benzyloxycarbonyl)-3-[2-(methoxycarbonyl)ethyl]-4-methylpyrrol-2-yl]methyl]-3,4-dimethylpyrrole (22). Obtained as a light yellow solid in 59% yield: mp 145−146 °C; ^{1}H-NMR ($CDCl_3$) δ 2.02, 2.24 (each s, 6 H), 2.32, 2.66 (each t, J = 7.8 Hz, 4 H), 3.58 (s, 4 H), 3.62 (s, 6 H), 4.39 (br s, 4 H), 7.02 (m, 4 H), 7.26 (m, 6 H), 8.83 (br s, 1 H), 10.97 (br s, 2 H). Anal. Calcd for $C_{42}H_{47}N_3O_8$: C, 69.88; H, 6.56; N, 5.82. Found: C, 69.75; H, 6.56; N, 5.85%.

2,5-Bis[[5-(benzyloxycarbonyl)-3-[2-(methoxycarbonyl)ethyl]-4-methylpyrrol-2-yl]methyl]-3,4-butanopyrrole (23). Obtained as a white powder in 66% yield: mp 149−151 °C; ^{1}H-NMR ($CDCl_3$) δ 1.73 (s, 4 H), 2.23 (s, 6 H), 2.33, 2.67 (each t, J = 7.8 Hz, 4 H), 2.52 (s, 4 H), 3.53 (s, 4 H), 3.61 (s, 6 H), 4.46 (br s, 4 H), 7.03 (m, 4 H), 7.26 (m, 6 H), 8.78 (br s, 1 H), 10.80 (br s, 2 H). Anal. Calcd for $C_{44}H_{49}N_3O_8$: C, 70.66; H, 6.60; N, 5.62. Found: C, 70.98; H, 6.66; N, 5.65%.

2,5-Bis[[5-(benzyloxycarbonyl)-3-ethyl-4-methylpyrrol-2-yl]methyl]-3,4-butanopyrrole (24). Obtained as a light pink powder in 77% yield: mp 204.5−206 °C; ^{1}H-NMR ($CDCl_3$) δ 0.99 (t, J = 7.5 Hz, 6 H), 1.73 (s, 4 H), 2.25 (s, 6 H), 2.36 (q, J = 7.5 Hz, 6 H), 2.52 (s, 4 H), 3.48 (s, 4 H), 4.39 (br s, 4 H), 7.02 (m, 4 H), 7.24 (m, 6 H), 8.80 (br s, 1 H), 11.04 (br s, 2 H). Anal. Calcd for $C_{40}H_{45}N_3O_4$: C, 76.04; H, 7.18; N, 6.65. Found: C, 75.76; H, 6.82; N, 6.62%.

7,8-Diethyl-3,12-bis[2-(methoxycarbonyl)ethyl]-2,13-dimethyl-17,18-diphenylporphyrin (32). Tripyrrane **20** (0.33 g, 0.45 mmol) was dissolved in THF (80 mL), and 10% Pd−C (0.07 g) and a drop of NEt_3 were added. The resulting mixture was stirred under H_2 at rt for 10 h. The catalyst was removed, and the solvent was evaporated to dryness. Recrystallization from CH_2Cl_2/*n*-hexane afforded tripyrrane dicarboxylic acid **27** as a white powder in quantitative yield; because of spontaneous decarboxylation at room temperature, this was used immediately in the following way. Tripyrrane diacid **27** (0.26 g, 0.45 mmol) was dissolved in MeOH (100 mL) and heated at reflux for 15 min before pyrrole **18** (0.28 g, 0.45 mmol) and $K_3Fe(CN)_6$ (0.96 g, 2.93 mmol) were added. The resulting mixture was heated at reflux for another 6 h. The MeOH was removed and the residue was redissolved in CH_2Cl_2. Some insoluble material was filtered off and the filtrate was washed with H_2O, 5% ammonium hydroxide (2×), H_2O, and brine and dried over anhydrous Na_2SO_4. The solvent was evaporated, and the crude mixture was chromatographed on silica gel eluting with CH_2Cl_2. Recrystallization from CH_2Cl_2/cyclohexane afforded the title compound as a purple crystalline solid (52 mg, 16%): mp 195−196 °C; vis λ_{max} (CH_2Cl_2) 404 nm (ϵ 196000), 502 (14400), 538 (14300), 568 (8500), 622 (3100); ^{1}H-NMR ($CDCl_3$) δ −3.59 (br s, 2 H), 1.96 (t, J = 7.5 Hz, 6 H), 3.30, 4.46 (each t, J = 7.8 Hz, 4 H), 3.57, 3.68 (each s, 6 H), 4.10 (q, J = 7.5 Hz, 4 H), 7.69 (m, 6 H), 8.03 (m, 4 H), 10.12 (s, 2 H), 10.17 (s, 2 H). Anal. Calcd for $C_{46}H_{46}N_4O_4$: C, 76.85; H, 6.45; N, 7.79. Found: C, 76.59; H, 6.29; N, 7.86%.

Porphyrins 33−36 were prepared from the appropriate tripyrranes dibenzyl esters and pyrrole **10** using the procedure described for porphyrin **32**:

17,18-Diethyl-3,12-bis[2-(methoxycarbonyl)ethyl]-2,13-dimethyl-7,8-diphenylporphyrin (33). Obtained in 31% yield: mp 238.5−240 °C; vis λ_{max} (CH_2Cl_2) 404 nm (ϵ 190000), 502 (13200), 538 (13300), 570 (8400), 624 (2900); ^{1}H-NMR ($CDCl_3$) δ −3.65 (br s, 2 H), 1.93 (t, J = 7.5 Hz, 6 H), 3.25, 4.33 (each t, J = 7.8 Hz, 4 H), 3.64, 3.67 (each s, 6 H), 4.05 (q, J = 7.5 Hz, 4 H), 7.66−7.75 (m, 6 H), 8.08 (m, 4 H), 10.07 (s, 2 H), 10.16 (s, 2 H). Anal. Calcd for $C_{46}H_{46}N_4O_4 \cdot H_2O$: C, 74.98; H, 6.57; N, 7.60. Found: C, 75.12; H, 6.28; N, 7.65%.

17,18-Diethyl-3,12-bis[2-(methoxycarbonyl)ethyl]-2,7,8,-13-tetramethylporphyrin (34). Obtained in 17% yield: mp 170−172 °C; vis λ_{max} (CH_2Cl_2) 400 nm (ϵ 172000), 498 (12900), 532 (10100), 566 (7200), 620 (4200); ^{1}H-NMR ($CDCl_3$) δ −3.90 (br s, 2 H), 1.93 (t, J = 7.5 Hz, 6 H), 3.27, 4.36 (each t, J = 7.8 Hz, 4 H), 3.61, 3.71 (each s, total 18 H), 4.12 (q, J = 7.5 Hz, 4

H), 9.96 (s, 2 H), 10.06 (s, 2 H). Anal. Calcd for $C_{36}H_{42}N_4O_4$: C, 72.70; H, 7.12; N, 9.42. Found: C, 72.56; H, 7.19; N, 9.54%.

7,8-Butano-17,18-diethyl-3,12-bis[2-(methoxycarbonyl)ethyl]-2,13-dimethylporphyrin (35). Obtained in 25% yield: mp 221−222.5 °C; vis λ_{max} (CH_2Cl_2) 399 nm (ϵ 172000), 498 (13500), 534 (10900), 566 (6800), 620 (4500); ^{1}H-NMR ($CDCl_3$) δ −3.84 (br s, 2 H), 1.94 (t, J = 7.5 Hz, 6 H), 2.57 (s, 4 H), 3.28, 4.36 (each t, J = 7.8 Hz, 4 H), 3.62, 3.73 (each s, 6 H), 4.16 (m, 8 H), 9.93 (s, 2 H), 10.09 (s, 2 H). Anal. Calcd for $C_{38}H_{44}N_4O_4$: C, 73.52; H, 7.14; N, 9.02. Found: C, 73.17; H, 7.21; N, 9.14%.

7,8-Butano-3,12,17,18-tetraethyl-2,13-dimethylporphyrin (36). Obtained in 27% yield: mp > 300 °C; vis λ_{max} (CH_2Cl_2) 398 nm (ϵ 141000), 498 (14500), 530 (10500), 566 (6500), 618 (4900); ^{1}H-NMR ($CDCl_3$) δ −3.75 (br s, 2 H), 1.90 (m, 12 H), 2.55 (s, 4 H), 3.66 (s, 6 H), 4.12 (m, 12 H), 9.99 (s, 2 H), 10.12 (s, 2 H). Anal. Calcd for $C_{34}H_{40}N_4$: C, 80.91; H, 7.99; N, 11.10. Found: C, 80.79; H, 7.82; N, 11.11%.

Crystal Structure Determinations[27] (19). Crystals were grown from $CHCl_3$/MeOH. Crystal data for $C_{52}H_{46}N_4 \cdot CHCl_3$ at 130 K (Cu Kα radiation, λ = 1.54178 Å, $2\theta_{max}$ = 115°), monoclinic, space group $P2_1/c$, a = 13.793(4) Å, b = 19.101(7) Å, c = 17.500(5) Å, β = 108.43(2)°, V = 4374(2) Å^3, Z = 4, R = 0.0695, wR = 0.088, S = 1.68 for 4320 reflections with $F > 4.0\sigma(F)$ and 541 parameters. **35:** Crystals were grown from CH_2Cl_2/MeOH. Crystal data for $C_{38}H_{44}N_4O_4 \cdot 2CH_2Cl_2$ at 126 K (Cu Kα radiation, λ = 1.54178 Å, $2\theta_{max}$ = 112°), triclinic, space group $P-1$, a = 7.802(4) Å, b = 15.463(9) Å, c = 15.975(10) Å, α = 90.91(2)°, β = 93.00(2)°, γ = 96.42(2)°, V = 1912(2) Å^3, Z = 2, R = 0.082, wR = 0.098, S = 1.79 for 3240 reflections with $F > 4.0\sigma$(F) and 478 parameters.

(27) The authors have deposited atomic coordinates and a full structure description for **19** and **35** with the Cambridge Crystallographic Data Centre. The structures can be obtained, upon request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

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Supporting Information Available: ^{1}H NMR spectra (300 MHz, $CDCl_3$) of compounds **10**, **12**, and **17** (3 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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