was heated at reflux for 16 h. Elimination of the solvent and excess of the amine in vacuo yielded a crude product which appeared to be an equimolar mixture of **13** and *N*-nitrosodiethylamine.

Reaction of 13b with Ammonia and Diethylamine. (From 1.766 g of **13**, 6 mL of concentrated HNO_3, and 20 mL of Ac_2O left overnight—method A—2.01 g (92%) of **13b** were obtained after purification by column chromatography with CH_2Cl_2 as the eluent.) *N*-Nitrosulfonamide **13b** (345 mg), 4 mL of 7 M methanolic ammonia, and ca. 50 mL of CH_2Cl_2 were mixed together and stirred at room temperature for 5 days. Evaporation of the solvent and column chromatography with CH_2Cl_2–MeOH 95:5 afforded 174 mg (68%) of *p*-toluenesulfonamide and 42 mg (14%) of **13**.

Treatment of 120 mg (0.52 mmol) of **13b** with 0.1 mL (1 mmol) of Et_2NH in 30 mL of refluxing CH_2Cl_2 for 3 days yielded *N,N*-diethyl-*p*-toluenesulfonamide as the only sulfomamide obtained (as indicated by TLC). Washing the final solution with diluted aqueous HCl and evaporation of the solvent gave 108 mg of that compound (88% yield).

Acknowledgment. We are indebted to the INAPE, Ministerio de Educación y Ciencia, Spain, for a fellowship (1979–1982) to the first author, and to Elisenda Pairó for her help in the preparation of some nitroamides.

Registry No. 1, 613-93-4; **1a**, 63412-06-6; **1b**, 59476-39-0; **2**, 6212-93-7; **2a**, 19211-35-9; **2b**, 91083-84-0; **3**, 42474-15-7; **3a**, 91083-85-1; **4**, 7438-09-7; **4a**, 16514-82-2; **5**, 91084-04-7; **5a**, 91083-86-2; **6**, 1119-49-9; **6a**, 14300-06-2; **7**, 105-60-2; **7a**, 35784-01-1; **7b**, 91083-87-3; **8**, 947-04-6; **8a**, 91083-88-4; **8b**, 91083-89-5; **9**, 1205-08-9; **9a**, 91083-90-8; **9b**, 91083-91-9; **10**, 51514-00-2; **10b**, 91083-92-0; **10c**, 91083-93-1; **11**, 1492-11-1; **11a**, 91083-94-2; **11b**, 91083-95-3; **12**, 91084-05-8; **12b**, 91083-96-4; **13**, 640-61-9; **13a**, 80-11-5; **13b**, 23114-01-4; $PhCONH_2$, 55-21-0; n-$C_8H_{17}CONH_2$, 1120-07-6; n-$C_{13}H_{27}CONH_2$, 638-58-4; $PhCONEt_2$, 1696-17-9; n-$C_8H_{17}CONMe_2$, 6225-08-7; n-$C_8H_{17}CONCH_2CH_2CH_2CH_2$, 20308-70-7; n-$C_{13}H_{27}CON(CH_2$(6-methylpyridin-2-yl))Me, 91083-97-5; n-$C_{13}H_{27}CONCH_2CH_2CH_2CH_2$, 70974-47-9; AcNMe($c$-$C_6H_{11}$), 41273-78-3; NH_3, 7664-41-7; PhCONHBu-*n*, 2782-40-3; $PhCONCH_2CH_2CH_2CH_2$, 3389-54-6; PhCONHPh, 93-98-1; $NO_2NH(CH_2)_5CONH_2$, 91083-98-6; $NO_2NH(CH_2)_5CONHMe$, 91083-99-7; $NO_2NH(CH_2)_5CONHPh$, 91084-00-3; n-$C_{13}H_{27}CONCH_2CH_2OCH_2CH_2$, 5338-53-4; diethylamine, 109-89-7; dimethylamine, 124-40-3; pyrrolidine, 123-75-1; morpholine, 110-91-8; 2-Me-6-(*N*-methylaminomethyl)pyridine, 6971-57-9; *N*-methylcyclohexylamine, 100-60-7; aniline, 62-53-3; methylamine, 74-89-5; methyl *N*-nitroglycinate, 74386-85-9; *N,N*-tetramethylene-2-(nitroamino)acetamide, 91084-01-4; *N*-acetylpyrrolidine, 4030-18-6; methyl 4-methyl-2-(nitroamino)-pentanoate, 91084-02-5; *N*-(ethoxycarbonyl)pyrrolidine, 5470-26-8; methyl *N,p*-dinitrophenylalaninate, 91084-03-6; butylamine, 109-73-9; cyclododecanone oxime, 946-89-4; methyl glycinate, 616-34-2; methyl leucinate, 2666-93-5; methyl phenylalaninate, 2577-90-4; *N,N*-tetramethylene-12-(nitroamino)dodecanamide, 91084-06-9.

Supplementary Material Available: Spectroscopic data (^1H NMR, ^{13}C NMR, IR) for compounds 1–6, 8–12 and *N*-methyl-*N*-[(6′-methylpyrid-2-yl)methyl]myristamide (1 page). Ordering information is given on any current masthead page.

Magnetic Circular Dichroism Studies. 66.[1] Synthesis of Demethyl Monosubstituted Porphyrins. The Effect of Substituent Conformation on the Magnetic Circular Dichroism Spectra of Ethoxycarbonyl Porphyrins

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The synthesis of a series of demethyl monosubstituted (acetyl, vinyl, formyl, cyano, and ethoxycarbonyl) free-base porphyrins (**6b–f**) is described. The key intermediates, 5-formyl-5′-methyldipyrrylmethanes **16a** and **26**, used in this synthesis are prepared in high yields by an improved procedure which entails decarboxylation of the 5-carboxy-5′-methyldipyrrylmethanes **15a** and **25** in trifluoroacetic acid and subsequent formylation of the decarboxylated dipyrrylmethane with a mixture of dimethylformamide and *p*-nitrobenzoyl chloride. The preparation of the demethylformylporphyrin **6d** from the demethylvinylporphyrin **6c** was successfully accomplished by the use of thallium(III) as a "protecting group" for the macrocycle. This series of monosubstituted porphyrins allows, for the first time, the assessment of the electronic and optical consequences of substituent effects on the porphyrin macrocycle on the same sterically unconstrained basis as now exists for a wide variety of other cyclic π-electron systems. This is illustrated by comparing the MCD spectra of the methyl and demethyl ethoxycarbonyl free-base porphyrins. The observed sign variations of the MCD bands for these two porphyrins are explained with the perimeter model approach previously elaborated for substituted porphyrins.

Introduction

Derivatives of the cyclic tetrapyrrolic compound porphine (**1**) are widely distributed in nature and play important roles in biological processes. For example, the iron complexes of porphyrins like iron protoporphyrin IX (**2**) serve in the hemoglobin and myoglobin[2a] of mammals in the transport and storage of dioxygen, in the transfer of electrons as exemplified by cytochrome c,[2b] and in the biological hydroxylation of a variety of substrates as typified by cytochrome P-450.[2c] Parallel in biological significance to the porphyrins are the chlorins and bacteriochlorins, the most important of which in the form of their magnesium derivatives are represented by chlorophyll *a* and *b* (**3**) and bacteriochlorophyll. These reduced porphyrins are involved in photosynthesis in green plants[3a] and bacteria,[3b] respectively. Chlorins which are not in-

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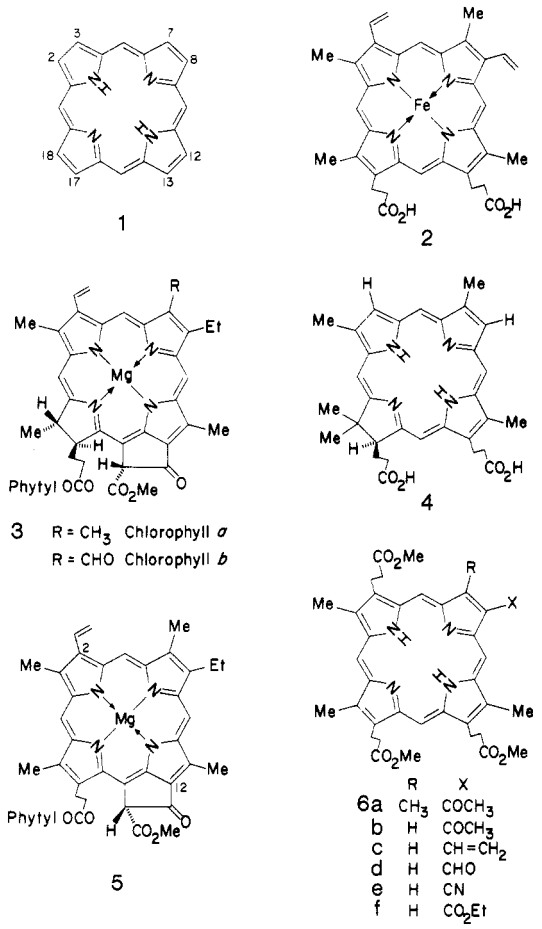
0022-3263/84/1949-3327$01.50/0

Chart I



volved in photosynthesis have also been isolated and identified. For instance, bonellin (**4**), which is not complexed with a metal ion, is a physiologically active pigment of the marine echurian worm *Bonellia viridis*[4] and heme d_1, an iron chlorin,[5] has been shown to be part of the electron-transfer system of *Pseudomonas* cytochrome oxidase.[6]

Apart from their biological significance, the porphyrins and reduced porphyrins have attracted the interest of both experimental[7] and theoretical[8] chemists to their magnetic optical activity[7f] as measured by the technique of magnetic circular dichroism (MCD). The MCD of porphyrins and heme proteins, in particular, has been extensively studied and these developments have recently been reviewed.[9] Notwithstanding, however, the large amount of effort devoted to the MCD of porphyrins, relatively few systematic studies of the relation between the sign variation of the MCD bands of porphyrin derivatives and the nature of the peripheral substituents on the macrocycle have been made. In the first report[10] on the MCD of chlorins it was noted that the signs of the MCD bands associated with the electronic visible and Soret transitions were inverted (i.e., in the sign pattern +−+− with increasing energy) as compared to the normal sign pattern (i.e., −+−+) for alkylporphyrins. Subsequent studies[7a,8a,b] have shown that although the observed sign inversions can be attributed to the effect of the chlorin chromophore, the actual occurrence of sign inversion is also modulated by the central and peripheral substituents.

Substituent-induced MCD band sign inversion for porphyrins was first observed[11] for protochlorophyll *a* (**5**), which has a vinyl and a carbonyl substituent at C-2 and C-12 of the macrocycle, and this was followed by reports of substituent-induced MCD band sign variations for other carbonyl-substituted porphyrins.[8i] Continuing work in this laboratory focuses on understanding and correlating the signs of MCD bands to the chemical nature and the relative positions of substituents in singly and multiply substituted porphyrins. In a preliminary study[12a] it was proposed that the signs of the MCD bands of free-base porphyrins are also delicately influenced by the phenomena of N–H tautomerism and/or the conformation of the substituents with respect to the plane of the porphyrin ring. These effects are illustrated in the MCD spectrum of the acetylporphyrin **6a** which showed two oppositely signed bands (Figure 1, ref 12a) associated with the lowest energy electronic transition. Recently, a more extensive qualitative theoretical treatment has considered the separate MCD contributions from two populations of trans N–H tautomers and from two populations of conformers of the acetyl substituent—one in which the carbonyl moiety of the acetyl group achieves the maximum degree of coplanarity with the plane of the macrocycle allowed by steric interaction and the other in which it is much more out of plane.[12b]

In order to further explore the problem of the substituent conformer effect, it was reasoned that if a hydrogen replaces the methyl group adjacent to the substituent, a more nearly coplanar arrangement with respect to the porphyrin macrocycle would be adopted by the substituent. Persuant to this proposition we wish to describe here the first total synthesis of a series of demethyl monosubstituted porphyrins containing acetyl, vinyl, formyl, cyano, and ethoxycarbonyl groups (**6b–f**). The singular importance of the present synthetic work and its value for ongoing theoretical MCD studies is illustrated in the comparison of the MCD and absorption spectra of the methyl- and demethyl(ethoxycarbonyl)porphyrins shown in Figure 1.

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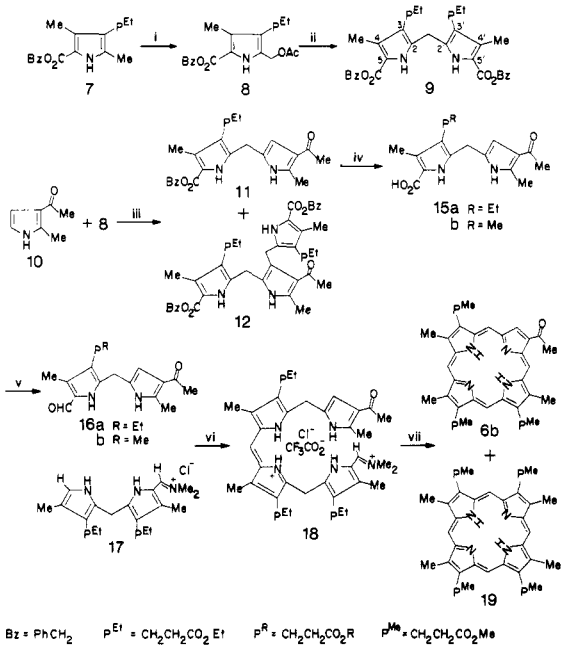
Scheme I[a]



[a] (i) $Pb(OAc)_4$, glacial AcOH, room temperature; (ii) aqueous 80% AcOH, 90 °C, N_2; (iii) glacial AcOH, 90 °C, N_2; (iv) 10% Pd/C, EtOH, H_2, room temperature, 1 atm; (v) TFA, room temperature, 3 min, DMF, *p*-$NO_2PhCOCl$, 0 °C, N_2; (vi) TFA-MeOH, N_2, room temperature; (vii) a, $Cu(OAc)_2$, glacial AcOH, MeOH, anhydrous NaOAc, N_2, 24 h; b, TFA-H_2SO_4 (1:4), MeOH, 24 h.

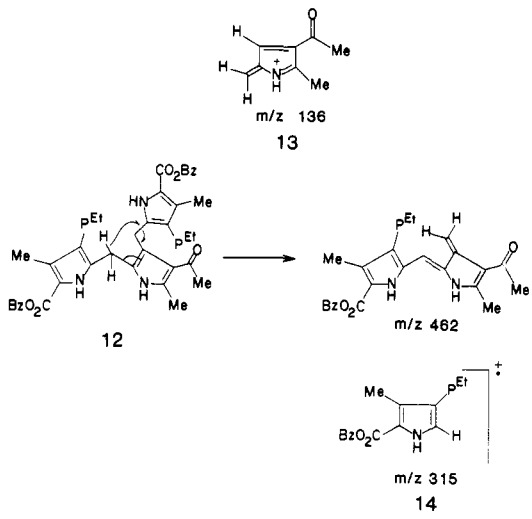
Results and Discussion

Synthesis. From the point of view of synthetic convenience it was decided to synthesize the demethylacetylporphyrin **6b** first and to subsequently convert the acetyl function to the vinyl, formyl, and cyano substituents. The synthesis (Scheme I) commenced with the preparation of pyrrole **10**[13] from 4-aminopent-3-ene-2-one[14] and α,β-dibromoethyl acetate. This pyrrole was condensed with the known α-(acetoxymethy)pyrrole **8**,[15] prepared by treating pyrrole **7** with lead tetraacetate, to give the required dipyrrylmethane **11** along with a small amount of **12**.

The notable feature in the ^1H NMR of **11** is the doublet centered at δ 6.32 with a coupling constant of 2.7 Hz which was assigned to the C-3′ hydrogen. The mass spectrum of **11** showed, apart from the molecular ion (m/z 450) and daughter ions derived from the loss of the tropylium ion (m/z 359) and the benzyloxycarbonyl moiety (m/z 315), characteristic ions at m/z 349 due to the loss of the (ethoxycarbonyl)ethyl moiety[16] and at m/z 241 attributed to the loss of a molecule of benzyl alcohol and the (ethoxycarbonyl)ethyl moiety. The peak at m/z 136 is due to the azafulvenium ion **13** (Scheme II) derived from cleavage at the methane bridge[16] of the dipyrrylmethane **11**.

The minor compound was assigned the structure **12** on the basis of its ^1H NMR. When directly compared with the ^1H NMR of **11**, it showed the absence of the doublet centered at δ 6.32 attributed to the C-3′ hydrogen and the

Scheme II



presence of additional singlets at δ 2.27 due to the methyl protons of the C-3′ pyrrolylmethyl moiety, at δ 4.03 due to the C-3′ methylene protons, and at δ 5.20 assigned to the benzyl methylene protons of the C-3′ pyrrolylmethyl moiety. Further structural confirmation was derived from its mass spectrum. The molecular ion (M^+ 777) was not observed but a fragment ion at m/z 686 was obtained due to the facile loss of a tropylium ion. Other salient features are the ions at m/z 462 due to the loss of pyrrole **14** (m/z 315) (Scheme II) with subsequent loss of tropylium ion and a molecule of ethylene to give the ion at m/z 343 and further loss of a methyl radical from the acetyl function to give the base peak at m/z 328.

The dipyrrylmethane **11** was hydrogenated over 10% palladized charcoal in absolute alcohol at room temperature and atmospheric pressure to give the dipyrrylmethane acid **15a**. This acid was then formylated using the modified Vilsmeier–Haack[17,18] procedure to give a disappointingly low yield (36%) of **16a**. The trifluoroacetic acid–triethyl orthoformate method[19] was also tried, but on the methyl ester acid analogue **15b**, and the formyl compound **16b** was obtained only in 48% yield. Moreover, this method was found to require careful optimization of reaction conditions such as the time of exposure of the dipyrrylmethane of trifluoroacetic acid and the temperature of the reaction during addition of triethyl orthoformate. As a result of these low yields we have investigated other ways of formylation and have found[20] that brief treatment of **15a** with trifluoroacetic acid,[19,21,22] quenching of the trifluoroacetic acid solution, isolation of the decarboxylated dipyrrylmethane, and formylation with dry dimethylformamide/*p*-nitrobenzoyl chloride[18] gave a good yield (71%) of **16a**. The ^1H NMR of **16a** was in agreement with the structure; the expected doublet centered at δ 6.33 (J = 2.5 Hz) was due to the C-3′ hydrogen and the aldehydic proton resonated as a singlet at δ 9.45. The mass spectrum gave the molecular ion (m/z 344) as the base peak and

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(18) We have employed *p*-nitrobenzoyl chloride instead of benzoyl chloride because of *p*-nitrobenzoate anion is a better leaving group, consequently increasing the reactivity of the Vilsmeier–Haack complex.
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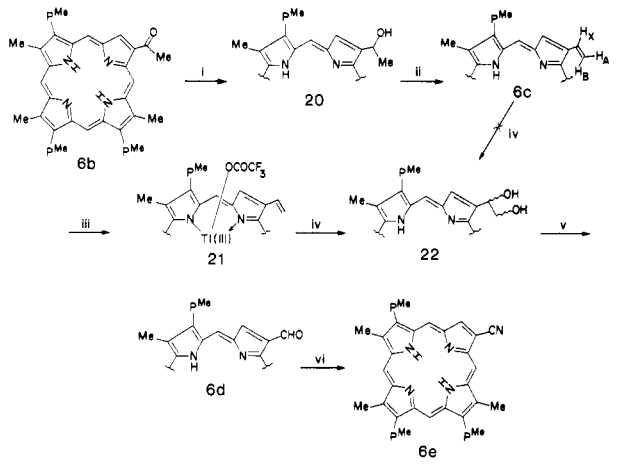
other characteristic peaks at m/z 243 and m/z 136 are due to the loss of the (ethoxycarbonyl)ethyl moiety[16] and to **13**, respectively.

The symmetrical dipyrrylmethane **9**[15b] was prepared by self condensation of the α-(acetoxymethyl)pyrrole **8** in aqueous 80% acetic acid. The benzyl protecting groups of **9** were removed by hydrogenation over 10% palladized charcoal in absolute ethanol at room temperature and atmospheric pressure to give the corresponding diacid in quantitative yield. Decarboxylation of the diacid was achieved in refluxing dry dimethylformamide and the dimethylformamide solution was subsequently treated with 1 equiv of *p*-nitrobenzoyl chloride in dry dimethylformamide to yield the *mono*iminium salt **17**. Protection of one of the α-free positions of the decarboxylated dipyrrylmethane with a *N,N*-dimethylformaldiminio group has been shown[23] to be necessary in order to prevent condensation of two molecules of **16a** with one molecule of the decarboxylated dipyrrylmethane.

The α-formyldipyrrylmethane **16a** and the monoiminium salt **17** were condensed in methanol containing trifluoroacetic acid to give the *b*-bilene intermediate **18**. Subsequent oxidative cyclization of this *b*-bilene was brought about by anhydrous copper(II) acetate in a mixture of glacial acetic acid and methanol[24] to yield the demethylacetylporphyrin **6b**. This porphyrin showed the expected rhodo-type visible spectrum which is characteristic of porphyrins bearing a single electron-withdrawing function.[25] A small amount of a porphyrin which exhibited an etio type spectrum[25] was also obtained as a product from the above cyclization reaction. An examination of its ^{1}H NMR showed only two *meso*-methine proton singlets at δ 10.81 and 10.99, each having an integral equivalent of 2 protons; a group of methyl singlets between δ 3.69 and δ 3.71 which integrated to 24 protons; and methylene envelopes between δ 3.14 and 3.20 and between δ 4.54 and 4.60, each having an integral of 8 protons. This led us to tentatively assign the coproporphyrin II tetramethyl ester structure (**19**) to this porphyrin. Furthermore, elemental analysis corresponded to an empirical formula of $C_{40}H_{46}N_4O_8$ and its melting point agreed closely with reported literature values[26] for coproporphyrin II tetramethyl ester. The formation of **19** may be attributed to the hydrolysis of unreacted monoimimum salt **17** to give the corresponding 5-unsubstituted-5′-formyldipyrrylmethane which then self condensed under the acidic reaction conditions.

The demethylacetylporphyrin **6b** was then reduced with sodium borohydride in a chloroform–ethanol mixture at a temperature of 60 °C since reduction was found to be slow at room temperature. The intermediate α-(hydroxyethyl)porphyrin **20** (Scheme III) was treated with benzoyl chloride in dry dimethylformamide[27] to yield the vinylporphyrin **6c**. Its visible absorption spectrum indicated an etio-type spectrum as expected and its elemental analyses corresponded to an empirical formula of $C_{37}H_{40}N_4O_6$. The salient features of the ^{1}H NMR spectrum, run in deuteriotrifluoroacetic acid, are the resonances due to the vinyl protons, which can be analyzed as an ABX system.[28] The doublet centered at δ 6.48 (J = 11.1 Hz) was assigned to H_A resulting from coupling to H_X; the doublet centered at δ 6.92 (J = 17.4 Hz) was attributed to H_B resulting from coupling to H_X; the double doublet centered at δ 8.46 (J = 17.4 and 11.1 Hz) is due to H_X. Surprisingly, the coupling between H_A and H_B, which has a typical J value of 0.5 Hz,[28a] was not observed. This may be due to solvent effects since the spectrum run in deuteriochloroform showed J_{AB} to be 1.1 Hz.

Scheme III[a]



[a] (i) $NaBH_4$, $CHCl_3$, EtOH, 60 °C, N_2; (ii) DMF, PhCOCl; (iii) TTFA, CH_2Cl_2, dioxane, room temperature; (iv) a, pyridine, 2% w/w OsO_4 in pyridine, room temperature, 3 h; b, aqueous 10% Na_2SO_3, 90 °C, 45 min; (v) a, aqueous 2.5% $NaIO_4$, aqueous 80% dioxane, Δ; b, 5% H_2SO_4-MeOH, room temperature; (vi) a, NH_2OH·HCl, aqueous pyridine, Δ; b, SeO_2, $CHCl_3$, 24 h.

With the vinylporphyrin **6c** in hand, the next step was to convert the vinyl function to the formyl group. The method of choice was the osmium tetraoxide oxidation of the vinyl group and subsequent sodium periodate cleavage of the derived glycol **22**. However, treatment of **6c** according to the literature procedure[29] with 1 equiv of osmium tetraoxide in a mixture of dry dioxane and ether containing pyridine for 24 h followed by reductive cleavage of the intermediate osmate ester with aqueous sodium sulfite resulted in a complex mixture of products as revealed by thin-layer chromatography. Moreover, the visible spectrum of this mixture showed substances absorbing at wavelengths (498 and 640 nm) characteristic of chlorin-type compounds. The formation of chlorin-type species has been attributed[29] to osmium tetraoxide oxidation of one of the peripheral double bonds of the porphyrin macrocycle.[30]

It has been reported[27] that osmylation of vinyl functions carried out using pyridine as the solvent rather than a mixture of dioxane and ether containing a small amount of the base generally resulted in rapid and clean oxidation. Prompted by this observation, we treated **6c**, dissolved in pyridine, with 1 equiv of osmium tetraoxide for 24 h. Again to our disappointment the product showed a chlorin-type visible spectrum. Using a large exces of osmium tetraoxide, so as to reduce the reaction time, did not improve the situation.

These studies showed that a peripheral double bond of **6c** is particularly susceptible to attack by osmium tetraoxide and it is interesting to note that for the vinyl-

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porphyrin having a methyl group adjacent to the vinyl function osmylation proceeded without much complication.[31] Therefore we sought a way to protect the macrocycle from oxidation. Perusal of the porphyrin literature indicated that certain metal ions like iron(III), nickel(II), copper(II), and thallium(III) when complexed with the porphyrin are able to impart a high oxidation potential to the macrocycle.[32] Furthermore, there have been a few reports describing the use of metal ions for the protection of the porphyrin macrocycle while allowing the peripheral functionalities to be chemically manipulated.[32,33] Encouraged by these observations we decided to protect the vinylporphyrin **6c** with a metal ion. Thallium(III) was chosen because of its ease of insertion and removal (by mild reduction) compared to the other metal ions mentioned above.[33b,34] In addition, it has been shown that when vinylporphyrins were treated with 1 equiv of thallium(III) reagent only the thallium(III) chelate was obtained.[32b,c,35]

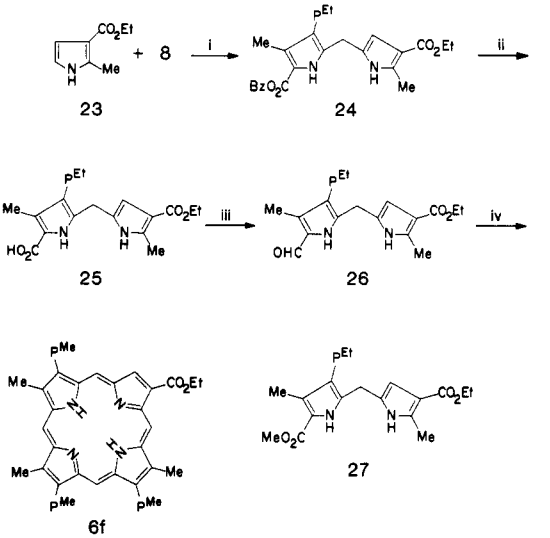
Therefore **6c** was treated with 1 equiv of thallium trifluoroacetate[36] to give the chelate **21**. The visible spectrum showed absorption bands (λ_{max} 416, 546, and 582 nm) characteristic for metalloporphyrins.[25] The complex **21** was dissolved in pyridine and then treated with 1.1 equiv of osmium tetroxide for 3 h to give the intermediate osmate ester which was then reductively cleaved with aqueous sodium sulfite, with concomitant removal of thallium, to yield the glycol **22**. No attempts were made to optimize reaction conditions for the osmylation step. Sodium periodate oxidation of **22** in aqueous dioxane followed by esterification of the propionic acid side chains (5% methanolic sulfuric acid) and column chromatography provided the formylporphyrin **6d** albeit in low yield. Elemental analysis showed that **6d** was obtained as a hydrate and its visible spectrum showed the expected characteristic rhodo-type absorption.[25]

Condensation of **6d** with hydroxylamine hydrochloride in aqueous pyridine gave the corresponding oxime which was dehydrated with selenium dioxide in ethanol-free chloroform[37] to provide the cyanoporphyrin **6e** in 70% yield. Its infrared spectrum indicated the nitrile absorption at 2240 cm^{-1}.

The preparation of the (ethoxycarbonyl)porphyrin **6f** was also undertaken in parallel with the above described synthesis. Initially, we had planned to prepare **6f** by the "Baeyer-Villiger" type oxidation of the formyl function of **6d**.[27,38] However, the difficulties and low yields encountered in the preparation of **6d** resulted in the abandonment of this plan. Consequently, 3-(ethoxycarbonyl)-2-methylpyrrole (**23**)[39] was condensed with the α-(acetoxymethyl)pyrrole **8** to yield the dipyrrylmethane **24** as an uncrystallizable oil. The ^1H NMR spectrum, however, showed the C-3′ hydrogen as a doublet at δ 6.36 (J = 2.9 Hz). For further characterization, **24** was hydrogenated over 10% palladized charcoal in absolute ethanol at room temperature and atmospheric pressure to give the corresponding acid **25** which was then treated with ethereal diazomethane in dry dioxane to give the crystalline methyl ester **27**. The ^1H NMR showed the absence of singlets at δ 5.25 and 7.35 attributable to the methylene and phenyl protons, respectively, of the benzyl group and the presence of a new singlet at δ 3.78 assigned to the methyl protons of the methoxycarbonyl moiety. The mass spectrum showed the molecular ion at m/z 404; other diagnostic ions are the ones at m/z 303 derived from the loss of the (ethoxycarbonyl)ethyl moiety and the base peak m/z 271 due to the further loss of a molecule of methanol.[16]

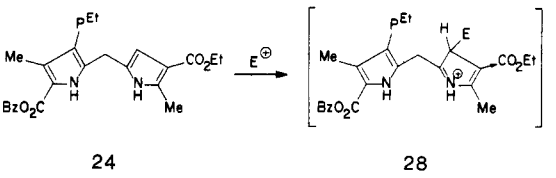
Interestingly, no compound analogous to **12** resulting from the condensation of **23** with two molecules of **8** was obtained as was the case in the preparation of **11**. This may be due to the possibility that for dipyrrylmethanes the ethoxycarbonyl group is a stronger inductively electron-withdrawing substituent than Taft parameters would indicate.[40] If so, the consequences of this effect are 2-fold: the first will result in the decrease of electron density at the C-3′ carbon and the other may act to destabilize the transition states **28** (Scheme V). On the whole this will make aromatic electrophilic substitution at C-3′ an unfavorable process. An alternative possibility is that it is the greater effective steric bulk of the ethoxycarbonyl group as compared to the acetyl group which discourages substitution at C-3′.

Scheme IV[a]



[a] (i) glacial AcOH, 90 °C, N_2; (ii) 10% Pd/C, EtOH, H_2, room temperature, 1 atm; (iii) TFA, room temperature, 3 min, DMF, p-$NO_2PhCOCl$, 0 °C, N_2; (iv) a, **17**, MeOH-TFA, room temperature; b, $Cu(OAc)_2$, glacial AcOH, MeOH, anhydrous NaOAc, N_2; c, TFA-H_2SO_4 (1:4), MeOH, room temperature, 24 h.

Scheme V



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Formylation of the acid **25** was accomplished in the same way as described for the preparation of **16a** to give **26** in 88% yield. Compound **26** was condensed with the previously described monoiminium salt **17** to give the *b*-bilene intermediate. This intermediate was cyclized, in the same manner as described earlier, to give **6f** (after removal of the copper and transesterification of the propionic ester side chains) along with an insignificant amount of coproporphyrin II tetramethyl ester **19**. The (ethoxycarbonyl)porphyrin **6f** showed the expected rhodo-type visible spectrum.[25] The notable features in the ^{1}H NMR spectrum are the triplet centered at δ 1.94 (J = 7.2 Hz) and the quartet centered at δ 5.11 (J = 7.2 Hz) assigned to the methyl and methylene protons, respectively, of the nuclear ethoxycarbonyl moiety indicating that this group has survived the transesterification conditions.

Magnetic Circular Dichroism. MCD, like the CD exhibited by optically active molecules, is a signed optical phenomenon and carries with it the intrinsic potential of providing information about the structure and electronic properties of substances that either are not evident or else are not as clearly evident in an ordinary absorption spectrum. MCD, however, unlike CD which arises out of the chiral molecular geometry of the substance, has its origin in the details of the ways in which the excited states of a molecule are coupled (mixed) by the external magnetic field. Consequently, the perspectives of the electronic and molecular structure of a substance obtained by the two techniques, even if applied to the same optically active molecule, are different. Approaches for understanding the molecular basis of CD are well documented[41] and a perimeter model approach for understanding how the occurrence of MCD band sign inversion relates to the molecular structures of cyclic π-electron systems has been provided by Michl.[8c,d,42] We have also utilized the perimeter model in a number of studies of porphyrin systems[7a,8a,b,12,43,44] for the purpose of obtaining useful structural and electronic information.

Since the application of the perimeter model to substituted porphyrins of the type of concern here has now been documented,[12] we note here only those aspects which are particularly relevant to the spectra of the methyl- and demethyl(ethoxycarbonyl)porphyrins shown in Figure 1. According to the perimeter model, the occurrence of MCD band sign variation in the four lowest energy purely electronic transitions of cyclic π-electron systems (here, the Q_0^x, Q_0^y, B_0^x, and B_0^y transitions) depends on the relative magnitudes of the differences in the energies of the highest occupied (ΔHOMO) and lowest unoccupied (ΔLUMO) molecular orbitals. If ΔHOMO > ΔLUMO, the perimeter model predicts the $[\theta]_M$ sign patern −+−+, in the order of increasing energy. On the other hand, if ΔHOMO < ΔLUMO and if the value |ΔHOMO − ΔLUMO| is large, the expected sign pattern is +−+−. In the event, however, that ΔHOMO < ΔLUMO and |ΔHOMO − ΔLUMO| is relatively small, MCD band sign inversion may occur for only the lowest energy Q_0^x and Q_0^y transitions and not for the higher energy MCD bands associated with the first two of the Soret region transitions.

The condition ΔHOMO > ΔLUMO is the one imposed on the energy levels of the four frontier molecular orbitals

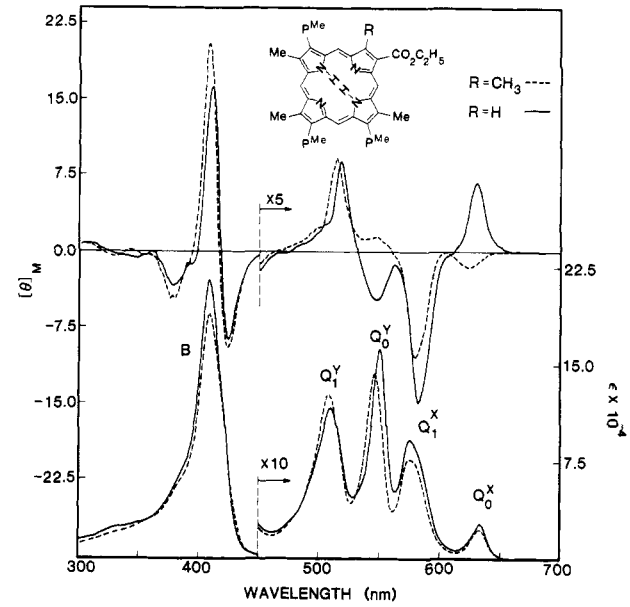

Figure 1. Absorption and MCD spectra of the demethyl(ethoxycarbonyl)porphyrin (—) and the methyl(ethoxycarbonyl)-porphyrin (−−) in chloroform.

of octaalkyl free-base porphyrins by the presence of the internal *trans*-protons and by the alkyl or alkyl-like substituents at the pyrrole positions.[8b,d,12] Consequently, common alkyl free-base porphyrins exhibit the normal −+−+ MCD band sign pattern. The condition ΔHOMO < ΔLUMO is a condition which *may be imposed* on the orbital energies of free-base porphyrins having a π-acceptor substituent at one pyrrole position since the effect of such substituents is to widen the gap between the LUMO orbitals while leaving the HOMO splitting little changed. Whether the condition ΔHOMO < ΔLUMO actually obtains for a particular monosubstituted porphyrin depends on the effective π-acceptor character (i.e., its intrinsic π-acceptor capability as modulated by steric effects which may diminish maximum overlap of the porphyrin and substituent π-orbitals) of the substituent and is a condition which may further be modulated by the conjunctive effects of N–H proton tautomerism.[12] Since the Q_0^x and Q_0^y MCD bands of the methyl(ethoxycarbonyl)porphyrin are not inverted whereas those of the demethyl(ethoxycarbonyl)porphyrin are (Figure 1), it appears that for the former porphyrin conformer species wherein the ethoxycarbonyl group is well out of plane are highly populated whereas much more nearly coplanar conformer species are well populated for the latter porphyrin. Consequently, it can be seen that theoretical studies[45] of substituted porphyrins will, in general, be the more well guided by access to optical information derived from sterically unhindered reference porphyrins.

The MCD spectra of the two (ethoxycarbonyl)-porphyrins in Figure 1 also illustrate in a most effective manner the way in which the bisignate Q_0^x MCD observed[12] for the acetyl porphyrin **6a** may arise. Notice that the peak position of the negative Q_0^x MCD band of the sterically encumbered methyl(ethoxycarbonyl)porphyrin is higher in energy than that of the positive MCD band of the unhindered demethyl(ethoxycarbonyl)porphyrin. In the case of the acetyl porphyrin **6a**, the acetyl group has less effective steric bulk than the ethoxycarbonyl group and consequently a larger range of conformations can be accessed by the acetyl group in porphyrin **6a**. Since MCD

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effectively "sees" all molecular species present in solution, the bisignate nature of the Q_0^x MCD of the acetyl porphyrin **6a** receives a quite natural and satisfying explanation as the summation of oppositely signed MCD bands analogous to those of the (ethoxycarbonyl)porphyrins in Figure 1. The way in which the MCD of substituted free-base porphyrins may be further affected by tautomeric equilibria is discussed elsewhere.[12]

Conclusion

In the present work we have presented the synthetic procedures leading to a series of monosubstituted (acetyl, vinyl, formyl, cyano, and ethoxycarbonyl) free-base porphyrins which lack the usual adjacent alkyl substituents in moderate detail since we believe the availability of these porphyrins will, for the first time, allow the electronic and optical consequences of substituent effects on the porphyrin macrocycle to be assessed on the same sterically unconstrained basis as now exists for a wide variety of other cyclic π-electron systems. We have illustrated some aspects of this for a pair of (ethoxycarbonyl)porphyrins and plan to present the results of a more detailed investigation in subsequent publications.

Experimental Section

General Procedures. All melting points were determined by using a Thomas Hoover capillary melting point apparatus and are uncorrected. Absorption spectra were recorded for chloroform solutions on a Cary 14M spectrophotometer. Infrared spectra were recorded on a Beckman Acculab 3 spectrophotometer. ^1H NMR spectra of porphyrins were recorded on a 300-MHz Nicolet NT 300 WB instrument and the spectra of simpler molecules were recorded on a Varian XL-100 FT instrument. Tetramethylsilane was used as an internal standard for all NMR measurements. In the subsequent synthesis description the abbreviation for multiplicities are: b, broad; s, singlet; m, multiplet; d, doublet; dd, double doublet; q, quartet. Microanalyses were performed by the microanalytical service laboratories either at Stanford or at the University of California, Berkeley. Mass spectra were obtained on a Ribermag R10-10B spectrometer. The high-resolution mass spectra measurement was obtained by Dr. Arnold Fallik at the University of California, Berkeley.

Alumina refers to neutral alumina, grade III, prepared by addition of an appropriate quantity of water to neutral alumina, Brockman activity I, obtained from Fischer Scientific Company and the silica gel was Davisil type 62. Thin-layer chromatography was performed on Merck silica gel 60F-254, precoated on aluminum sheets (0.2 mm).

All solutions in water immiscible solvents were dried over anhydrous sodium sulfate. *N,N*-dimethylformamide and dichloromethane were dried by distillation over calcium hydride before use. Pyridine, dried over potassium hydroxide pellets, was distilled over barium oxide before use. Commercial anhydrous ether (Baker) was dried over sodium wire. Petroleum ether refers to the petroleum fraction bp 35–60 °C. Thallium(III) trifluoroacetate was prepared from thallic oxide.[36]

Removal of copper from porphyrin complexes was achieved by the following procedure. The complex (ca. 100 mg) was moistened with trifuoracetic acid (1 mL) and concentrated sulfuric acid (4 mL) was added. The mixture was shaken vigorously for 15 min and then carefully added to cold methanol (100 mL) to transesterify the porphyrin propionic ester side chains. After standing overnight at room temperature in the dark, the acidic methanolic solution was diluted with water (300 mL) and then extracted with dichloromethane.

Pyrroles. Benzyl 3,5-Dimethyl-4-[2′-(ethoxycarbonyl)ethyl]pyrrole-2-carboxylate (7). Prepared, according to the literature procedure[15a] from benzyl acetoacetate (57.3 g) and ethyl 4-acetyl-5-oxohexanoate (65 g): the yield was 35 g (36%); mp (aqueous ethanol) 78–79 °C (lit.[15] mp 75–76 °C); IR (nujol) 3310 (NH), 1730 (ester C=O) and 1670 (nuclear ester C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.23 (t, 3 H, J = 7.1 Hz, CH_3CH_2O), 2.20 (s, 3 H, $ArCH_3$), 2.28 (s, 3 H, $ArCH_3$), 2.35–2.45 (m, 2 H, CH_2CO), 2.62–2.79 (m, 2 H, $ArCH_2$), 4.11 (q, 2 H, J = 7.1 Hz, CH_3CH_2O), 5.28 (s, 2 H, $PhCH_2$), 7.30–7.45 (m, 5 H, PhH), 8.50–8.80 (b, 1 H, NH). Anal. Calcd for $C_{19}H_{23}NO_4$: C, 69.28; H, 7.03; N, 4.25. Found: C, 69.29; H, 7.04; N, 4.27.

Benzyl 5-(Acetoxymethyl)-4-[2′-(ethoxycarbonyl)ethyl]-3-methylpyrrole-2-carboxylate (8). Prepared as described in the literature[15] from **7** (12.0 g): the yield was 8.7 g (62%); mp (acetone) 120–121.5 °C (lit.[15] mp 121–122 °C); IR (nujol) 3300 (NH), 1710–1740 (2 × ester C=O) and 1670 (nuclear ester C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.23 (t, 3 H, J = 7.1 Hz, CH_3CH_2O), 2.08 (s, 3 H, CH_3CO_2), 2.28 (s, 3 H, $ArCH_3$), 2.42–2.55 (m, 2 H, CH_2O), 2.70–2.90 (m, 2 H, $ArCH_2$), 4.10 (q, 2 H, J = 7.1 Hz, CH_3CH_2O), 5.05 (s, 2 H, CH_2OAc), 5.30 (s, 2 H, $PhCH_2$), 7.34–7.38 (m, 5 H, PhH), 8.90–9.10 (b, 1 H, NH). Anal. Calcd for $C_{21}H_{25}NO_6$: C, 65.10; H, 6.50; N, 3.62. Found: C, 65.16; H. 6.48; N, 3.65.

3-Acetyl-2-methylpyrrole (10). A mixture of acetylacetone (102 mL) and concentrated ammonia (1 L, d = 0.880) were heated over a steam bath for 15 min with stirring. The mixture was then allowed to cool and sodium chloride (200 g) was added. Diethyl ether (200 mL) was added and the ethereal layer was separated from the alkaline aqueous layer. The aqueous layer was extracted several times with diethyl ether and the combined ethereal extracts were washed with water and brine and then dried. The filtered solution was evaporated in vacuo to give 4-aminopent-3-ene-2-one as a light yellow oil. This oil and α,β-dibromoethyl acetate, prepared by bromination (52 mL of bromine) of vinyl acetate (86 g) in dry carbon tetrachloride (180 mL), were added dropwise into concentrated aqueous ammonia at −10 °C, with efficient stirring. After the addition was complete, the reaction mixture was allowed to warm to room temperature. After 20 h of stirring the mixture was heated at 90 °C for 30 min, cooled, and evaporated in vacuo. Water (200 mL) was added to the residue and the mixture was acidified to pH 2 with concentrated hydrochloric acid. The acidic aqueous mixture was subjected to continuous ether extraction. The ethereal layer was washed with water, brine, and dried. The filtered ethereal solution was evaporated in vacuo. The residue was chromatographed over silica gel with dichloromethane–diethyl ether (4.8–0.2, v:v) as eluent to give the title compound **10** (9.5 g, 7%): mp (H_2O) 95.5–96.5 °C (lit.[13] mp 94.5–95.5 °C); IR (nujol) 3200–3300 (NH) and 1640 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 2.41 (s, 3 H, CH_3CO), 2.55 (s, 3 H, $ArCH_3$), 6.48–6.62 (m, 2 H, ArH), 8.10–8.50 (b, 1 H, NH). Anal. Calcd for C_7H_9NO: C, 68.21; H, 7.37; N, 11.35. Found: C, 68.27; H, 7.36; N, 11.37.

3-(Ethoxycarbonyl)-2-methylpyrrole (23). Vinyl acetate (172 g) was dissolved in dry carbon tetrachloride (100 mL) and bromine (102 mL) in dry carbon tetrachloride (100 mL) was added dropwise with vigorous stirring, under nitrogen. When addition was complete, the reaction mixture was stirred for 30 min and then the carbon tetrachloride was evaporated in vacuo. The crude α,β-dibromoethyl acetate was mixed with ethyl acetoacetate (260 g), and aqueous 10% ammonium hydroxide (2 L) was added dropwise. After addition was complete the reaction mixture was stirred for an additional 2 h and left to stand overnight at room temperature. The aqueous layer was decanted and the semisolid product was taken into dichloromethane. The dichloromethane layer was washed with water and then dried. The filtered solution was evaporated in vacuo and the residue was further evaporated under reduced pressure (5 torr) at a water bath temperature of 80 °C. The solid was pressed between Whatman No. 1 filter paper for 2 days. Recrystallization from benzene furnished 3-(ethoxycarbonyl)-2-methylpyrrole (131 g, 43%): mp 81–82.5 °C (lit.[39] mp 75 °C); IR (nujol) 3300 (NH) and 1680 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.34 (t, 3 H, J = 7.1 Hz, CH_3CH_2O), 2.53 (s, 3 H, $ArCH_3$), 4.26 (q, 2 H, J = 7.1 Hz, CH_3CH_2O), 6.55 (d, 2 H, J = 2.6 Hz, ArH), 7.80–8.40 (b, 1 H, NH). Anal. Calcd for $C_8H_{11}NO_2$: C, 62.73; H, 7.24; N, 9.14. Found: C, 62.57; H, 7.22; N, 9.09.

Dipyrrylmethanes. Benzyl 4-Acetyl-4′,5-dimethyl-3′-[2-(ethoxycarbonyl)ethyl]dipyrrylmethane-5′-carboxylate (11). The acetylpyrrole **10** (2.5 g) and α-(acetoxymethyl)pyrrole **8** (8.0 g) were dissolved in glacial acetic acid (60 mL) and heated under nitrogen, at 70 °C for 2 h. The reaction mixture was allowed to cool and then poured onto crushed ice (100 g). The aqueous mixture was extracted several times with dichloromethane. The combined dichloromethane extracts were washed with water, saturated aqueous sodium bicarbonate, and water and then dried.

The filtered solution was evaporated in vacuo to give an oil which was chromatographed over silica gel with dichloromethane–diethyl ether (3.5–1.5 v:v) as eluent. The required dipyrrylmethane (6 g, R_f (TLC) 0.32, dichloromethane–diethyl ether, 3.5–1.5, v:v) was obtained as an oil which crystallized on tituration with diethyl ether: mp (diethyl ether–petroleum ether) 137–139 °C; IR (nujol) 3280 and 3310 (NH), 1710 (ester C=O) and 1660 (acetyl C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.21 (t, 3 H, J = 7.1 Hz, CH_3CH_2O), 2.28 (s, 3 H, $ArCH_3$), 2.38 (s, 3 H, CH_3CO), 2.45 (s, 3 H, $ArCH_3$), 2.50–2.65 (m, 2 H, CH_2CO), 2.65–2.77 (m, 2 H, $ArCH_2$), 3.84 (s, 2 H, CH_2), 4.05 (q, 2 H, J = 7.1 Hz, CH_3CH_2O), 5.26 (s, 2 H, $PhCH_2$), 6.32 (d, 1 H, J = 2.7 Hz, ArH), 7.31 (s, 5 H, PhH), 8.40–8.60 (b, 1 H, NH), 9.00–9.20 (b, 1 H, NH); MS, m/z (relative intensity) 450 (M^+, 100), 407 (14), 359 (90), 349 (46), 341 (40), 315 (79), 299 (13), 241 (48), 136 (59). Anal. Calcd for $C_{26}H_{30}N_2O_5$: C, 69.31; H, 6.71; N, 6.22. Found: C, 69.06; H, 6.74; N, 6.15.

Fractions containing the trimer **12** at R_f (TLC) 0.40 (dichloromethane–diethylether, 3.5–1.5, v:v) were collected and the solvent evaporated in vacuo to give a yellow orange foam (0.2 g): IR (nujol) 3160–3350 (NH) and 1620–1730 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.23 (t, 6 H, J = 7.1 Hz, 2 × CH_3CH_2O), 2.25 (s, 3 H, $ArCH_3$), 2.27 (s, 3 H, $ArCH_3$), 2.40 (s, 3 H, CH_3CO), 2.43 (s, 3 H, $ArCH_3$), 2.30–2.90 (m, 8 H, 2 × CH_2CO and 2 × $ArCH_2$), 3.85 (s, 2 H, CH_2), 4.03 (s, 2 H, CH_2), 4.05 (q, 4 H, J = 7.1 Hz, 2 × CH_3CH_2O), 5.20 (s, 2 H, $PhCH_2$), 5.24 (s, 2 H, $PhCH_2$), 7.31–7.50 (m, 10 H, PhH), 8.20–8.35 (b, 1 H, NH), 9.19–9.28 (b, 1 H, NH), 9.80–9.95 (b, 1 H, NH); MS, m/z (relative intensity) 686 (40), 462 (46), 343 (62), 328 (100), 315 (94), 196 (81).

4-Acetyl-4′,5-dimethyl-3′-[2-(ethoxycarbonyl)ethyl]-5′-formyldipyrrylmethane (16a). (i) Formylation of 15a Using Trifluoroacetic Acid–Dimethylformamide/*p*-Nitrobenzoyl Chloride. The dipyrrylmethane benzyl ester **11** (6.0 g) was dissolved in ethanol and then hydrogenated over 10% palladized charcoal (0.6 g) at room temperature and atmospheric pressure for 24 h. The solvent was evaporated in vacuo and then aqueous 4 M ammonium hydroxide (100 mL) was added to the residue. The aqueous mixture was extracted twice with dichloromethane. The alkaline aqueous layer was filtered, and the filtrate was cooled in an ice bath and then acidified with glacial acetic acid to pH 6. After cooling at 0 °C for 1 h, the white precipitate was filtered, sucked dry, and then dried over phosphorous pentoxide in a vacuum desiccator. The yield of the acid was 4.6 g (96%).

The dipyrrylmethane acid (3.3 g) was finely ground and then added, in one portion, to trifluoroacetic acid (6 mL) under nitrogen. After the evolution of carbon dioxide had ceased the reaction mixture was stirred for an additional 3 min and then poured into a mixture of crushed ice (20 g) and aqueous 4 M ammonium hydroxide (60 mL). The alkaline aqueous mixture was extracted several time with dichloromethane and the combined dichloromethane layers were washed with water and brine and dried. The filtered solution was evaporated in vacuo to give the decarboxylated dipyrrylmethane which was immediately dissolved, under nitrogen, in dry dimethylformamide (5 mL). The solution was efficiently stirred and cooled to 0 °C in an ice bath, and then *p*-nitrobenzoyl chloride (1.8 g) in dry dimethylformamide (1 mL) was added dropwise. There was an almost instantaneous precipitation of the iminium salt. After addition was complete, the reaction mixture was stirred at 0 °C for 15 min and then dry diethyl ether was added. The reaction mixture was left to stand at 0 °C for another 15 min. The iminium salt was filtered and subsequently hydrolyzed in aqueous 50% ethanol (50 mL) containing sodium carbonate (1.5 g) at 70 °C. After 15 min, the aqueous ethanolic solution was diluted with water during which time the formyldipyrrylmethane precipitated. The product was filtered off, sucked dry, and recrystallized from aqueous ethanol: the yield was 2.2 g (71%); mp 193–194 °C; IR (nujol) 3180–3310 (NH), 1760 (ester C=O), and 1610–1660 (acetyl and formyl C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.24 (t, 3 H, J = 7.1 Hz, CH_3CH_2O), 2.29 (s, 3 H, $ArCH_3$), 2.32 (s, 3 H, CH_3CO), 2.49 (s, 3 H, $ArCH_3$), 2.49–2.59 (m, 2 H, CH_2CO), 2.74–2.90 (m, 2 H, $ArCH_2$), 3.90 (s, 2 H, CH_2), 4.12 (q, 2 H, J = 7.1 Hz, CH_3CH_2O), 6.33 (d, 1 H, J = 2.5 Hz, ArH), 9.45 (s, 1 H, CHO), 9.70–9.90 (b, 1 H, NH), 10.05–10.2 (b, 1 H, NH), MS, m/z (relative intensity) 344 (M^+, 100), 315 (14), 301 (29), 243 (47), 227 (12), 136 (53). Anal. Calcd for $C_{19}H_{24}N_2O_4$: C, 66.26; H, 7.02; N, 8.13. Found: C, 66.04; H, 6.99; N, 8.01.

(ii) Formylation of 15a Using the Modified Vilsmeier–Haack Method.[17,18] The dipyrrylmethane acid **15a** (1.5 g) was dissolved in dry dimethylformamide (5 mL) and the solution refluxed, under nitrogen, for 30 min. The reaction mixture was allowed to attain room temperature and then cooled to 0 °C in an ice bath. *p*-Nitrobenzoyl chloride (0.8 g) in dry dimethylformamide (1 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 1 h. Anhydrous diethyl ether (30 mL) was added and the mixture placed in a refrigerator. After 1 h, the iminium salt was filtered and subsequently hydrolyzed in aqueous 50% ethanol (20 mL) containing sodium carbonate (1.0 g) at 70 °C for 15 min. Water was then added to precipitate the formyldipyrrylmethane. The product was filtered, dried, and recrystallized from aqueous ethanol. Yield was 0.5 g (36%), identical in mp, mixture mp, and NMR to the product obtained above.

4-Acetyl-4′,5-dimethyl-3′-[2-(methoxycarbonyl)ethyl]-5′-formyldipyrrylmethane (16b). 4-Acetyl-5′-carboxy-4′,5-dimethyl-3′-[2-(methoxycarbonyl)ethyl]dipyrrylmethane **15b** (3 g), obtained by hydrogenolysis of the benzyl ester over 10% palladized charcoal (0.2 g) in dry tetrahydrofuran containing a few drops of triethylamine was added to trifluoroacetic acid, under nitrogen, at 40 °C. After 3 min, the trifluoroacetic acid solution was cooled to 0 °C in an ice bath followed by dropwise addition of triethyl orthoformate (5 mL). The mixture was stirred for 15 min and poured into cold water (200 mL). Reddish solids precipitated which were collected by filtration. The residue was added to a mixture of methanol (10 mL) and water (150 mL) and concentrated ammonium hydroxide solution (8 mL) with vigorous stirring. The golden yellow product was filtered, washed with water, and dried. The product was chromatographed over neutral alumina (10% water) with dichloromethane–methanol as the eluent. Recrystallization from aqueous methanol afforded the title compound (1.3 g, 48%): mp 200–201 °C; IR (film, $CHCl_3$) 3249 (NH), 1734 (ester C=O), and 1627 (aldehyde and ketone C=O) cm^{-1}; NMR ($CDCl_3$) δ 2.30 (s, 3 H, $ArCH_3$), 2.36 (s, 3 H, CH_3CO), 2.45 (s, 3 H, $ArCH_3$), 2.50–3.00 (m, 4 H, $CH_2CH_2CO_2Me$), 3.68 (s, 3 H, CO_2CH_3), 3.91 (s, 2 H, CH_2), 6.38 (d, 1 H, J = 2.6 Hz, ArH), 9.44 (s, 1 H, CHO), 10.07 (b, 1 H, NH), 10.63 (b, 1 H, NH). Anal. Calcd for $C_{18}H_{22}N_2O_4$: C, 65.42; H, 6.72; N, 8.48. Found: C, 65.38; H, 6.58; N, 8.48.

Dibenzyl 3,3′-Bis[2-(ethoxycarbonyl)ethyl]-4,4′-dimethyldipyrrylmethane-5,5′-dicarboxylate (9). α-(Acetoxymethyl)pyrrole **8** (5.0 g) was dissolved in aqueous 80% acetic acid (100 mL) and heated, under nitrogen, at 70 °C for 24 h. After this period, the cooled reaction mixture was poured over crushed ice (200 g). The aqueous mixture was extracted several times with dichloromethane and the combined dichloromethane extracts were washed with water and saturated aqueous sodium bicarbonate water and dried. The filtered solution was evaporated in vacuo to give an oil which slowly crystallized on standing. Recrystallization from ethanol gave **9** (2.3 g, 56%): mp 103.5–105 °C (lit.[15b] mp 102–103 °C); IR (nujol) 3300–3400 (NH), 1720 and 1705 (ester C=O) and 1690 (nuclear ester C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.14 (6 H, t, J = 7.1 Hz, CH_3CH_2O), 2.28 (6 H, s, 2 × $ArCH_3$), 2.40–2.60 (4 H, m, 2 × CH_2CO), 2.65–2.85 (m, 4 H, 2 × $ArCH_2$), 3.96 (s, 2 H, CH_2), 4.04 (4 H, q, J = 7.1 Hz, CH_3CH_2O), 5.25 (4H, s, $PhCH_2$), 7.34 (s, 10 H, PhH), 8.95–9.10 (b, 2 H, NH). Anal. Calcd for $C_{37}H_{42}N_2O_8$: C, 69.14; H, 6.59; N, 4.36. Found: C, 68.94; H, 6.64; N, 4.37.

Benzyl 4′,5-Dimethyl-3′-[2-(ethoxycarbonyl)ethyl]-4-(ethoxycarbonyl)dipyrrylmethane-5′-carboxylate (24). 3-(Ethoxycarbonyl)-2-methylpyrrole (4.0 g) and α-(acetoxymethyl)pyrrole **8** (10 g) were dissolved in glacial acetic acid and heated, under nitrogen, at 90 °C for 2 h. After this period, aqueous 1% sodium acetate (300 mL) was added to the cooled reaction mixture. The aqueous mixture was extracted several times with dichloromethane. The combined organic extracts were washed with water, saturated aqueous sodium bicarbonate, and water and dried. The filtered solution was evaporated in vacuo to give an oil which was chromatographed over silica gel with dichloromethane–diethyl ether (4.85–0.15, v:v) as eluent to give the dipyrrylmethane **24** (9.7 g, 78%) as an uncrystallizable pale yellow viscous oil: IR (film, $CHCl_3$) 3280–3380 (NH) and 1650–1710 (alkyl and nuclear ester C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.20 (t, 3 H, J = 7 Hz, CH_3CH_2O), 1.33 (t, 3 H, J = 7.1 Hz, CH_3CH_2OCOAr), 2.28 (s, 3 H, $ArCH_3$), 2.43 (s, 3 H, $ArCH_3$), 2.52–2.64 (m, 2 H, CH_2CO),

2.65–2.82 (m, 2 H, ArCH_2), 3.98 (s, 2 H, CH_2), 4.05 (q, 2 H, J = 7.1 Hz, CH_2CH_2O), 4.24 (q, 2 H, J = 7.1 Hz, CH_3CH_2OCOAr), 5.25 (s, 2 H, PhCH_2), 6.36 (d, 1 H, J = 2.9 Hz, ArH), 7.35 (s, 5 H, PhH), 8.42–8.59 (b, 1 H, NH), 8.95–9.09 (b, 1 H, NH).

A small amount of **24** was hydrogenolyzed over 10% palladized charcoal in absolute ethanol at room temperature and atmospheric pressure for 24 h. The filtrate ethanolic solution was evaporated in vacuo and the residue was dissolved in dry dioxane. The dioxane solution was treated with excess ethereal diazomethane. The reaction mixture was allowed to stand at room temperature for 2 h. After this period dioxane was removed under reduced pressure and the residue chromatographed over neutral alumina (grade III) with dichloromethane–diethyl ether (4.5–0.5, v:v) as eluent to give an oil **27** which was crystallized from ether–petroleum ether, mp 120–121.5 °C; NMR ($CDCl_3$) δ 1.21 (t, 3 H, J = 7.1 Hz, CH_3CH_2O), 1.35 (t, 3 H, J = 7.1 Hz, CH_3CH_2OCOAr), 2.28 (s, 3 H, ArCH_3), 2.49 (s, 3 H, ArCH_3), 2.50–2.82 (m, 4 H, $CH_2CH_2CO_2Et$), 3.78 (s, 3 H, CH_3O), 3.84 (s, 2 H, CH_2), 4.05 (q, 2 H, J = 7.1 Hz, CH_3CH_2O), 4.26 (q, 2 H, J = 7.1 Hz, CH_3CH_2OCOAr), 6.45 (d, 1 H, J = 2.9 Hz, ArH), 8.35–8.50 (b, 1 H, NH), 8.90–9.10 (b, 1 H, NH); MS, m/z (relative intensity) 404 (M^+, 90), 389 (10), 358 (39), 303 (90), 271 (100), 166 (45). Anal. Calcd for $C_{21}H_{28}N_2O_6$: C, 62.36; H, 6.98; N, 6.93. Found: C, 62.52; H, 7.02; N, 6.89.

4′,5-Dimethyl-4-(ethoxycarbonyl)-3′-[2-(ethoxycarbonyl)ethyl]-5′-formyldipyrrylmethane (26). Compound **24** (7.3 g) was dissolved in absolute ethanol and hydrogenated over 10% palladized charcoal (0.7 g) for 24 h. Then the solvent was evaporated in vacuo, and aqueous 4 M ammonium hydroxide (100 mL) was added to the residue. The alkaline aqueous mixture was extracted twice with dichloromethane. The alkaline aqueous layer was then filtered, and the filtrate cooled in an ice bath and subsequently acidified with glacial acetic acid. After cooling in ice for 1 h, the white precipitate was filtered, sucked dry, and further dried over phosphorous pentoxide in a vacuum desiccator; the yield was 4.3 g (72%). The acid **25** (4.3 g) was decarboxylated in trifluoroacetic acid (10 mL) and formylated with dry dimethylformamide–*p*-nitrobenzoyl chloride (2.3 g) according to the procedure (i) described for the preparation of **16a**. The formyldipyrrylmethane **26** was obtained in 88% (3.7 g) yield: mp (aqueous methanol) 107–109 °C; IR (film, $CHCl_3$) 3240–3340 (NH), 1720 (ester C=O), 1690 (nuclear ester C=O) and 1640 (aldehyde C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.24 (t, 3 H, J = 7.1 Hz, CH_3CH_2O), 1.33 (t, 3 H, J = 7.1 Hz, CH_3CH_2OCOAr), 2.29 (s, 3 H, ArCH_3), 2.43 (s, 3 H, ArCH_3), 2.53–2.60 (m, 2 H, CH_2CO), 2.75–2.90 (m, 2 H, ArCH_2), 3.88 (s, 2 H, CH_2), 4.12 (q, 2 H, J = 7.1 Hz, CH_3CH_2O), 4.25 (q, 2 H, J = 7.1 Hz, CH_3CH_2OCOAr), 6.37 (d, 1 H, J = 2.8 Hz, ArH), 9.46 (s, 1 H, CHO), 9.40–9.60 (b, 1 H, NH), 9.70–9.80 (b, 1 H, NH), MS, m/z (relative intensity) 374 (M^+, 100), 345 (35), 328 (33), 273 (61), 227 (19), 166 (60), 120 (29). Anal. Calcd for $C_{20}H_{26}N_2O_5$: C, 64.12; H, 6.99; N, 7.48. Found: C, 63.92; H, 6.76; N, 7.33.

Porphyrins. 2-Acetyl-7,13,17-tris[2-(methoxycarbonyl)ethyl]-8,12,18-trimethyl[21*H*,23*H*]porphine (6b). Dipyrrylmethane **9** (4.0 g) suspended in absolute ethanol (150 mL) was hydrogenated over 10% palladized charcoal (0.4 g) at room temperature and atmospheric pressure for 24 h. After this period ethanol was evaporated in vacuo and aqueous 4 M ammonium hydroxide (50 mL) was added to the residue. The alkaline aqueous mixture was extracted twice with dichloromethane and filtered and the filtrate was cooled in an ice bath and then acidified with glacial acetic acid. The precipitate was filtered and dried over phosphorus pentoxide in a vacuum desiccator. The yield of the diacid was 2.5 g (90%).

This acid (2.5 g) was suspended in dry dimethylformamide (7 mL) and refluxed under nitrogen for 30 min. The dimethylformamide solution was cooled to 0 °C in an ice bath and then *p*-nitrobenzoyl chloride (1.1 g) in dry dimethylformamide (1 mL) was added dropwise. After addition was complete, the reaction mixture was stirred for 15 min at 0 °C and then diluted with dry diethyl ether (30 mL). After standing at 0 °C for 1 h the precipitated monoiminium salt **17** (2.2 g, 88%) was filtered off and dried over calcium chloride in a vacuum desiccator for 24 h.

The iminium salt **17** (2.2 g) and α-formyldipyrrylmethane **16b** (1.7 g) were dissolved under nitrogen in absolute methanol (7 mL) and the mixture was efficiently stirred. Trifluoroacetic acid (10 mL) was added slowly and the reaction mixture stirred in the dark for 1.5 h. *b*-Bilene formation was monitored spectrophotometrically by the appearance of an absorption band at λ_{max} 502 nm. The red solution was poured into a hot mixture of glacial acetic acid (300 mL), absolute methanol (200 mL), copper(II) acetate (11 g), and anhydrous sodium acetate (6 g). The reaction mixture was then refluxed, under nitrogen, in the dark for 24 h. After this period, the reaction mixture was cooled and diluted with water (800 mL), and the aqueous mixture was extracted several times with dichloromethane. The combined dichloromethane extracts were washed with water, dilute sodium bicarbonate solution, and water and then dried. The filtered solution was evaporated in vacuo and the residue chromatographed over silica gel with dichloromethane–diethyl ether (4.5–0.5 v:v) as eluent. The copper(II) porphyrin complex (R_f (TLC) 0.27) was demetalated and then esterified with 5% methanolic sulfuric acid. The demethylacetylporphyrin **6b** was chromatographed over alumina with the above solvent mixture. The yield of porphyrin was 0.327 g, 11%: mp (dichloromethane-methanol) 228–229 °C; IR (CH_2Cl_2) 1700–1720 (ester C=O) and 1650 (ketone C=O) cm^{-1}; NMR (CF_3CO_2D) δ 3.22–3.45 (m, 6 H, 3 × CH_2CO), 3.62 (3 H), 3.78 (3 H), 3.79 (3 H), 3.82 (6 H), 3.84 (3 H), and 3.87 (3 H) (s, 3 × ArCH_3, CH_3CO, 3 × CO_2CH_3), 4.62–4.78 (m, 6 H, 3 × ArCH_2), 10.47 (s, 1 H, ArH), 10.97 (1 H), 11.14 (1 H), 11.38 (1 H), and 11.89 (1 H) (s, methine protons); vis λ_{max} (log ϵ_{max}) 412 (5.32), 515 (4.03), 555 (4.26), 579 (4.05), 638 (3.36) nm. Anal. Calcd for $C_{37}H_{40}N_4O_7$: C, 68.08; H, 6.18; N, 8.58. Found: C, 67.99; H, 6.30; N, 8.55.

A faster moving (R_f (TLC) 0.60, dichloromethane–diethyl ether, 4.5–0.5, v:v) red fraction was also obtained from chromatography over silica gel of the crude copper(II) porphyrin complex. After demetalation, esterification, and chromatography over alumina with the above mentioned solvent mixture gave **19** (8.7 mg): mp (dichloromethane–methanol) 284–285 °C (lit.[26] mp 285–287 °C, lit.[26] mp 286–289 °C); NMR (CF_3CO_2D) δ 3.14–3.20 (m, 8 H, 4 × CH_2CO_2Me), 3.69–3.71 (m, 24 H, 4 × ArCH_3, 4 × CO_2CH_3), 4.54–4.60 (m, 8 H, 4 × ArCH_2), 10.81 (2 H), 10.99 (2 H) (s, methine protons); vis λ_{max} (log ϵ_{max}) 400 (5.24), 498 (4.16), 533 (3.99), 568 (3.84), 6.21 (3.71) nm. Anal. Calcd for $C_{40}H_{46}N_4O_8$: C, 67.59; H, 6.52; N, 7.88. Found: C, 67.42; H, 6.56; N, 7.68.

2-Ethenyl-7,13,17-tris[2-(methoxycarbonyl)ethyl]-8,12,18-trimethyl[21*H*,23*H*]porphine (6c). Demethylacetylporphyrin **6b** (400 mg) was dissolved, under nitrogen, in a mixture of chloroform (200 mL) and absolute alcohol (60 mL). Sodium borohydride (400 mg) in absolute alcohol (20 mL) was added and the reaction mixture was stirred at 60 °C, in the dark, for 1 h. After this period, aqueous 5 M acetic acid was added dropwise to destroy unreacted sodium borohydride. Water (400 mL) was added and the chloroform layer was separated. The aqueous layer was further extracted with dichloromethane, and the combined organic extracts were washed with water, dilute sodium bicarbonate solution, and water and dried. The filtered solution was evaporated in vacuo and the residue chromatographed over silica gel with dichloromethane–diethyl ether (85–15, v:v) as eluent to provide the demethyl-α-(hydroxyethyl)porphyrin **20** (345 mg).

Porphyrin **20** was dissolved in dry dimethylformamide (100 mL), under nitrogen, and the solution heated at 80 °C in the dark. Benzoyl chloride (3 mL) was added dropwise to the solution and then the reaction mixture was stirred for 1 h. The reaction mixture was cooled and water (200 mL) and triethylamine (3.7 mL) were added. The aqueous mixture was stirred at room temperature overnight. The precipitate was filtered off, dried, and then chromatographed over silica gel with dichloromethane–diethyl ether (4.8–0.2, v:v) as eluent to give the vinylporphyrin **6c** (183 mg): mp (dichloromethane–methanol) 187–189 °C; IR (CH_2Cl_2) 1710–1740 (ester C=O) cm^{-1}; NMR (CF_3CO_2D) δ 3.25–3.42 (m, 6 H, 3 × CH_2CO), 3.77 (3 H), 3.78 (3 H) and 3.84 (12 H) (s, 3 × ArCH_3, 3 × CO_2CH_3), 4.65–4.80 (m, 6 H, 3 × ArCH_2), 6.48 (d, 1 H, J_{AX} = 11.1 Hz, H_A), 6.92 (d, 1 H, J_{BX} = 17.4 Hz, H_B), 8.46 (dd, 1 H, J_{BX} = 17.4 and J_{AX} = 11.1 Hz, H_X), 9.98 (s, 1 H, ArH), 11.02 (1 H), 11.18 (1 H), 11.20 (1 H) and 11.23 (1 H) (s, methine protons); vis λ_{max} (log ϵ_{max}) 406 (5.23), 504 (4.14), 542 (4.08), 573 (3.86), 631 (3.65) nm. Anal. Calcd for $C_{37}H_{40}N_4O_6$: C, 69.80; H, 6.33; N, 8.80. Found: C, 69.95; H, 6.40; N, 8.67.

2-Formyl-7,13,17-tris[2-(methoxycarbonyl)ethyl]-8,12,18-trimethyl[21*H*,23*H*]porphine (6d). Porphyrin **6c** (132 mg) was dissolved in dry dichloromethane (12 mL) and dry dioxane (3 mL)

under nitrogen. Thallium trifluoroacetate (123 mg) dissolved in dry dioxane (3 mL) was then added and the reaction mixture stirred, in the dark, for 5 min. The solution was filtered over Celite (prewashed with dichloromethane) and the filtrate evaporated in vacuo to provide the thallium(III) complex (λ_{max} 416, 546, and 582 nm). This complex was dissolved in dry pyridine and osmium tetroxide (2% w/w in pyridine) was added portionwise (total volume added was 2 mL) over a period of 1 h. The reaction mixture was stirred at room temperature, in the dark, for an additional 2 h. Aqueous 10% sodium sulfite (5 mL) was added and the reaction mixture was heated at 90 °C for 45 min. The hot mixture was filtered over Celite, the Celite pad washed (3 ×) with aqueous 50% pyridine (15 mL), and the filtrate evaporated in vacuo. The residue was partitioned between water (100 mL) and dichloromethane (100 mL). The dichloromethane layer was separated and sufficient concentrated hydrochloric acid was added to the aqueous layer. The acidified aqueous layer was extracted with dichloromethane. This was repeated until almost all the porphyrin had been transferred to the dichloromethane layer. The combined dichloromethane layers were washed with water and then dried. The filtered solution was evaporated in vacuo to give the porphyrin glycol which was dissolved in aqueous 80% dioxane. Aqueous 2.5% sodium periodate (5 mL) was added and the reaction mixture was heated, under nitrogen in the dark, at 80 °C for 2.5 h and then stirred at room temperature overnight. The reaction mixture was evaporated in vacuo and was worked up as described above for the isolation of the porphyrin glycol. The crude formylporphyrin was treated overnight with 5% methanolic sulfuric acid (100 mL) to esterify acidic groups. Water (300 mL) was added and the aqueous mixture was extracted several times with dichloromethane; the combined dichloromethane extracts were washed with aqueous 4 M hydrochloric acid and water and dried. The filtered solution was evaporated in vacuo and the residue chromatographed over silica gel with dichloromethane–diethyl ether (4–4, v:v) and then over alumina (III, dichloromethane–diethyl ether, 4.8–0.2, v:v) to yield the formylporphyrin **6d** (23 mg) which was recrystallized from dichloromethane–methanol: mp 206–208 °C; IR (CH_2Cl_2) 1705 (ester C=O) and 1610 (aldehyde C=O) cm^{-1}; NMR (CF_3CO_2D) δ 3.27–3.42 (m, 6 H, 3 × CH_2CO), 3.79 (3 H), 3.81 (9 H), 3.85 (3 H) and 3.86 (3 H) (s, 3 × ArCH_3, 3 × CO_2CH_3), 4.62–4.84 (m, 6 H, 3 × ArCH_2), 10.46 (s, 1 H, ArH), 10.97 (1 H), 11.13 (1 H), 11.37 (1 H), 11.45 (1 H) and 11.77 (1 H) (s, CHO and methine protons); vis λ_{max} (log ϵ_{max}) 414 (5.22), 516 (3.91), 557 (4.20) 579 (3.99), 638 (3.32) nm. Anal. Calcd for $C_{36}H_{38}N_4O_7 \cdot {}^1/_4H_2O$: C, 66.19; H, 736; N, 7.72. Found: C, 66.21; H, 7.31; N, 7.76.

2-Cyano-7,13,17-tris[2-(methoxycarbonyl)ethyl]-8,12,18-trimethyl[21*H*,23*H*]porphine (6e). The formylporphyrin **6d** (13.0 mg) was dissolved in pyridine (5 mL) and hydroxylamine hydrochloride (23 mg) in water (1 mL) was added. The reaction mixture was heated in the dark under nitrogen at 90 °C for 1 h. and stirred at room temperature for 2 h. Pyridine was removed under reduced pressure and the residue was taken into dichloromethane. The dichloromethane solution was washed several time with aqueous 0.05 M hydrochloric acid and water and then dried. The filtered solution was evaporated in vacuo to provide the formylporphyrin oxime. This compound was dissolved in ethanol-free chloroform (40 mL) and selenium dioxide (2 mg) was added. The reaction mixture was refluxed, under nitrogen, for 24 h and then the cooled solution was filtered over Celite. The filtrate was evaporated in vacuo and the residue chromatographed over alumina (grade III) with dichloromethane–diethyl ether (4.9–0.1, v:v) as the eluent to provide the cyanoporphyrin **6e** (9 mg): mp (dichloromethane–methanol) 219–221 °C; IR (CH_2Cl_2) 2240 (C≡N), and 1700–1730 (ester C=O) cm^{-1}; NMR (CF_3CO_2D) δ 3.28–3.50 (m, 6 H, 3 × CH_2CO), 3.79 (3 H), 3.80 (3 H), 3.82 (6 H), 3.86 (3 H) and 3.87 (3 H) (s, 3 × ArCH_3, 3 × CO_2CH_3), 4.62–4.80 (m, 6 H, 3 × ArCH_2), 10.30 (s, 1 H, ArH), 11.00 (1 H), 11.19 (2 H) and 11.35 (1 H) (s, methine protons); vis λ_{max} (log ϵ_{max}) 407 (5.33), 512 (4.01), 551 (4.31), 572 (4.05), 626 (3.17) nm; high-resolution MS, M^+ 635.2755, calcd for $C_{36}H_{37}N_5O_6$ M^+ 635.2744.

2-(Ethoxycarbonyl)-7,13,17-tris[2-(methoxycarbonyl)ethyl]-8,12,18-trimethyl[21*H*,23*H*]porphine (6f). Formyldipyrrylmethane **26** (1.0 g) was dissolved, under nitrogen, in trifluoroacetic acid (3 mL) followed by addition of **17** (1.2 g) in absolute methanol (5 mL). The mixture was efficiently stirred, in the dark, for 1.5 h. The *b*-bilene solution was poured into a hot mixture of glacial acetic acid (400 mL), absolute methanol (200 mL), anhydrous copper(II) acetate (4 g), and anhydrous sodium acetate (2 g). This mixture was refluxed for 24 h. The cooled reaction mixture was diluted with water (800 mL) and extracted several times with dichloromethane. The combined organic extracts were washed with water, dilute aqueous sodium bicarbonate, and water and dried. The filtered solution was evaporated in vacuo. The residue was chromatographed over silica gel with dichloromethane–diethyl ether (4.5–0.5, v:v) as eluent to give the copper(II) complex. After demetalation and reesterification of the propionic acid side chains with 5% methanolic sulfuric acid (200 mL, 24 h) and the usual aqueous workup, the free-base **6f** was chromatographed over alumina (grade III) with dichloromethane–diethyl ether (85–15, v:v) as eluent. The yield was 122.2 mg: mp (dichloromethane–methanol) 171–172 °C; IR (CH_2Cl_2) 1680–1720 (nuclear and alkyl ester C=O) cm^{-1}; NMR (CF_3CO_2D) δ 1.95 (t, 3 H, J = 7.2 Hz, CH_3CH_2OCOAr), 3.22–3.41 (m, 6 H, 3 × CH_2CO), 3.78 (3 H), 3.80 (3 H), 3.83 (6 H), 3.85 (3 H) and 3.86 (3 H) (s, 3 × ArCH_3 and 3 × CO_2CH_3), 4.62–4.80 (m, 6 H, 3 × ArCH_2), 5.11 (q, 2 H, J = 7.2 Hz, CH_3CH_2OCOAr), 10.48 (s, 1 H, ArH), 10.99 (1 H), 11.16 (1 H), 1137 (1 H) and 11.91 (1 H) (s, methine protons); vis λ_{max} (log ϵ_{max}) 409 (5.33), 510 (4.06), 551 (4.21), 574 (3.97), 633 (3.43) nm. Anal. Calcd for $C_{38}H_{42}N_4O_8$: C, 66.85; H, 6.20; N, 8.21. Found: C, 66.84; H, 6.24; N, 8.16.

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Registry No. **6b**, 91238-14-1; **6b** Cu(II) complex, 91230-46-5; **6c**, 91238-15-2; **6d**, 91238-16-3; **6d** oxime, 91238-33-4; **6e**, 91238-17-4; **6f**, 91238-18-5; **6f** Cu(II) complex, 91230-47-6; **7**, 68999-92-8; **8**, 51741-18-5; **9**, 52091-11-9; **10**, 6009-46-7; **11**, 91238-19-6; **12**, 91238-20-9; **15a**, 91238-21-0; **15b**, 91238-22-1; **16a**, 91238-23-2; **16b**, 91238-24-3; **17**, 58684-52-9; **19**, 865-16-7; **19** Cu(II) complex, 14552-44-4; **20**, 91238-25-4; **21**, 91230-48-7; **22**, 91238-32-3; **23**, 936-12-9; **24**, 91238-26-5; **25**, 91238-27-6; **26**, 91238-28-7; **27**, 91238-29-8; $CH_3C(O)CH_2C(O)OCH_2Ph$, 5396-89-4; $(CH_3C(O))_2CH(CH_2)_2C(O)OEt$, 2832-10-2; $CH_3C(O)CH_2C(O)CH_3$, 123-54-6; $CH_3C(NH_2)=CHC(O)CH_3$, 1118-66-7; $CH_3C(O)OCHBrCH_2Br$, 24442-57-7; $CH_3C(O)OCH=CH_2$, 108-05-4; $CH_3C(O)CH_2C(O)OEt$, 141-97-9; [4-methyl-3-[2-(ethoxycarbonyl)ethyl]-2-pyrryl](4-acetyl-5-methyl-2-pyrryl)methane, 91238-30-1; 5-[(4-acetyl-5-methyl-2-pyrryl)methyl]-4-[2-(ethoxycarbonyl)ethyl]-3,*N*,*N*-trimethyl-2-pyrrolemethaniminium chloride, 91238-31-2; bis[5-carboxy-4-methyl-3-[2-(ethoxycarbonyl)ethyl]-2-pyrryl]-methane, 52091-10-8; 2-(ethoxycarbonyl)-1,8,12,18,*N*,*N*-hexamethyl-7,13,17-tris[2-(ethoxycarbonyl)ethyl]-5,6,15,16-tetrahydro-21*H*-bilinemethaniminium chloride–trifluoroacetic acid, 91265-27-9.