Concerning the Synthesis of 3,7,13,17-Tetramethyl-5,15-diphenylporphyrin, a Sterically Hindered Porphyrin

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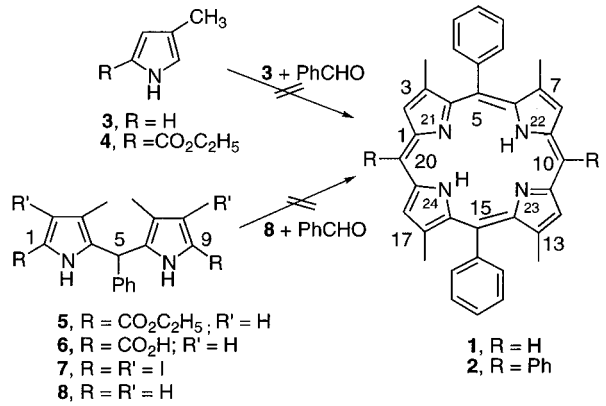
The synthesis of the sterically hindered porphyrin **1** (3,7,13,17-tetramethyl-5,15-diphenylporphyrin) could only be achieved by first preparing a 5,15-meso substituted octaalkylporphyrin. Thus, the synthesis of a 2,8,12,18-tetrakis(2-hydroxyethyl)-3,7,13,17-tetramethyl-5,15-diphenylporphyrin (**12**) had to precede the synthesis of **1**. The 2-hydroxyethyl side chains were then converted into vinyl residues via the corresponding 2-chloroethyl intermediates. The four vinyl residues (at C2, C8, C12, C18) were cleaved using a resorcinol melt, and the tetra β-unsubstituted porphyrin **1** was then obtained. Porphyrin **1** could not be prepared by direct condensation of benzaldehyde with 3-methylpyrrole nor with a meso-phenyl β-unsubstituted dipyrrylmethane.

Free-base porphyrins have two inner hydrogens that can migrate between four central nitrogens, giving rise to two possible tautomers and therefore to a hydrogen-migration process that has been extensively studied by means of solution[1−3] and solid state[4−8] NMR. Since this reaction can also be activated by photochemical means,[9] N−H tautomerism has been proposed as a possible mechanism for performing data storage in the frequency domain by means of photochemical hole burning.[10,11] Solution ^{1}H NMR studies revealed that the free energies involved in the N−H tautomerism of porphyrins are affected by the presence of substituents in the β-positions of the pyrrole rings.[12,13] Similar effects on the hydrogen migration process were observed when electron-donor or electron-acceptor groups were employed. The observed changes were assumed to reflect the effects that are introduced by bulky substituents in the geometry of the macrocycle; a fact that if further confirmed could help to explain (and therefore to control) the N−H tautomerization process. It was known that meso-substituents introduce steric hindrances in the porphyrin ring by

Scheme 1



interaction with the β-substituents,[14,15] which are relieved by forcing a distortion of the planar macrocycle.[16−21] It can therefore be expected that steric crowding will affect the central cavity of the porphyrin ring. The cavity is usually a square with side lengths of 2.89 Å. Steric crowding will result in the formation of a rectangle where the shorter N21−N22 and N23−N24 axes (Scheme 1) will favor the dynamics of hydrogen migration along these axes. To probe into the latter, the sterically crowded porphyrin should also carry free β-pyrrole hydrogens to help in the analysis of the N−H tautomerism process.[1−8]

Porphyrin **1** (Scheme 1) seems to fulfill the above-mentioned requisites. The interaction between the *meso*-phenyl residues and the methyl groups at the 3, 7, 13, and 17 positions will shorten the distance between N21

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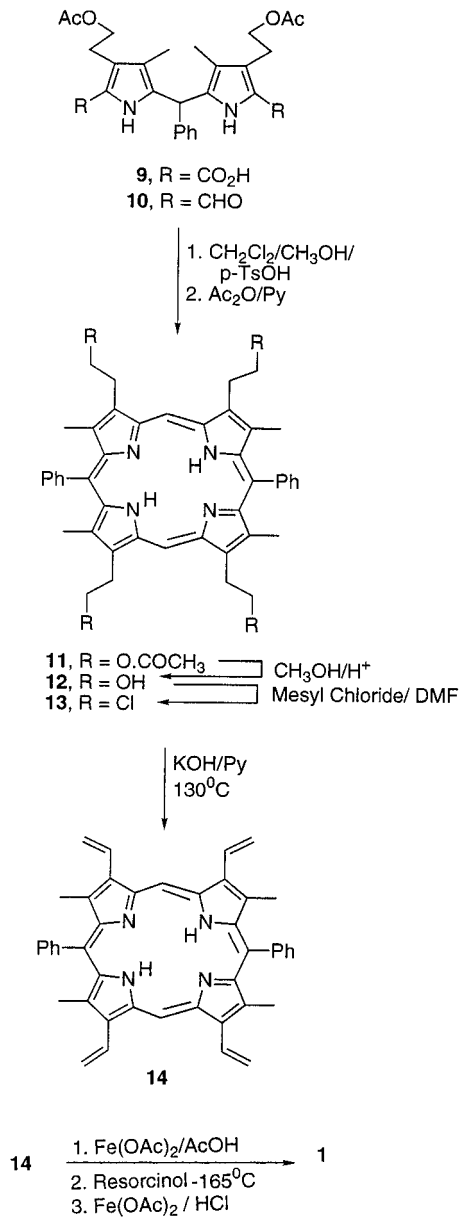
and N22 and between N23 and N24 (as is the case of porphycene and its alkyl derivatives[22,23]) while H2, H8, H12, and H18 will be available to study the tautomerism rates among the central protons. Surprisingly, the synthesis of **1** posed major challenges which were solved as reported below. Bringing 3-methyl pyrrole **3** into reaction with benzaldehyde by means of known procedures[24−27] led to mixtures of porphyrins that showed (by ^{1}H NMR analysis) different patterns of meso-substitution.

Although the synthesis of porphyrin **2** has been reported[28] as arising from the reaction of **3** with benzaldehyde (Scheme 1), we could not duplicate the procedure.[29] To carry out the synthesis of **1** under more restricted conditions we prepared the hitherto unknown *meso*-phenyl dipyrrylmethane **8**. Reaction of **4** with benzaldehyde gave dipyrrylmethane **5**. It was saponified to **6**, the latter was decarboxylated by treatment with iodine in basic medium, and the resulting tetraiodide **7** was dehalogenated to **8** by hydrogenolysis in the presence of sodium acetate. Reaction of **8** with benzaldehyde following established procedures[24−27] gave a mixture of porphyrins with random meso-substitutions. It was therefore concluded that **1** can only be obtained if the free β-pyrrole positions in the reacting dipyrrylmethanes are "protected" by substituents that could be removed after the porphyrin ring was formed. The most simple choice appeared to be the use of β-vinyl residues which can be removed from a porphyrin by established procedures.[30,31]

Scheme 2 outlines the synthetic approach used. By condensation of the meso-substituted dipyrrylmethanes **9** and **10** using procedures established for meso-unsubstituted porphyrins,[32] followed by a reacetylation step of the partially deacetylated reaction product, it was possible to obtain porphyrin **11** in fair yields. Removal of the acetate ester groups by transesterification with 5% sulfuric acid in methanol gave **12**. Treatment of the tetra β-hydroxyethyl porphyrin **12** with mesyl chloride in dimethylformamide gave the tetra β-chloroethyl porphyrin **13**, which was transformed into the tetravinyl porphyrin **14** by dehalogenation with potassium hydroxide in pyridine. Cleavage of the vinyl residues using the resorcinol melt of iron−porphyrin **14**, followed by demetalation[33] gave **1** as a pure and simple porphyrin.

The synthetic approach to **9** and **10** is outlined in Scheme 3. The known trichloromethyl pyrrole **15** was converted into the triester **16** by treatment with methanol and sodium acetate. The latter was converted into the acid **17** by hydrogenolysis of the benzyl ester, the acid **17** was decarboxylated by treatment with iodine-iodide in a sodium bicarbonate solution, and the resulting iodide **18** was reduced with hydrogen to the β-free pyrrole **19**. Condensation of **19** with benzaldehyde in acid medium gave the meso-substituted dipyrrylmethane **20** as the sole reaction product. Reduction of the acetate side chains with diborane yielded **21**, as was the case with analogous pyrrylmethanes that were not substituted at the meso-bridge.[34,35] Saponification of the nuclear esters of **21** gave the diacid **22**, which could be decarboxylated with simultaneous formylation to **23** when reacted with trimethyl orthoformate in trifluoroacetic acid. Both **22** and **23** were esterified to **9** and **10** (Scheme 2) using acetic anhydride in pyridine.

Scheme 2



In conclusion, the synthesis of a 5,15-meso-substituted porphyrin β-substituted only at C3, C7, C13, and C17

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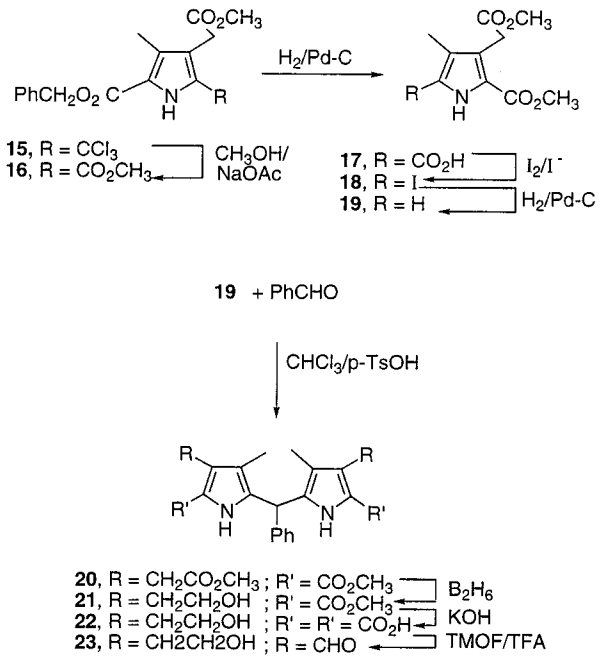
Scheme 3



could only be achieved by first preparing a β-octasubstituted porphyrin. The more direct approach, using meso-substituted dipyrrylmethanes with β-free positions led to a mixture of porphyrins. Porphyrin **1** was very insoluble in the usual solvents, therefore the ^{1}H NMR spectrum of its dication was recorded. The spectrum showed an upfield shift of the methyl groups flanking the phenyl meso-substituents, as expected from the steric repulsions among the substituents. Steric repulsions between meso- and β-substituents cause distortions in the planarity of the macrocycle, which result in a general decrease in the ring current and a nonuniform perturbation of the chemical shifts throughout the molecule.[36,37] The dynamics of the tautomerism of the nitrogen bound protons of **1** will be discussed elsewhere.

Experimental Section

General. NMR spectra were obtained using a Bruker MSL 300 spectrometer. Reactions were monitored using TLC on silica gel plates (0.25 mm thick, with the fluorescent dye F-254, Merck Darmstadt). Flash chromatography was performed on silica gel columns packed with TLC−Kieselgel (Merck or Riedel de Hann). Pyrroles and dipyrrylmethanes were spotted on TLC using a 2% *p*-dimethylaminobenzaldehyde solution in 6 N hydrochloric acid. Melting points were determined on a Köfler block.

Benzyl 3-Methyl-4-methoxycarbonylmethyl-5-methoxycarbonyl-2-pyrrolecarboxylate (16). A mixture of the trichloromethylpyrrole **15**[38] (20 g) and 10 g of anhydrous sodium acetate was dissolved in 350 mL of dry methyl alcohol and the solution was stirred at 50 °C for 72 h. It was then poured over ice water, the precipitate was collected and crystallized from methanol; 15 g (70%) of **16** was obtained; mp 90−91 °C; ^{1}H NMR ($CDCl_3$) δ 9.60 (b, 1H), 7.35 (s, 5H), 5.35 (s, 2H), 3.85 (s, 3H), 3.80 (s, 3H), 3.70 (s, 2H), 2.30 (s, 3H). Anal. Calcd for $C_{18}H_{19}NO_6$: C, 62.60; H, 5.50; N, 4.05. Found: C, 62.63; H, 5.59; N, 14.15

Methyl 3-Methoxycarbonylmethyl-4-methyl-5-carboxy-2-pyrrolecarboxylate (17). A solution of 13 g of pyrrole **16** in 300 mL of ethanol was reduced with hydrogen at 50 psi over 2 g of 10% Pd on charcoal during 2 h. The catalyst was filtered, the solvent was evaporated to dryness in vacuo, and the resulting acid crystallized from ethanol−water: 8.7 g (68%); mp >200 °C (dec). Anal. Calcd for $C_{11}H_{11}NO_6$: C, 52.17; H, 4.35; N, 5.53. Found: C, 52.07; H, 4.39; N, 5.71.

Methyl 3-Methoxycarbonylmethyl-4-methyl-5-iodo-2-pyrrolecarboxylate (18). Carboxypyrrole **17** (10 g, 40 mmol) was dissolved in a solution of 20 g (200 mmol) of $NaHCO_3$ in 200 mL of water, the mixture was heated to 65 °C, and a solution of 10 g (80 mmol) of iodine and 20 g of potassium iodide in ethanol−water was slowly added with stirring. After a further heating for 1 h, the suspension was filtered and crystallized from ethanol−water; 11.6 g (97%) of **18** were obtained: mp 127−128 °C; ^{1}H NMR ($CDCl_3$) δ 9.40 (s, 1H), 3.85 (s, 3H), 3.80 (s, 3H), 3.73 (s, 2H), 2.00 (s, 3H). Anal. Calcd for $C_{10}H_{12}NO_4I$: C, 35.60; H, 3.56; N, 4.15. Found: C, 35.49; H, 3.60; N, 4.20.

Methyl 3-(Methoxycarbonylmethyl)-4-methyl-2-pyrrolecarboxylate (19). Iodopyrrole **18** (10 g) dissolved in 200 mL of methanol was reduced with hydrogen over 1 g of 10% Pd−C in the presence of 2.5 g of sodium acetate. After 2 h at 50 psi, the catalyst was filtered-off, the solution was evaporated to dryness in vacuo, the residue was partitioned between chloroform−water, and the chloroform layer was separated and evaporated to dryness. The residue was crystallized from benzene−hexane; 5.5 g (74%) of **19** was obtained; mp 81 °C; ^{1}H NMR ($CDCl_3$) δ 9.20 (s, 1H), 6.65 (d, 1H), 3.85 (s, 2H), 3.80 (s, 3H), 3.70 (s, 3H), 2.00 (s, 3H). Anal. Calcd for $C_{10}H_{13}NO_4$: C, 56.87; H, 6.16; N, 6.63. Found: C, 57.00; H, 6.27; N, 6.71.

Dimethyl 2,8-Bis(methoxycarbonylmethyl)-3,7-dimethyl-5-phenyl-1,9-dipyrrylmethanedicarboxylate (20). Benzaldehyde (5.3 g, 50 mmol) was added to a solution of 4.2 g (20 mmol) of **19** in 100 mL of chloroform, 0.7 g of *p*-toluensulfonic acid was added, and the mixture was heated under reflux for 2 h. The solution was then cooled, washed with a $NaCO_3H$ solution and then with water, dried (Na_2SO_4), and evaporated to dryness. The residue was purified by flash chromatography on a silica gel column using chloroform as an eluant followed by 3% methanol in chloroform to elute the dipyrrylmethane. The latter was recovered from the eluates by evaporation in vacuo and was crystallized from methanol−water: 8.1 g (80%); mp 137−138 °C; ^{1}H NMR ($CDCl_3$) δ 8.52 (b, 2H), 7.36 (m, 3H), 7.14 (m, 2H), 5.55 (s, 1H), 3.85 (s, 4H), 3.78 (s, 6H), 3.70 (s, 6H), 1.80 (s, 6H). Anal. Calcd for $C_{27}H_{30}N_2O_8$: C, 63.53; H, 5.88; N, 5.49. Found: C, 63.50; H, 5.92; N, 5.53.

Dimethyl 2,8-Bis(2-hydroxyethyl)-3,7-dimethyl-5-phenyl-1,9-dipyrrylmethanedicarboxylate (21). Dipyrrylmethane **20** (5 g) was dissolved in 250 mL of dry tetrahydrofuran and a stream of diborane was slowly bubbled through the solution using nitrogen gas as a carrier during 2 h. The solution was kept in the closed vessel for a further 24 h at 25 °C, it was then cooled to 5 °C, excess methanol was added to decompose the borates, and the mixture was evaporated to dryness. The solid residue was partitioned between chloroform and water, the organic layer was repeatedly washed with water, dried (Na_2SO_4), and evaporated to dryness, and the residue was purified by flash chromatography on silica gel using chloroform as an eluant. The product recovered after evaporation of the eluates was crystallized from methanol−water; 3.0 g (66%) of **21** was obtained: mp 161−162 °C; ^{1}H NMR ($CDCl_3$) δ 8.87 (b, 2H), 7.30 (m, 3H), 7.10 (m, 2H), 5.55 (d, 1H), 3.51 (s, 2H), 3.48 (s, 6H), 3.03 (t, 4H), 2.40 (b, 2H), 1.90 (s, 6H). Anal. Calcd for $C_{25}H_{30}N_2O_6$: C, 66.08; H, 6.61; N, 6.17. Found: C, 66.19; H, 6.72; N, 6.25.

2,8-Bis(methoxycarbonylmethyl)-3,7-dimethyl-5-phenyl-1,9-dicarboxydipyrrylmethane (22). Dipyrrylmethane **21** (3 g) was dissolved in 20 mL of ethanol, 20 mL of a 10% KOH solution in water was added, and the mixture was heated to dryness with stirring at 110 °C in an open vessel. The residue was dissolved in water, the solution adjusted to pH 5 with concentrated HCl, and the precipitate was filtered,

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washed with water and dried: 2.1 g (74%); ^{1}H NMR (Py-d_6-D_2O) δ 7.10 (s, 2H), 6.30 (m, 5H), 5.10 (d, 1H), 3.60 (s, 4H), 3.10 (t, 4H), 1.90 (s, 6H); EI-MS, *m*/*z* 426 (M^+).

2,8-Bis(2-hydroxyethyl)-3,7-dimethyl-5-phenyl-1,9-diformyldipyrrylmethane (23). Dipyrrylmethane **22** (1.7 g, 4 mmol) was dissolved in 25 mL of trifluoroacetic acid, the solution was cooled to 0−5 °C under a stream of nitrogen, and trimethylorthoformate (4.2 g, 40 mmol) was added after 10 min. The mixture was kept for additional 15 min, ice water was then added followed by concentrated ammonium hydroxide to adjust to pH 7, the oily layer that separated was dissolved in chloroform, and the latter was separated, washed with $NaHCO_3$ and then with water, dried (Na_2SO_4), and evaporated to dryness in vacuo. The residue was purified by flash chromatography on a silica gel column using 6% methanol in chloroform as an eluant. Evaporation of the eluates left behind an oily residue: 800 mg (51%); ^{1}H NMR ($CDCl_3$) δ 9.84 (b, 2H), 9.18 (s, 2H), 6.88 (b, 5H), 5.42 (d, 1H), 3.78 (s, 4H), 2.85 (t, 4H), 1.80 (s, 6H); EI-MS, *m*/*z* 396 (M^+), 367 (M^+ − CHO), 338 (M^+ − 58, 2CHO).

2,8-Bis(2-acetoxyethyl)-3,7-dimethyl-5-phenyl-1,19-diformyldipyrrylmethane (10). Diformyldipyrrylmethane **23** (800 mg) was dissolved in 60 mL of dry pyridine, and acetic anhydride (12 mL) was added at 25 °C. After 2 h the solvent was evaporated to dryness in vacuo, and the residue was purified by flash chromatography on silica gel using 3% methanol in chloroform. The diacetate **10** was recovered from the eluate as an oil that crystallized from chloroform−heptane: 640 mg (66%); mp 140−141 °C; ^{1}H NMR ($CDCl_3$) δ 9.75 (b, 2H), 9.55 (s, 2H), 7.35 (m, 3H), 7.05 (m, 2H), 5.55 (d, 1H), 4.10 (t, 4H), 2.90 (t, 4H), 1.95 (s, 6H), 1.83 (s, 6H). Anal. Calcd for $C_{27}H_{30}N_2O_6$: C, 67.78; H, 6.27; N, 5.86. Found: C, 67.81; H, 6.30; N, 5.82.

2,8-Bis(2-acetoxyethyl)-3,7-dimethyl-5-phenyl-1,19-dicarboxydipyrrylmethane 9 was obtained from **22** (600 mg) following the procedure described for the preparation of **10**; 450 mg (62%) of **9** was obtained as an oil: ^{1}H NMR ($CDCl_3$) δ 10.85 (b, 2H), 9.85 (b, 2H) 7.25 (m, 3H), 7.00 (m, 2H), 5.50 (d, 1H), 4.10 (t, 4H), 2.95 (t, 4H), 1.95 (b, 6H), 1.85 (s, 6H); EI-MS *m*/*z* 510 (M^+), 420 (M^+ − $2CO_2H$).

2,8,12,18-Tetrakis(2-acetoxyethyl)-3,7,13,17-tetramethyl-5,15-diphenylporphyrin (11). A mixture of 300 mg (0.3 mmol) of **10** and 300 mg (0.31 mmol) of **9** was dissolved in 250 mL of dry methylene chloride and 25 mL of dry methanol, 700 mg (5 mmol) of *p*-toluensulfonic acid was added, and the solution was kept in the dark for 72 h at 25 °C. The solution was first washed with water (100 mL), with a 5% solution of $NaHCO_3$ (100 mL), and then with water again (100 mL), dried (Na_2SO_4), and evaporated to dryness. The porphyrin residue was redissolved in 12 mL of dry pyridine and 3 mL of acetic anhydride, the mixture was kept for 2 h in the dark and then evaporated to dryness, and the residue was purified by flash chromatography on silica gel using 1% methanol in chloroform as eluant. Pure porphyrin tetracetate (160 mg, 26%) was thus obtained: mp 245−247 °C (methylene chloride−hexane); ^{1}H NMR ($CDCl_3$) δ 10.38 (s, 2H) 8.06 (d, 4H), 7.77 (q, 6H), 4.80 (t, 8H), 4.40 (t, 8H), 2.54 (s, 12H), 2.04 (s, 12), −2.32 (b, 2H). Anal. Calcd for $C_{52}H_{54}N_4O_8$: C, 72.39; H, 6.26; N, 6.49. Found: C, 72.30; H, 6.23; N, 6.46.

2,8,12,18-Tetrakis(2-hydroxyethyl)-3,7,13,17-tetramethyl-5,15-diphenylporphyrin (12). Tetracetoxyporphyrin **11** (120 mg) was dissolved in 20 mL of 5% sulfuric acid in dry methanol, the mixture was kept during 24 h in the dark at 25 °C and then diluted with water, and the porphyrin was extracted into chloroform (100 mL plus 1 mL of triethylamine). The latter was evaporated to dryness and left behind 87 mg (90%) of porphyrin **12** which could not be purified further due to its insolubility: ^{1}H NMR ($CDCl_3$−TFA) δ 10.43 (b, 2H), 8.22 7.87 (qd, 10H), 4.70 (t, 8H), 4.05 (t, 8H), 2.14 (s, 12H), −1.81 (b, 4H); EI-MS, *m*/*z* 695 (M^+ + 1).

2,8,12,18-Tetrakis(2-chloroethyl)-3,7,13,17-tetramethyl-5,15-diphenylporphyrin (13). Tetrahydroxyethylporphyrin **12** (87 mg, 0.125 mmol) was dissolved in 9 mL of dry dimethylformamide, mesyl chloride (1.1 mL, 6.6 mmol) was added, and the mixture was heated at 75 °C during 18 h. It was then cooled and diluted with 50 mL of water, a drop of triethylamine was added, and the solution was extracted with methylene chloride (3 × 30 mL). The pooled extracts were dried (Na_2SO_4) and evaporated to dryness, and the residue was dissolved in chloroform and purified by flash chromatography on silica gel using the same solvent as eluant; 48 mg (52%) of porphyrin **13** was obtained: mp dec above 300 °C (chloroform−heptane); ^{1}H NMR ($CDCl_3$-TFA) α 10.17 (s, 2H), 8.04 (d, 4H), 7.75 (m, 6H), 4.46 (t, 8H), 4.22 (t, 8H), 2.52 (s, 12H), −2.34 (b, 4H); FAB-MS (4-nitrobenzyl alcohol used as matrix) 769 (M^+ + 1). Anal. Calcd for $C_{44}H_{42}Cl_4N_4$: C, 68.75; H, 5.47, N, 7.29. Found: C, 68.66; H, 5.52; N, 7.31.

2,8,12,18-Tetravinyl-3,7,13,17-tetramethyl-5,15-diphenylporphyrin (14). Tetrachloroethylporphyrin **13** (48 mg) was dissolved in 10 mL of dry pyridine heated under reflux, 3 mL of a 3% aqueous KOH was added, and the mixture was heated under reflux for 3 h. It was then evaporated to dryness in vacuo, the residue was dissolved in chloroform, the latter was washed with water, dried (Na_2SO_4), and evaporated to dryness, and the residue was purified by flash chromatography on silica gel using chloroform as eluant; 28 mg (72%) of **14** was obtained: mp dec above 300 °C (chloroform−heptane); ^{1}H NMR ($CDCl_3$-CF_3CO_2H) δ 10.11 (s, 2H) 8.34 (m, 4H), 7.87 (m, 6H), 7.70 (dd, J_{trans} = 17.6 Hz, J_{cis} = 12.9 Hz, 4H), 6.25 (d, J_{cis} = 12.9 Hz, 4H), 5.82 (d, J_{trans} = 17.6 Hz), 2.28 (s, 12H), −1.42 (b, 4H); EI-MS, *m*/*z* 623 (M^+ + 1), 311 (M^{2+}). Anal. Calcd for $C_{44}H_{38}N_4$: C, 84.89; H, 6.11; N, 9.00. Found: C, 84.86; N, 6.09; N, 8.96.

3,7,13,17-Tetramethyl-5,15-diphenylporphyrin (1). Tetravinylporphyrin **14** (62.2 mg, 0.1 mmol) was dissolved in 10 mL of boiling glacial acetic acid, and a saturated ferrous acetate solution in acetic acid was then added (4 × 0.25 mL). The mixture was heated under reflux under nitrogen for 5 min and then cooled and diluted with 40 mL of chloroform. The solution was washed with 25% HCl (2 × 10 mL) and then with brine, dried (Na_2SO_4), and evaporated to dryness, and the residue was purified by flash chromatography on silica gel using 1% methanol−chloroform to elute nonreacted **14** followed by 2% methanol−chloroform to elute the iron−porphyrin. The latter was mixed with 190 mg of resorcinol, and the mixture was heated at 180 °C for 30 min under oxygen-free nitrogen. The fused mass was dissolved in 5 mL of boiling glacial acetic acid, 0.5 mL of a saturated ferrous acetate solution of glacial acetic acid was added, the reflux continued for further 5 min, 0.1 mL of concentrated HCl was then added, and the solution was allowed to cool to 25 °C. Chloroform (20 mL) was added, the mixture was washed with a 7% $NaHCO_3$ solution and then with water, dried (Na_2SO_4), and evaporated to dryness, and the residue was purified by flash chromatography on silica gel using 5% hexane in chloroform as eluant; 6.2 mg (27%) of **1** was obtained after crystallization from methylene chloride−methanol: mp dec above 300 °C; ^{1}H NMR ($CDCl_3$-TFA) δ 10.37 (s, 2H), 8.90 (s, 4H), 8.26 (d, 4H), 7.95 (m, 6H), 2.45 (s, 12H), −2.05 (b, 4H). EI-MS *m*/*z* 519 (M^+ + 1), 518 (M^+). Anal. Calcd for $C_{36}H_{30}N_4$: C, 83.40; H, 5.79; N, 9.00. Found: C, 83.37; H, 5.74; N, 8.97.

Diethyl 3,7-Dimethyl-5-phenyl-1,9-dipyrrylmethanedicarboxylate (5). Ethyl 3-methyl-2-pyrrole carboxylate **4** (7.65 g, 50 mmol)[39] was dissolved in 150 mL of dry ethanol, benzaldehyde (4 g, 38 mmol) and *p*-toluensulfonic acid (160 mg, 0.9 mmol) were added, and the mixture was heated under reflux during 2 h. The mixture was then poured over ice water, the dipyrrylmethane was extracted into chloroform, the latter was washed with water, dried (Na_2SO_4), evaporated to dryness, and the residue crystallized from ethanol: 7.0 g (76%); mp 104−106 °C; ^{1}H NMR ($CDCl_3$) δ 8.95 (b, 2H), 7.30 (m, 3H), 7.10 (m, 2H), 6.70 (b, 2H), 5.55 (b, 1H), 4.15 (q, 6H), 1.90 (s, 6H), 1.20 (t, 6H). Anal. Calcd for $C_{23}H_{26}N_2O_4$: C, 70.05; H, 6.60; N, 7.11. Found: C, 70.09; H, 6.58; N, 7.15.

3,3′-Dimethyl-5-phenyl-1,2,8,9-tetraiododipyrrylmethane (7). Dipyrrylmethane **5** (7 g) was dissolved in 50

(39) Alonso Garrido, D. O.; Buldain, G.; Ojea, M. I.; Frydman, B. *J. Org. Chem.* **1988**, *53*, 403.

mL of ethanol and 50 mL of 10% NaOH and heated in an open vessel at 110 °C until dry. The residue was dissolved in water and the diacid **6** was precipitated by adjusting the solution to pH 3 with concentrated HCl. The precipitate was filtered, dried, and dissolved in a solution of 10 g of $NaHCO_3$ in 200 mL of water. The mixture was cooled to 5 °C and a solution of 16 g of iodine in 150 mL of ethanol was added dropwise with constant stirring. After the addition was completed, the mixture was kept at 25 °C for 30 min, 200 mL of water was then added, and the precipitate was filtered, dried, and crystallized from ethanol−water: 11.8 g (76%); mp 98−99 °C; ^{1}H NMR ($CDCl_3$) δ 7.70 (b, 2H), 7.30 (m, 3H), 7.05 (m, 2H), 5.50 (s, 1H), 1.85 (s, 6H). Anal. Calcd for $C_{17}H_{14}I_4N_2$: C, 27.05; H, 1.86; N, 3.71. Found: C, 27.10; H, 1.95; N, 3.76.

3,3′-Dimethyl-5-phenyldipyrrylmethane (8). Tetraiododipyrrylmethane **7** (5.0 g) dissolved in 250 mL of methanol was reduced with hydrogen at 40 psi over 2 g of 10% Pd−charcoal in the presence of 17 g of anhydrous sodium acetate. After 2 h the catalyst was filtered-off, the solution was evaporated to dryness in vacuo, the residue was partitioned between chloroform and water, the chloroform layer was evaporated to dryness, and the residual oil was purified by flash chromatography on silica gel using dichloromethane as eluant; 1.4 g (86%) of **8** was obtained as an oil: ^{1}H NMR ($CDCl_3$) δ.50 (b, 2H), 7.30 (m, 3H), 7.05 (m, 2H), 6.55 (t, 2H), 6.05 (t, 2H), 5.50 (s, 1H), 1.90 (s, 3H). EI-MS *m*/*z* 250 (M^+), 169 (M^+ − 3-methylpyrrole), 81 (3-methylpyrrole).

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