An efficient route to vinylporphyrins

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This paper is dedicated to Professor Ross Stewart on the occasion of his 65th birthday

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The use of 1-bromo-19-methylbiladienes-ac in the synthesis of vinylporphyrins is described. The effect of the vinyl precursors on the reactions of the dipyrromethene intermediates and the construction of the linear tetrapyrrole are discussed. High-yield syntheses of a methylvinylporphyrin, an H-vinyl analogue, as well as two A,C-divinylporphyrins are presented.

Key words: pyrrole, dipyrromethene, acetoxyethylpyrrole, chloroethylpyrrole, biladiene-ac, porphyrin, vinylporphryin, benzoporphyrin, decarboxylation, transesterification.

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On décrit l'utilisation des 1-bromo-19-méthylbiladiènes-ac dans la synthèse des vinylporphyrines. On discute de l'effet des précurseurs vinyles sur les réactions des intermédiaires dipyrrométhènes et sur la construction du tétrapyrrole linéaire. On rapporte des synthèses avec rendements élevés d'une méthylvinylporphyrine, d'un analogue H-vinyle ainsi que de deux A,C-divinylporphyrines.

Mots clés: pyrrole, dipyrrométhène, acétoxyéthylpyrrole, chloroéthylpyrrole, biladiène-ac, porphyrine, vinylporphyrine, benzoporphyrine, dicarboxylation, transesterification.

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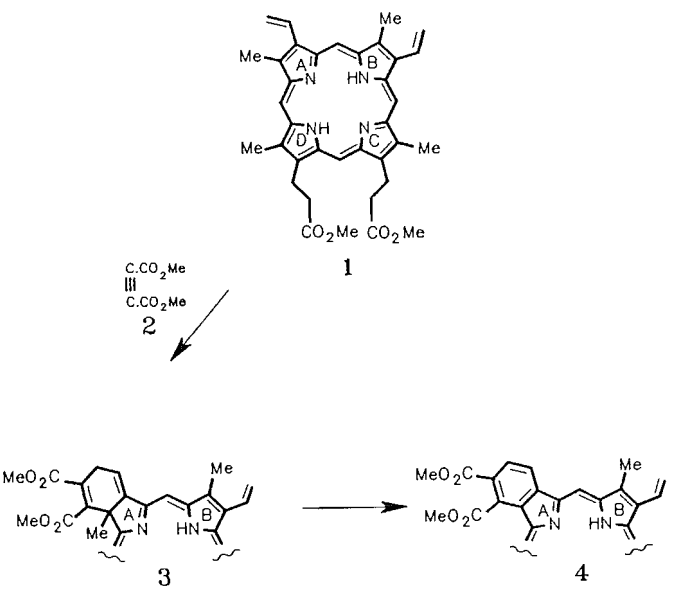
Introduction

Porphyrins and related macrocycles bearing peripheral vinyl substituents play an important role in the vital functioning of living organisms (1). Of particular interest is heme, the iron(II) complex of protoporphyrin IX (**1**), which is the prosthetic group of hemoglobin, myoglobin, and several heme enzymes. Because of their biological significance, synthesis of vinylporphyrins has received special attention, particularly in structure/function (2–6) and isotopic labelling studies (7–9). In addition, the vinyl and cross-conjugated porphyrinic β,β′ double bonds of protoporphyrin IX (**1**) have been shown (10, 11) to undergo [4+2] cycloaddition reactions with electron-deficient dienophiles to give compounds (**3**) having essentially a *chlorin* chromophore (Scheme 1). With alkynes (**2**), the initially formed cycloadducts, under certain reaction conditions, undergo aromatization (12) with the concomitant loss of the angular methyl group to give benzoporphyrins (**4**). To study this cycloaddition reaction further, we have developed, and describe here, an efficient synthesis of vinylporphyrins.

Although peripheral substituent manipulations of protoporphyrin IX have been used to prepare several useful porphyrins (13), synthesis of a totally unsymmetrical porphyrin involves the stepwise coupling of individual pyrroles, leading to a linear tetrapyrrole, which is cyclized in the final step. Two of the most commonly used tetrapyrrolic precursors are 1,19-dimethylbilenes-b and 1,19-dimethylbiladienes-ac (14), which are converted to the porphyrin using cupric salts in refluxing solvents (e.g., dimethylformamide). This method, originally developed by Johnson and Kay (15), has since been successfully modified for the synthesis of several vinylporphyrins (2–9) and other unsymmetrically substituted porphyrins. However, the varying yields (20–50%) of porphyrin produced and the harsh acidic conditions required (H_2SO_4–CF_3CO_2H) to remove coordinated Cu after cyclization are notable disadvantages of this method.

Our approach to unsymmetrical porphyrins has been via 1-bromo-19-methylbiladienes-ac (**7**), which are prepared by the stannic chloride mediated coupling of a 5′-unsubstituted



SCHEME 1

5-methyldipyrromethene (**5**) with a 5-bromo-5′-bromomethyldipyrromethene (**6**) and cyclized to the porphyrin (**8**) in DMSO–pyridine at room temperature, each reaction producing a greater than 80% yield (Scheme 2). This method, originally described by Johnson and co-workers (16, 17), suffered from a major drawback, viz. the traditional preparation of dipyrromethene **6** by the bromination of dipyrromethene **5** in hot anhydrous acetic or formic acid produced varying results, with yields of 50% being considered exceptional. However, the mild room temperature bromination procedure developed by us (18) (bromine in 10–15% TFA–1,2-dichloroethane) increased the accessibility of this important dipyrrolic intermediate and thereby made this route more versatile (19). We report here the syntheses of four vinylporphyrins using this method: a methylvinyl and an H-vinyl analogue (**8***a* and **8***b*), which have been used to study the regio- and stereochemistry of Diels–Alder additions as well as transformation to benzoporphyrins, and, in

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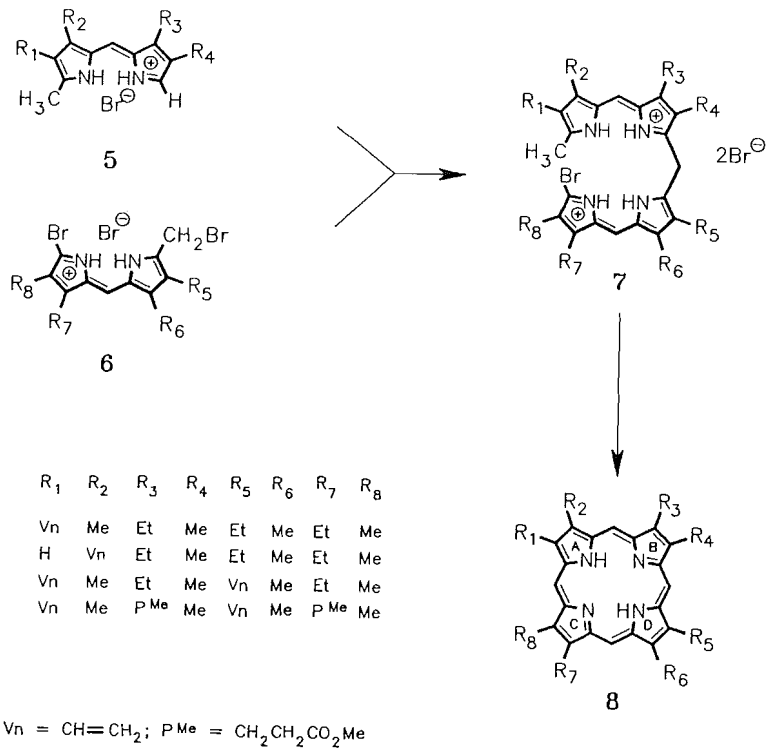


8	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8
a.	Vn	Me	Et	Me	Et	Me	Et	Me
b.	H	Vn	Et	Me	Et	Me	Et	Me
c.	Vn	Me	Et	Me	Vn	Me	Et	Me
d.	Vn	Me	P^{Me}	Me	Vn	Me	P^{Me}	Me

SCHEME 2

addition, ring A,C-divinylporphyrins (**8***c* and **8***d*) have been prepared and used for a high yield synthesis of bacteriochlorins via two simultaneous Diels–Alder reactions.

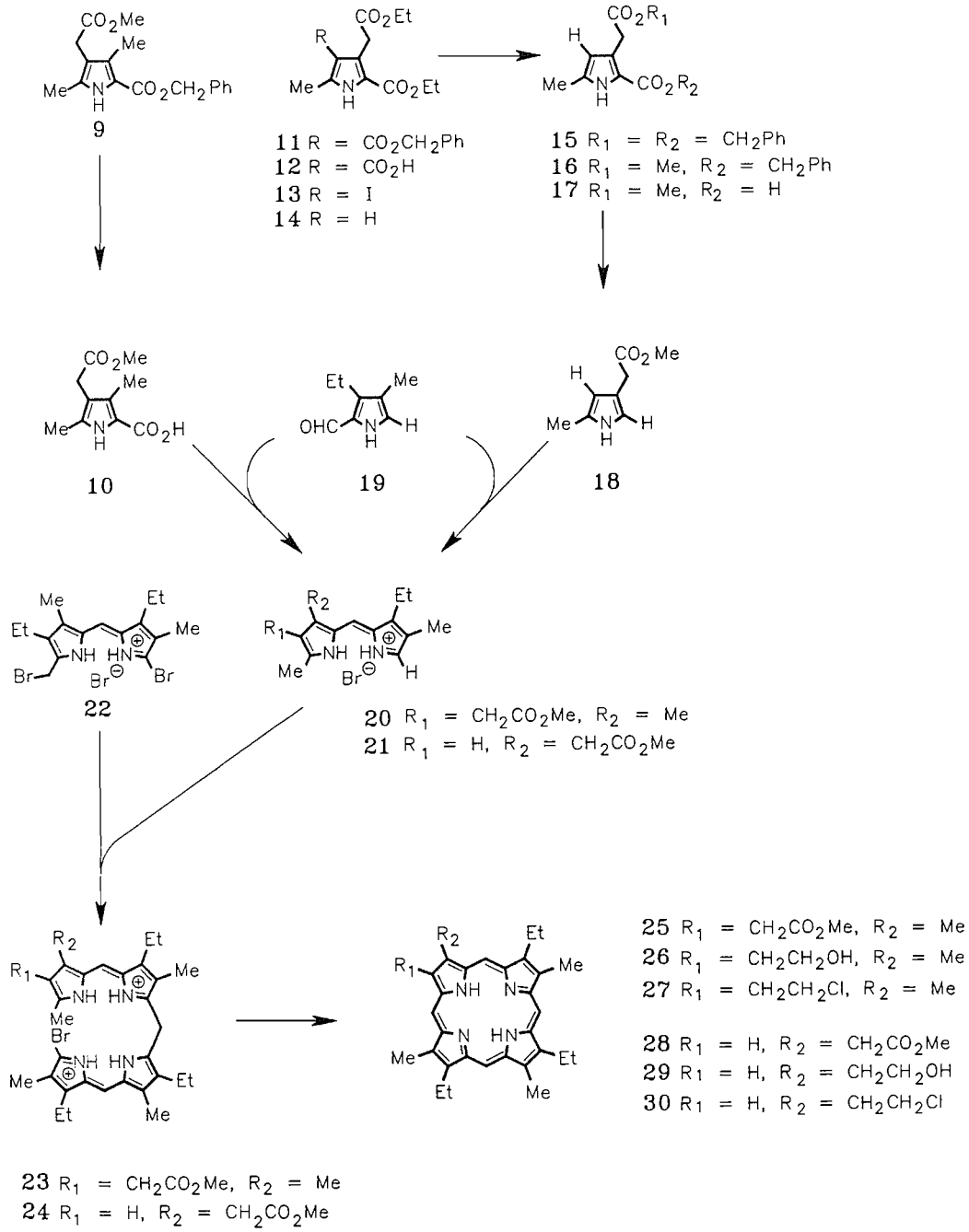
Results and discussion

The sensitive nature of the vinyl substituent requires that a two-carbon vinyl precursor be carried through most of the synthetic sequence, with generation of the vinyl group being delayed until the final stages. The two most commonly used precursors are the 2-chloroethyl group (20) (derived from methoxycarbonylmethyl) and the acetyl group (21), the latter being transformed to the vinyl via the 1-hydroxyethyl moiety. Scheme 3 outlines the synthesis of the unsymmetrical porphyrins **8***a* and **8***b*; the cycloaddition reactions of the latter leading to benzoporphyrins have already been reported (22). Retrosynthetic analysis of the target porphyrins clearly indicated that the northern half carrying the reactive centres should constitute the 5′-unsubstituted 5-methyldipyrromethene components **20** and **21**. Of the two monopyrrolic precursors required for each synthesis, the common 5-unsubstituted 2-formylpyrrole (**19**) was prepared in high yield as reported earlier (23). The dipyrromethene **20** was obtained in 90% yield by coupling pyrrole **19** with 4-(methoxycarbonyl)methyl-3,5-dimethylpyrrole-2-carboxylic acid (**10**) (24) in the presence of 48% aqueous hydrobromic acid, the decarboxylation occurring *in situ*.

The α,β-diunsubstituted pyrrole **18** necessary for the synthesis of the dipyrromethene **21** was obtained from pyrrole **11** (Scheme 3), which in turn was prepared from benzyl acetoacetate and diethyl 3-oxopentanedioate as described earlier (25). Following catalytic debenzylation using 10% Pd–C, the resulting pyrrole-4-carboxylic acid (**12**) was decarboxylated by an indirect iodinative–deiodinative procedure (the electron-withdrawing 2-ethoxycarbonyl group prevents direct decarboxylation) to give the β-unsubstituted pyrrole (**14**) in 60% overall yield (from **11**). To manipulate the α-ester for pyrrole coupling, compound **14** was transbenzylated to the bis-benzyl ester **15** and preferentially transmethylated with sodium methoxide in methanol–THF at room temperature to give benzyl 3-(methoxycarbonyl)methyl-5-methylpyrrole-2-carboxylate (**16**) in 77% overall yield. Debenzylation of **16** to pyrrole-2-carboxylic acid **17** and coupling with the formylpyrrole **19** in the usual manner resulted in a low yield of the dipyrromethene **21**, suggesting that the replacement of an alkyl group at the 4-position by a hydrogen atom deactivated the ring towards electrophilic substitution. To overcome this problem, **17** was first decarboxylated to the diunsubstituted pyrrole **18** with trifluoroacetic acid at room temperature. Removal of the electron-withdrawing carboxyl group increased the nucleophilicity of the ring system and the coupling with **19** proceeded smoothly.

The dipyrromethenes **20** and **21** in dichloromethane were condensed separately with the 5-bromo-5′-bromomethyldipyrromethene **22** (18) using stannic chloride as the catalyst to give the biladienes **23** and **24** respectively in over 90% yield. They in turn, when treated with DMSO–pyridine, cyclized to the porphyrins **25** and **28** in over 80% yield. The transformation of the methoxycarbonylmethyl to the required vinyl substituent was effected via 2-hydroxyethyl and 2-chloroethyl groups. For best results, the porphyrins **25** and **28** were metalated (Zn) prior to reduction with lithium aluminum hydride and subsequently demetalated; this avoids any complications that may arise due to the possible irreversible insertion of aluminum. The porphyrins **26** and **29** so obtained (>95% yield) were converted to the 2-chloroethyl analogs **27** and **30** using thionyl chloride (95% yield) and dehydrochlorinated (aqueous NaOH in pyridine) to the vinylporphyrins **8***a* and **8***b* in 85% yield.

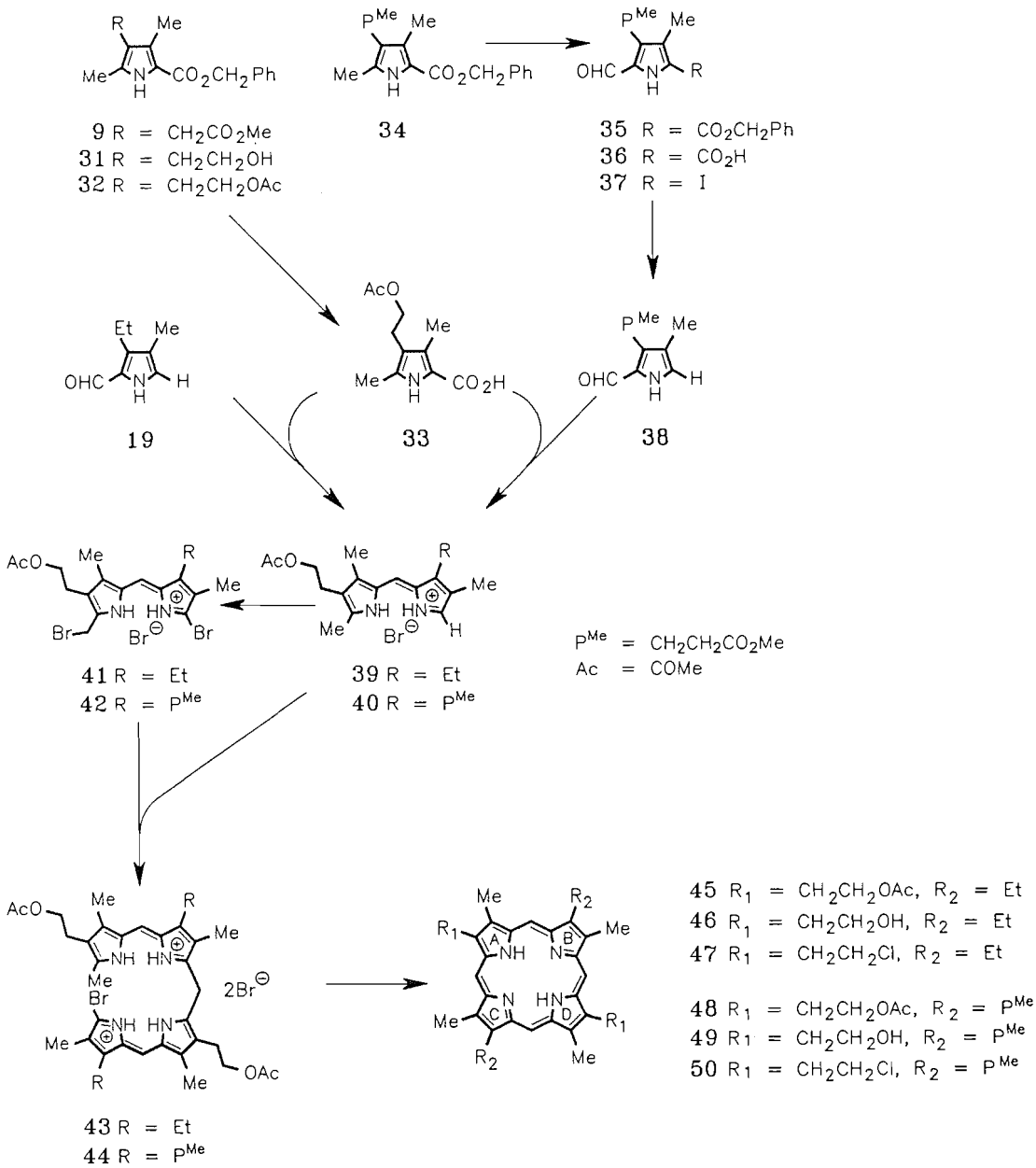
The substituents in the ring A,C-divinylporphyrins **8***c* and **8***d* (Scheme 2) were arranged to give the molecules a twofold axis of symmetry so that the 5-bromo-5′-bromomethyldipyrromethene (**6**) could be obtained by the direct bromination of 5′-unsubstituted 5-methyldipyrromethene (**5**). However, bro-



SCHEME 3

mination of the dipyrromethene **20** (Scheme 3), using bromine in 10–15% trifluoroacetic acid/1,2-dichloroethane turned out to be rather slow, giving at best a 70% yield of the bromomethyl derivative in 2 weeks. This required that the vinyl precursor be modified prior to bromination.

Scheme 4 outlines the synthetic sequence used. The common monopyrrolic precursor **33** was prepared starting from 4-(methoxycarbonyl)methylpyrrole **9**, by diborane reduction to 4-(2-hydroxyethyl)pyrrole **31**, protecting as the 4-(2-acetoxyethyl) derivative (**32**) followed by catalytic debenzylation of the α-ester group. 2-Formyl-3-ethyl-4-methylpyrrole (**19**) (23) and 2-formyl-3-(2-methoxycarbonyl)ethylpyrrole (**38**) (25) were synthesized according to literature procedures. Acid-catalyzed condensation of the pyrrole pairs **19, 33** and **38, 33** afforded the dipyrromethenes **39** and **40** in high yield. The former was successfully brominated (85% yield) with bromine in 10–15% TFA–1,2-dichloroethane, and the product, 5-bromo-5′-bromomethyldipyrromethene (**41**), coupled with **39** itself in the presence of anhydrous stannic chloride to give the biladiene-ac **43** in 79% yield. However, the bromination of the 2-(methoxycarbonyl)ethyl analog **40** under the same conditions was incomplete after 1 week, with the isolated material exhibiting approximately 80% reaction at the α-methyl group. To maximize the yield of the biladiene-ac **44**, the brominated product **42** was coupled, *without isolation* (after removal of excess bromine), with the α-unsubstituted dipyrromethene **40** to give an overall yield of 59% (from **40**). The biladienes **43** and **44** were subsequently cyclized in DMSO–pyridine to give the bis(2-acetoxyethyl)porphyrins **45** and **48** in over 85% yield. Removal of the acetoxy protection using 5% H_2SO_4 – methanol,



SCHEME 4

chlorination with thionyl chloride, and dehydrochlorination with aqueous NaOH in pyridine afforded the ring A,C-divinyl porphyrins **8***c* and **8***d* in high yield.

Experimental

The ^{1}H nmr spectra were recorded in the indicated solvents on a Varian XL-300 or a Bruker WH-400 spectrometer. Low resolution mass spectra were recorded on either a Varian MAT CH4B or a Kratos-AEI MS-50 instrument while high resolution measurements were obtained on the latter instrument. Melting points were determined using a Thomas Kofler Micro Hot Stage apparatus (dipyrromethenes and biladienes decompose rather than melt cleanly).

*Ethyl 4-carboxy-3-(ethoxycarbonyl)methyl-5-methylpyrrole-2-carboxylate (**12**)*

Ethyl-4-benzyloxycarbonyl-3-ethoxycarbonylmethyl-5-methylpyrrole-2-carboxylate (**11**) (37.3 g, 0.10 mol) in THF (500 mL) containing triethylamine (5 drops) and 10% Pd–C (1.5 g) was hydrogenated to completion at room temperature and atmospheric pressure. The catalyst was filtered, the filtrate evaporated to dryness, and the residue redissolved in hot ethanol (300 mL) and crystallized by the addition of water. The product, a white powder, was collected by filtration, washed with water, and dried. Yield 25.0 g (88%), mp 244–246°C; ^{1}H nmr (DMSO-d_6) δ: 1.25 (t, 3H, OCH_2CH_3), 1.32 (t, 3H, OCH_2CH_3), 4.10 (q, 2H, OCH_2CH_3), 4.15 (s, 2H, $CH_2CO_2C_2H_5$), 4.30 (q, 2H, OCH_2CH_3), 8.00 (s, 1H, NH), 11.80 (s, 1H, CO_2H); ms (*m/z*); 283 (M^+), 265, 236. Anal. calcd. for $C_{13}H_{17}NO_6$: C 55.12, H 6.05, N 4.94; found: C 55.07, H 6.10, N 4.85.

*Ethyl 3-(ethoxycarbonyl)methyl-4-iodo-5-methylpyrrole-2-carboxylate (**13**)*

To a hot solution of $NaHCO_3$ (35.0 g) in water (150 mL) was added the carboxypyrrole **12** (23.0 g, 81.3 mmol), and 1,2-dichloroethane (150 mL) added with stirring. A solution of I_2 (25 g) and NaI (30 g) in water (150 mL) was carefully added over 5 min and the reaction mixture refluxed for 15 min. The excess I_2 was destroyed by cautious

addition of aqueous $NaHSO_3$ and the reaction mixture extracted with dichloromethane. The organic phase was filtered, the solvent removed under reduced pressure, and the residual yellowish-brown oil dissolved in warm ethanol. Water was added until the solution turned turbid and, on cooling, the iodopyrrole crystallized out as pale yellow crystals that were filtered, washed with 65% aqueous ethanol, and air dried. Yield 25.6 g (86%), mp 110–111°C; ^{1}H nmr ($CDCl_3$) δ: 1.30 (2t, overlapping, 6H, 2 × OCH_2CH_3), 2.30 (s, 3H, CH_3), 3.80 (s, 2H, $CH_2CO_2C_2H_5$), 4.20 (q, 2H, OCH_2CH_3), 4.30 (q, 2H, OCH_2CH_3), 9.50 (br s, 1H, NH); ms (*m/z*): 365 (M^+), 320, 319, 292. Exact mass calcd. for $C_{12}H_{16}NO_4I$: 365.0123; found: 365.0123.

*Ethyl 3-(ethoxycarbonyl)methyl-5-methylpyrrole-2-carboxylate (**14**)*

The iodopyrrole **13** (21.3 g, 58 mmol) was dissolved in boiling methanol (150 mL) and treated with a solution of NaI (18 g) in water (20 mL), followed immediately by concentrated HCl (10 mL). The solution turned dark brown with liberation of iodine. The mixture was refluxed for 10 min, cooled to room temperature, and solid $NaHSO_3$ was added to destroy the iodine. Water (150 mL) was added to dissolve the excess bisulfite and the mixture extracted with dichloromethane (3 × 100 mL). The combined organic layers were washed with saturated $NaHCO_3$ (2 × 200 mL) and water (200 mL), dried over anhydrous $MgSO_4$, and concentrated to give a pale yellow oil. The oil was dissolved in ether (30 mL) and *n*-hexane added dropwise to induce crystallization. The white crystals were collected by filtration, washed with *n*-hexane, and air dried. Yield 11.0 g (79%), mp 80–81°C; ^{1}H nmr ($CDCl_3$) δ: 1.28 (t, 3H, OCH_2CH_3), 1.35 (t, 3H, OCH_2CH_3), 2.30 (s, 3H, CH_3), 3.82 (s, 2H, $CH_2CO_2C_2H_5$), 4.18 (q, 2H, OCH_2CH_3), 4.30 (q, 2H, OCH_2CH_3), 5.95 (s, 1H, pyr-H), 8.92 (br s, 1H, NH); ms (*m/z*): 239 (M^+), 193, 166. Exact mass calcd. for $C_{12}H_{17}NO_4$: 239.1158; found: 239.1155.

*Benzyl 3-(benzyloxycarbonyl)methyl-5-methylpyrrole-2-carboxylate (**15**)*

The pyrrole (**14**) (6.0 g, 25.2 mmol) in refluxing benzyl alcohol (150 mL) was treated, under nitrogen, with 1-mL portions of a concentrated solution of sodium benzyloxide (prepared from freshly cut sodium in benzyl alcohol) until no further evolution of ethanol vapors occurred. The hot solution was poured into a stirred solution of methanol (100 mL) and acetic acid (10 mL), diluted with water, and cooled. The precipitated solid was collected by filtration, washed with 50% aqueous methanol, then with water, and air dried to give the desired product as colourless crystals. Yield 7.78 g (85%), mp 92–93°C; ^{1}H nmr ($CDCl_3$) δ: 2.24 (s, 3H, CH_3), 2.86 (s, 2H, $CH_2CO_2CH_2C_6H_5$), 5.08 (s, 2H, $CH_2C_6H_5$), 5.21 (s, 2H, $CH_2C_6H_5$), 5.92 (s, 1H, pyr-H), 7.32 (m, 10H, 2 × C_6H_5), 8.70 (br s, 1H, NH); ms (*m/z*): 363 (M^+), 228, 91. Exact mass calcd. for $C_{22}H_{21}NO_4$: 363.1471; found: 363.1470.

*Benzyl 3-(methoxycarbonyl)methyl-5-methylpyrrole-2-carboxylate (**16**)*

A solution of the pyrrole **15** (6.0 g, 17 mmol) in dry tetrahydrofuran (20 mL) and anhydrous methanol (25 mL) was stirred at room temperature under argon with a solution of sodium methoxide (63.3 mg of sodium in 5 mL of methanol). When tlc indicated that no starting material remained, the reaction was quenched with acetic acid (10 mL) and the solution concentrated to a pale yellowish-brown oil, which was dissolved in a minimum of methanol and treated with water to afford a precipitate of tan crystals. The solid was recrystallized from ether–hexane to give the product as colourless crystals (4.30 g, 91%), mp 82–84°C; ^{1}H nmr ($CDCl_3$) δ: 2.25 (s, 3H, CH_3), 3.65 (s, 3H, CO_2CH_3), 3.82 (s, 2H, CH_2CO_2CH3), 5.30 (s, 2H, $CH_2C_6H_5$), 5.95 (s, 1H, pyr-H), 7.40 (m, 5H, C_6H_5), 8.90 (br s, 1H, NH); ms (*m/z*): 287 (M^+), 196, 153, 91. Anal. calcd. for $C_{16}H_{17}NO_4$: C 66.89, H 5.96, N 4.88; found: C 66.69, H 5.95, N 4.84.

*3-(Methoxycarbonyl)methyl-5-methylpyrrole-2-carboxylate (**17**)*

The pyrrole **16** (4.0 g, 14 mmol) in THF (400 mL) containing triethylamine (0.1 mL) and 10% Pd–C (0.4 g) was hydrogenated as described earlier and the resulting pale yellow oil was crystallized from THF–hexane to give the desired product as a white powder (2.6 g, 95%), mp 190°C (dec.); ^{1}H nmr (DMSO-d_6) δ: 2.10 (s, 3H, CH_3), 3.60 (s, 3H, OCH_3), 3.76 (s, 2H, $CH_2CO_2CH_3$), 5.80 (s, 1H, pyr-H), 11.22 (br s, 1H, NH), CO_2H too broad to be observed; ms (*m/z*): 153 ($M^+ - CO_2$), 94. Exact mass calcd. for $C_8H_{11}NO_2$: 153.0790; found: 153.0791.

*4-Methoxycarbonylmethyl-2-methylpyrrole (**18**)*

The foregoing pyrrolecarboxylic acid **17** (2.50 g, 12.7 mmol) was stirred in trifluoroacetic acid (20 mL) under nitrogen for 30 min (reaction monitored by tlc). The trifluoroacetic acid was evaporated *in vacuo*, the residual oil dissolved in dichloromethane (50 mL), washed twice with aqueous $NaHCO_3$, and dried ($MgSO_4$). The filtered solution was evaporated to a yellow oil, which was purified by column chromatography (silica gel 60, dichloromethane eluent) to give the product as a colourless oil (1.85 g, 95%) that could not be induced to crystallize; ^{1}H nmr ($CDCl_3$) δ: 2.30 (s, 3H, CH_3), 3.50 (s, 2H, $CH_2CO_2CH_3$), 3.70 (s, 3H, CO_2CH_3), 5.85 (s, 1H, 4-H), 6.56 (s, 1H, 2-H), 7.86 (br s, 1H, NH); ms (*m/z*): 153 (M^+), 94. Exact mass calcd. for $C_8H_{11}NO_2$: 153.0790; found: 153.0796.

*3′-Ethyl-4-(methoxycarbonyl)methyl-3,4′,5-trimethyl-2,2′-dipyrromethene hydrobromide (**20**)*

3-Ethyl-2-formyl-4-methylpyrrole (**19**) (23) (3.01 g, 21 mmol) and 2-carboxy-4-methoxycarbonylmethyl-3,5-dimethylpyrrole (**10**) (25) (4.22 g, 20 mmol) were dissolved in THF (110 mL) and treated with aqueous HBr (48%, 5 mL). The colour of the solution changed from yellow to dark orange. The solvent was replaced under reduced pressure by adding methanol at regular intervals. The reaction mixture was cooled in an ice bath, the precipitated product filtered, washed with 10% methanol – ether, then with ether, and air dried. Yield 5.15 g (90%), mp 160°C (dec.); ^{1}H nmr ($CDCl_3$) δ: 1.17 (t, 3H, J = 7.5 Hz, CH_2CH_3), 2.10 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 2.70 (q, 2H, CH_2CH_3), 2.75 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 3.71 (s, 2H, CH_2CO), 7.17 (s, 1H, bridge CH), 7.57 (d, 1H, J = 4.0 Hz, pyr-H), 13.23 (br s, 2H, 2 × NH); ms (*m/z*): 286 ($M^+ - HBr$), 271. Exact mass calcd. for $C_{17}H_{22}N_2O_2$: 286.1681; found: 286.1685.

*3′-Ethyl-3-(methoxycarbonyl)methyl-4′,5-dimethyl-2,2′-dipyrromethene hydrobromide (**21**)*

3-Ethyl-2-formyl-4-methylpyrrole (**19**) (1.66 g, 12.1 mmol) and 4-(methoxycarbonyl)methyl-2-methylpyrrole (**18**) in methanol were cooled to 0°C and treated with aqueous HBr (48%, 2 mL). The mixture was stirred for 30 min, when the solution darkened and the product crystallized. The crystals were collected, washed successively with cold methanol, ether, and hexane, and air dried. Yield 3.22 g in three crops (75%), mp 120–121°C; ^{1}H nmr ($CDCl_3$) δ: 1.22 (t, 3H, CH_2CH_3), 2.15 (s, 3H, CH_3), 2.76 (q, 2H, CH_2CH_3), 2.80 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 3.82 (s, 2H, CH_2CO), 6.40 (s, 1H, 4-H), 7.30 (s, 1H, bridge CH), 7.62 (d, 1H, J = 3.0 Hz, 5-H), 13.50 (br s, 2H, 2 × NH); ms (*m/z*): 272 ($M^+ - HBr$), 257, 243. Exact mass calcd. for $C_{16}H_{20}N_2O_2$: 272.1725; found: 272.1728.

*4-(2-Acetoxyethyl)-3′-ethyl-3,4′,5-trimethyl-2,2′-dipyrromethene hydrobromide (**39**)*

Benzyl-4-(2-acetoxyethyl)-3,5-dimethylpyrrole-2-carboxylate (**32**) (20 g, 63 mmol) in THF (300 mL) containing triethylamine (5 drops) and 10% Pd–C (2.0 g) was hydrogenated at room temperature and atmospheric pressure. The catalyst was filtered, and the filtrate treated with a solution of pyrrole **19** (9.6 g, 70 mmol) in THF (75 mL) followed by aqueous HBr (48%, 70 mL). The solvent was slowly replaced with methanol under reduced pressure until crystallization occurred. The orange crystals were filtered, washed with methanol, and air dried. Yield 19 g in two crops (79%), mp 146°C (dec.); ^{1}H nmr ($CDCl_3$/TFA) δ: 1.18 (t, 3H, J = 7.5 Hz, CH_2CH_3), 2.00 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.35 (s, 3H, $COCH_3$), 2.65 (s, 3H, CH_3), 2.75 (m, overlap, 4H, CH_2CH_3 and CH_2CH_2O-), 4.10 (t, 2H, J = 6.5 Hz, CH_2CH_2O-), 6.80 (s, 1H, bridge CH), 7.45 (d, 1H, J = 3.2 Hz, pyr-H), 12.80 (br s, 1H, NH), 13.00 (br s, 1H, NH). Anal. calcd. for $C_{19}H_{27}N_2BrO_2$: C 57.22, H 6.88, N 7.09; found: C 57.68, H 6.85, N 7.05.

*4-(2-Acetoxyethyl)-3'-[(methoxycarbonyl)ethyl]-3,4',5-trimethyl-2,2'-dipyrromethene hydrobromide (**40**)*

The pyrrole **32** (25), (1.35 g, 4.3 mmol) in THF (35 mL) containing triethylamine (5 drops) and 10% Pd–C (140 mg) was hydrogenated as described above. The 2-formylpyrrole **38** (24) (0.85 g, 4.4 mmol) was added, the catalyst filtered, and the volume reduced to 15 mL. Methanol (35 mL) was added, the solution warmed on a water bath and treated with aqueous HBr (1 mL). Following 5 min of heating, trimethyl orthoformate (1 mL) was added and heating was continued for a further 5 min. The solution was concentrated *in vacuo* (ca. 15 mL), diluted with diethyl ether (50 mL), and cooled. The solid was collected by filtration, washed with 5% methanol – diethyl ether, then with ether, and dried in air. Yield 1.67 g (89%), mp 157–159°C; ^{1}H nmr ($CDCl_3$/TFA) δ: 2.05 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.40 (s, 3H, $COCH_3$), 2.57 (t, 2H, CH_2), 2.75 (s, 3H, CH_3), 2.79 (t, 2H, CH_2), 3.02 (t, 2H, CH_2), 3.63 (s, 3H, OCH_3), 4.13 (t, 2H, OCH_2), 7.43 (s, 1H, bridge CH), 7.61 (d, 1H, pyr-H), 13.17 (br s, 1H, NH), 13.35 (br s, 1H, NH); ms (*m/z*): 358 (M^+ − HBr), 284, 223, 211. Exact mass calcd. for $C_{20}H_{26}H_2O_4$: 358.1892; found: 358.1891.

*4-(2-Acetoxyethyl)-5'-bromo-5-bromomethyl-3'-ethyl-3,4'-dimethyl-2,2'-dipyrromethene hydrobromide (**41**)*

4-(2-Acetoxyethyl)-3'-ethyl-3,4',5-trimethyl-2,2'-dipyrromethene hydrobromide **39** (1.5 g, 4 mmol), trifluoroacetic acid (1.5 mL), and bromine (1.9 g, 12 mmol) were stirred in 1,2-dichloroethane (12 mL) at room temperature with exclusion of moisture for 1 week. The solution was cooled and ether (20 mL) added with stirring until crystallization occurred. The crystals were collected, washed with ether, redissolved in dichloromethane (70 mL), and treated with cyclohexene (6 mL). The dichloromethane was replaced by ethyl acetate under reduced pressure, the resulting red crystals were collected, washed with ethyl acetate, then with hexane, and air dried. Yield 1.81 g (85%), mp 175°C (dec.); ^{1}H nmr ($CDCl_3$/TFA) δ: 1.25 (t, 3H, J = 7.5 Hz, CH_2CH_3), 2.10 (s, 3H, CH_3), 2.18 (s, 3H, $COCH_3$), 2.40 (s, 3H, CH_3), 2.75 (q, 2H, J = 7.5 Hz, CH_2CH_3), 3.00 (t, 2H, J = 6.5 Hz, CH_2CH_2O-), 4.50 (t, 2H, J = 6.5 Hz, CH_2CH_2O-), 4.95 (s, 2H, CH_2Br), 7.20 (s, 1H, bridge CH), 13.00 (br 2s, 2H, 2 × NH). Anal. calcd. for $C_{18}H_{23}N_2Br_3O_2$: C 40.10, H 4.30, N 5.20; found: C 39.45, H 4.15, N 4.85.

*1-Bromo-3,8,13-triethyl-18-(methoxycarbonyl)methyl-2,7,12,17,19-pentamethylbiladiene-ac dihydrobromide (**23**)*

The dipyrromethenes **20** (917 mg, 2.5 mmol) and **22** (1.202 g, 2.5 mmol) in dichloromethane (200 mL) were treated with stannic chloride (4 mL) and the mixture stirred for 1.5 h with exclusion of moisture. The reaction was quenched with aqueous HBr (4 mL of 48% HBr in 50 mL of water), the organic phase was poured into a mixture of methanol (100 mL) and aqueous HBr (48%, 25 mL), concentrated *in vacuo*, and allowed to stand in the refrigerator. The desired biladiene was collected by filtration, washed with ethyl acetate, then with *n*-hexane, and air dried. Yield 1.92 g (99%), mp 190°C (dec.); ^{1}H nmr ($CDCl_3$) δ: 0.67, 1.12, 1.22 (3t, 3H each, 3 × CH_2CH_3), 1.98, 2.09, 2.29, 2.35 (4s, 3H each, 4 × CH_3), 2.52 (q, 2H, CH_2CH_3), 2.64 (q, 2H, CH_2CH_3), 2.75 (s, overlap, 3H, CH_3), 2.75 (q, overlap, 2H, CH_2CH_3), 3.48 (s, 2H, CH_2CO), 3.72 (s, 3H, OCH_3), 5.25 (s, 2H, bridge CH_2), 7.12, 7.15 (2s, 1H each, 2 × bridge CH), 13.35, 13.52, 13.70, 13.92 (4 br s, 1H each, 4 × NH); ms (*m/z*): 522 (M^+; cyclized porphyrin product). Exact mass calcd. for $C_{33}H_{38}N_4O_2$: 522.2995; found: 522.2996.

*1-Bromo-3,8,13-triethyl-17-(methoxycarbonyl)methyl-2,7,12,19-tetramethylbiladiene-ac dihydrobromide (**24**)*

This biladiene was similarly prepared from the dipyrromethenes **21** (1.26 g, 3.56 mmol) and **22** (1.72 g, 3.56 mmol) and afforded 2.41 g (90%) of dark reddish-brown crystals, mp 182°C (dec.); ^{1}H nmr ($CDCl_3$) δ: 0.75, 0.92, 1.14 (3t, 3H each, 3 × CH_2CH_3); 1.99, 2.30, 2.31 (3s, 3H each, 3 × CH_3) 3.50 (q, 2H, CH_2CH_3), 2.65 (s, 3H, CH_3), 2.75 (2q, overlap, 2H each, 2 × CH_2CH_3), 3.59 (s, 3H, OCH_3), 3.95 s, 2H, CH_2CO), 5.18 (s, 2H, bridge CH_2), 7.14, 7.15 (2s, 1H each, 2 × bridge CH), 7.32 (s, 1H, β-H), 13.57, 13.65, 13.73, 13.79 (4 br s, 1H each, 4 × NH); ms (*m/z*): 508 (M^+; cyclized porphyrin product). Exact mass calcd. for $C_{32}H_{36}N_4O_2$: 508.2828; found: 508.2838.

*1-Bromo-8,18-bis(2-acetoxyethyl)-3,13-diethyl-2,7,12,17,19-pentamethylbiladiene-ac dihydrobromide (**43**)*

This biladiene was similarly prepared from the dipyrromethenes **39** (0.9 g, 2.4 mmol) and **41** (1.3 g, 2.4 mmol) to give 1.60 g (79%) of product, mp 195°C (dec.); ^{1}H nmr ($CDCl_3$) δ: 1.20 (2t, overlap, 6H, 2 × CH_2CH_3), 2.15 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 2.37 (s, 6H, 2 × $COCH_3$), 2.60–3.00 (m, overlap, 4H, 2 × CH_2CH_3), 2.65, 2.68, 2.70 (3s, 3H each, CH_3), 3.80 (2t, overlap, 4H, 2 × CH_2CH_2O-), 4.40 (2t, overlap, 4H, 2 × CH_2CH_2O-), 4.50 (s, 2H, bridge CH_2), 7.20, 7.26 (2s, 1H each, bridge CH), 11.70–12.60 (4s, 1H each, 4 × NH); ms (*m/z*): 594 (M^+; cyclized porphyrin product). Exact mass calcd. for $C_{32}H_{42}N_4O_4$: 594.3206; found: 594.3208.

*1-Bromo-8,18-bis(2-acetoxyethyl)-3,13-bis[(methoxycarbonyl)ethyl]-2,7,12,17,19-pentamethylbiladiene-ac dihydrobromide (**44**)*

The dipyrromethene **40** (355 mg; 0.81 mmol), trifluoroacetic acid (2.5 mL), bromine (390 mg; 2.4 mmol), and dichloromethane (10 mL) were stirred at room temperature for 2 weeks, protected from moisture. The solvent was removed *in vacuo*, the residue taken into dichloromethane and treated with cyclohexene. The solution was evaporated to dryness, redissolved in dichloromethane (20 mL), stirred in the dipyrromethene **40** (290 mg; 0.66 mmol), and treated with $SnCl_4$ (1 mL) in dichloromethane (1 mL). The solution was allowed to stand at room temperature for 2.5 h and quenched with a mixture of methanol (10 mL) and 48% aqueous HBr (1.5 mL). Dichloromethane (60 mL) was added, the solution extracted with water (2 × 30 mL) and concentrated to ca. 15 mL. Slow addition of diethyl ether resulted in the crystallization of the product, which was filtered, washed with 10% methanol – diethyl ether, and dried in air. Yield 456 mg; 59% overall for 2 steps; ^{1}H nmr ($CDCl_3$) δ: 1.86, 2.00, 2.06, 2.09, 2.37, 2.40 (6s, 3H each, 6 × CH_3), 2.53 (t, 2H, CH_2), 2.60 (t, 2H, CH_2), 2.75 (s, 3H, CH_3), 2.80 (t, 2H, CH_2), 2.96 (2t, overlap, 4H, 2 × CH_2), 3.07 (t, 2H, CH_2), 3.52 (t, 2H, CH_2), 3.62, 3.65, (2s, 3H each, 2 × OCH_3, 4.13 (t, 2H, CH_2), 5.25 (s, 2H, bridge CH_2), 7.35, 7.37, (2s, 1H each, bridge CH), 13.41, 13.54, 13.88, 14.12 (4s, 1H each, NH); ms (*m/z*): 710, (M^+; cyclized porphyrin product), 696, 651, 637. Exact mass calcd. for $C_{40}H_{46}N_4O_8$: 710.3316; found: 710.3322.

*7,12,17-Triethyl-2-(methoxycarbonyl)methyl-3,8,13,18-tetramethylporphyrin (**25**)*

The biladiene **23** (1.60 g, 2.08 mmols) dissolved in DMSO (200 mL) was treated with pyridine (10 mL) and allowed to stand in the dark at room temperature for 5 days. The porphyrin crystals were collected by filtration, washed with methanol, and air dried. Yield 0.89 g in two crops (82%), mp 289–290°C; visible spectrum (CH_2Cl_2) λ_{max} (nm) (relative intensities): 400 (18.5), 498 (2.00), 534 (1.57), 568 (1.08), 620 (1.00); ^{1}H nmr ($CDCl_3$) δ: −3.73 (br s, 2H, 2 × NH), 1.86 (3t, 3H each, 3 × CH_2CH_3), 3.60 (s, 3H, CH_3), 3.65 (s, 9H, 3 × CH_3), 3.76 (s, 3H, OCH_3), 4.03–4.14 (3q, overlap, 2H each, 3 × CH_2CH_3), 5.05 (s, 2H, CH_2CO), 10.07 (s, 2H, 2 × *meso*-H), 11.01, 11.04 (2s, 1H each, 2 × *meso*-H; ms (*m/z*): 522 (M^+). Anal. calcd. for $C_{33}H_{38}N_4O_2$: C 75.83, H 7.33, N 10.72; found: C 75.67, H 7.39, N 10.68.

*7,12,17-Triethyl-2-(2-hydroxyethyl)-3,8,13,18-tetramethylporphyrin (**26**)*

A solution of the porphyrin **25** (200 mg, 0.38 mmol) in dichloromethane (60 mL) was stirred with a saturated solution of zinc acetate in methanol (2 mL) and the metal insertion was monitored by ultraviolet–visible spectroscopy. More dichloromethane (100 mL) was added, the organic phase washed twice with water, and the solvent removed to afford the zinc complex (0.20 g, 90%), which was dried and used without further purification.

In a cooled 250-mL two-necked round-bottomed flask equipped with a magnetic stirring bar and an argon gas inlet was placed a slurry of

lithium aluminum hydride (49.0 mg, 1.28 mmol) in THF (30 mL), which was treated, dropwise, with a solution of the zinc complex (150 mg, 0.26 mmol) in THF. The reaction mixture was allowed to warm to room temperature and stirred for 2 h (progress monitored by tlc). Cold water was carefully added to quench the reaction (H_2 evolved), the mixture was extracted with dichloromethane, and the organic phase shaken with trifluoroacetic acid (3 mL) to demetalate the zinc complex. The excess acid was removed by washing the dichloromethane solution with 5% aqueous $NaHCO_3$, followed by water, and dried ($MgSO_4$). Evaporation of the solvent *in vacuo* afforded the desired porphyrin. Yield 122 mg (95%). A sample was recrystallized from chloroform–ether to give fine purple crystals, mp 275°C (dec.); visible spectrum (CH_2Cl_2) λ_{max} (nm) (relative intensities): 400 (25.2), 498 (2.78), 532 (2.24), 566 (1.65), 620 (1.00); ^{1}H nmr ($CDCl_3$) δ: −3.76 (br s, 2H, 2 × NH), 1.87 (3t, overlap, 9H, 3 × CH_2CH_3), 3.61, 3.64, 3.65, 3.66 (4s, 3H each, 4 × CH_3), 4.10 (3q, overlap, 6H, 3 × CH_2CH_3), 4.35 (t, 2H, CH_2CH_2OH), 4.48 (t, 2H, CH_2CH_2OH), 10.08 (s, 1H, *meso*-H), 10.09, (s, 2H, 2 × *meso*-H), 11.01 (s, 1H, *meso*-H); ms (*m/z*): 494 (M^+), 463. Exact mass calcd. for $C_{32}H_{38}N_4O$: 494. 3046; found: 494.3051.

2-(2-Chloroethyl)-7,12,17-triethyl-3,8,13,18-tetramethylporphyrin (27)

A mixture of the porphyrin (**26**) (200 mg, 0.405 mmol), dichloromethane (100 mL), DMF (20 mL), and K_2CO_3 (6 g) was stirred at room temperature and treated with thionyl chloride (6 mL). On completion of the reaction (monitored by tlc), water was added, the organic phase washed with $NaHCO_3$, followed by water, and dried ($MgSO_4$). After filtration, removal of solvent under reduced pressure gave a purple-brown solid, which was purified by chromatography (silica gel 70–230 mesh, dichloromethane eluent) and recrystallized from chloroform–methanol. Yield 180.4 mg (86%), mp 250°C (dec.); visible spectrum (CH_2Cl_2) λ_{max} (nm) (relative intensities): 398 (34.1), 498 (2.35), 534 (1.82), 566 (1.35), 620 (1.00); ^{1}H nmr ($CDCl_3$) δ: −3.75 (br s, 2H, 2 × NH), 1.88 (2t, overlap, 9H, 3 × CH_2CH_3), 3.61 (s, 3H, CH_3), 3.66 (s, 9H, 3 × CH_3), 4.04–4.14 (3q, overlap, 6H, 3 × CH_2CH_3), 4.32 (t, 2H, CH_2CH_2Cl), 4.52 (t, 2H, CH_2CH_2Cl), 10.01, 10.08, 10.09, 10.11 (4s 1H each, 4 × *meso*-H); ms (*m/z*): 512 (M^+), 497, 478, 463. Exact mass calcd. for $C_{32}H_{37}N_4Cl$: 512.2707; found: 512.2715.

7,12,17-Triethyl-3,8,13,18-tetramethyl-2-vinylporphyrin (8a)

The porphyrin **27** (150 mg, 0.293 mmol) in pyridine (100 mL) was heated at reflux under nitrogen for 10 min and treated with a 10% aqueous NaOH solution (10 mL). Heating was continued for an additional 2 h (completion of reaction shown by tlc), 50% aqueous acetic acid (40 mL) was added, and the mixture was extracted with dichloromethane (200 mL). The organic layer was washed with 5% aqueous $NaHCO_3$ (3 × 200 mL), followed by water (2 × 200 mL), dried ($MgSO_4$), and evaporated to dryness. The residue was chromatographed (silica gel 60, dichloromethane eluent) to give a pink residue after solvent evaporation. Recrystallization from chloroform–methanol gave the title porphyrin as purple prisms. Yield 121.3 mg (87%), mp 220°C (dec.); visible spectrum (CH_2Cl_2) λ_{max} (nm) (relative intensities): 400 (18.6), 502 (2.04), 538 (1.93), 570 (1.40), 624 (1.00); ^{1}H nmr ($CDCl_3$) δ: −3.68 (br s, 2H, 2 × NH), 1.90 (3t, overlap, 3H each, 3 × CH_2CH_3) 6.15 (dd, 1H, J = 1.5, 11.5 Hz, CH=CH_2), 6.36 (dd, 1H, J = 1.5, 17.5 Hz, CH=CH_2), 8.32 (dd, 1H, J = 11.5, 17.5 Hz, CH=CH_2), 10.07 (s, 2H, 2 × *meso*-H), 10.15, 10.23 (2s, 1H each, 2 × *meso*-H); ms (*m/z*): 476 (M^+), 461, 446. Exact mass calcd. for $C_{32}H_{36}H_4$: 476.2940; found: 476.2940. Anal. calcd. for $C_{32}H_{36}N_4$: C 80.63, H 7.61, N 11.76; found: C 80.54, H 7.63, N 11.74.

7,12,17-Triethyl-3-(methoxycarbonyl)methyl-8,13,18-trimethylporphyrin (28)

The biladiene **24** (2.00 g, 2.66 mmol) was cyclized in DMSO (300 mL) and pyridine (10 mL) as described earlier to afford 1.12 g (83%) of the pure product after chromatography and recrystallization; mp 228–230°C; visible spectrum (CH_2Cl_2) λ_{max} (nm) (relative intensities): 398 (29.9), 498 (3.00), 534 (2.37), 566 (1.80), 620 (1.00); ^{1}H nmr ($CDCl_3$) δ: −3.88 (br s, 2H, 2 × NH), 1.85 (3t, overlap, 9H, J = 7.5 Hz, 3 × CH_2CH_3), 3.55, 3.58, 3.62 (3s, 9H, 3 × CH_3), 3.85 (s, 3H, OCH_3), 3.97–4.11 (3q, overlap, 6H, J = 7.5 Hz, 3 × CH_2CH_3), 5.16 (s, 2H, $CH_2CO_2CH_3$), 9.24 (s, 1H, β-H), 10.00–10.12 (4s, 1H each, 4 × *meso*-H); ms (*m/z*): 508 (M^+), 493, 478, 449. Anal. calcd. for $C_{32}H_{36}N_4O_2$: C 75.56, H 7.13, N 11.01; found: C 75.40, H 7.25, N 10.86.

7,12,17-Triethyl-3-(2-hydroxyethyl)-8,13,18-trimethylporphyrin (29)

This was prepared in 95% yield from the porphyrin **28** as described earlier; mp 273–274°C; visible spectrum (CH_2Cl_2) λ_{max} (nm) (relative intensities): 400 (28.17), 498 (2.29), 532 (2.05), 568 (1.78), 620 (1.00); ^{1}H nmr ($CDCl_3$) δ: −3.75 (br s, 2H, 2 × NH), 1.88 (2t, overlap, 9H, 3 × CH_2CH_3), 3.62, 3.65, 3.69 (3s, 3H each, 3 × CH_3), 4.10 (3q, 6H, 3 × CH_2CH_3), 4.45 (t, 2H, CH_2CH_2OH), 4.62 (t, 2H, CH_2CH_2OH), 9.19 (s, 1H, β-H), 10.08–10.16 (4s, 1H each, 4 × *meso*-H); ms (*m/z*): 480 (M^+), 465, 449. Exact mass calcd. for $C_{31}H_{36}N_4O$: 480.2889; found: 480.2892.

3-(2-Chloroethyl)-7,12,17-triethyl-8,13,18-trimethylporphyrin (30)

This was prepared in 95% yield from 2-hydroxyethylporphyrin **29** as described earlier; mp 230–232°C; visible spectrum (CH_2Cl_2) λ_{max} (nm) (relative intensities): 400 (30.1), 502 (2.52), 542 (2.42), 570 (1.73), 626 (1.00); ^{1}H nmr ($CDCl_3$) δ: −3.80 (br s, 2H, 2 × NH), 1.08 (3t, overlap, 9H, 3 × CH_2CH_3), 3.61, 3.65, 3.69 (3s, 3H each, 3 × CH_3), 4.02–4.17 (3q, overlap, 6H, 3 × CH_2CH_3), 4.51 (t, 2H, CH_2CH_2Cl), 4.67 (t, 2H, CH_2CH_2Cl), 9.20 (s, 1H, β-H), 10.10–10.14 (4s, 1H each, 4 × *meso*-H); ms (*m/z*): 498 (M^+), 483, 462. Exact mass calcd. for $C_{31}H_{35}N_4Cl$: 498.2550; found: 498.2552.

7,12,17-Triethyl-8,13,18-trimethyl-3-vinylporphyrin (8b)

This was prepared in 88% yield by the dehydrochlorination of porphyrin **30** as described earlier; mp 221–222°C; visible spectrum (CH_2Cl_2) λ_{max} (nm) (relative intensities): 402 (22.35), 504 (2.27), 544 (2.51), 570 (1.69), 630 (1.00); ^{1}H nmr ($CDCl_3$) δ: −3.66 (s, 2H, 2 × NH), 1.90 (2t, overlap, 9H, 3 × CH_2CH_3), 3.60, 3,64, 3.66 (3s, 9H, 3 × -CH_3), 4.15 (2q, overlap, 6H, 3 × CH_2CH_3), 6.40 (d, 1H, J = 12.0 Hz, CH=CH_2), 6.63 (d, 1H, J = 17.0 Hz, CH=CH_2), 8.47 (dd, 1H, J = 12.0, 17.0 Hz, CH=CH_2), 9.44 (s, 1H, Ar-H), 10.06, 10.07, 10.10, 10.26 (4s, 1H each, 4 × *meso*-H); ms (*m/z*): 462 (M^+), 447, 432. Exact mass calcd. for $C_{31}H_{34}N_4$: 462.2783; found: 462.2784.

2,12-Bis(2-acetoxyethyl)-7,17-diethyl-3,8,13,18-tetramethylporphyrin (45)

The biladiene **43** (1.55 g, 1.85 mmol) was cyclized in DMSO–pyridine as described earlier to afford the title porphyrin in 81% yield. A pure sample was obtained for characterization by column chromatography (silica gel 60, 95:5, dichloromethane–methanol eluent); mp 320°C; visible spectrum (CH_2Cl_2) λ_{max} (nm) (relative intensities): 398 (26.81), 498 (2.66), 534 (2.10), 568 (1.52), 620 (1.00); ^{1}H nmr ($CDCl_3$) δ: −3.80 (br s, 2H, 2 × NH), 1.90 (t, 6H, J = 8.0 Hz, 2 × CH_2CH_3), 2.10 (s, 6H, 2 × C(=O)CH_3), 3.65 (s, 6H, 2 × CH3), 3.70 (s, 6H, 2 × CH_3), 4.15 (q, 4H, J = 8.0 Hz, 2 × CH_2CH_3), 4.38 (t, 4H, J = 8.0 Hz, 2 × CH_2CH_2O-), 4.90 (t, 4H, J = 8.0 Hz, 2 × CH_2CH_2O-), 10.10 (s, 2H, 2 × *meso*-H), 10.15 (s, 2H, 2 × *meso*-H); ms (*m/z*): 594 (M^+), 552, 536, 521. Anal. calcd. for $C_{26}H_{42}N_4O_4$: C 72.70, H 7.12, N 9.42; found: C 72.52, H 7.69, N 9.08.

7,17-Diethyl-2,12-bis(2-hydroxyethyl)-3,8,13,18-tetramethylporphyrin (46)

The bis(acetoxyethyl)porphyrin **45** (600 mg, 1.01 mmol) was dissolved in methanol (150 mL) containing 5% (w/v) concentrated H_2SO_4 and stirred in the dark for 16 h (reaction monitored by tlc). The mixture was poured onto ice (150 g) and the product extracted with dichloromethane. The organic phase was washed with 5% aqueous $NaHCO_3$, dried ($MgSO_4$), and evaporated to dryness to give a purple-red solid, which was recrystallized from chloroform–ether to give the bis(hy-

droxyethyl)porphyrin (505 mg, 98%), mp 240°C (dec.); visible spectrum (CH_2Cl_2) λ_{max} (nm) (relative intensities): 394 (18.41), 496 (2.14), 530 (1.65), 564 (1.28), 618 (1.00); ^{1}H nmr ($CDCl_3$) δ: −3.40 (br s, 2H, 2 × NH), 1.75 (t, 6H, 2 × CH_2CH_3), 3.66 (s, 6H, 2 × CH_3), 3.71 (s, 6H, 2 × CH_3), 4.16 (q, 4H, 2 × CH_2CH_3), 4.56 (t, 4H, 2 × CH_2CH_2OH), 5.04 (t, 4H, 2 × CH_2CH_2OH), 10.65 (s, 2H, 2 × *meso*-H), 10.70 (s, 2H, 2 × *meso*-H); ms (*m/z*): 510 (M^+), 495, 479, 448. Exact mass calcd. for $C_{32}H_{38}N_4O_2$: 510.2995; found: 510.2999.

*2,12-Bis(2-chloroethyl)-7,17-diethyl-3,8,13,18-tetramethylporphyrin (**47**)*

Porphyrin **46** was converted to its bis(chloroethyl) analog **47** in 85% yield as described earlier; mp 324–325°C; visible spectrum (CH_2Cl_2) λ_{max} (nm) (relative intensities): 398 (17.53), 498 (1.69), 534 (1.43), 570 (1.16), 620 (1.00); ^{1}H nmr ($CDCl_3$) δ: −3.75 (br s, 2H, 2 × NH), 1.88 (t, 6H, J = 7.5 Hz, 2 × CH_2CH_3), 3.65 (s, 6H, 2 × CH_3), 3.68 (s, 6H, 2 × CH_3), 4.13 (q, 4H, J = 7.5 Hz, 2 × CH_2CH_3), 4.32 (t, 4H, J = 8.0 Hz, 2 × CH_2CH_2Cl), 4.50 (t, 4H, J = 8.0 Hz, 2 × CH_2CH_2Cl), 10.03 (s, 2H, 2 × *meso*-H), 10.13 (s, 2H, 2 × *meso*-H); Exact mass calcd. for $C_{32}H_{36}N_4Cl_2$: 546.2307; found: 546.2307. Anal. calcd. for $C_{32}H_{36}N_4Cl_2$: C 70.19, H 6.63, N 10.23; found: C 70.25, H 6.58, N 10.20.

*7,17-Diethyl-3,8,13,18-tetramethyl-2,12-divinylporphyrin (**8**c)*

Dehydrochlorination of the porphyrin **47** was carried out as described earlier to afford the title compound in 84% yield; mp 225°C (dec.); visible spectrum (CH_2Cl_2) λ_{max} (nm) (relative intensities): 402 (19.2), 506 (2.05), 546 (2.68), 572 (1.80), 626 (1.00); ^{1}H nmr ($CDCl_3$) δ: −3.66 (br s, 2H, 2 × NH), 1.90 (t, 6H, 2 × CH_2CH_3), 3.68 (s, 6H, 2 × CH_3), 3.72 (s, 6H, 2 × CH_3), 4.15 (q, 4H, 2 × CH_2CH_3), 6.15 (dd, 2H, J = 2.0, 12.0 Hz, CH=CH_2), 6.34 (dd, 2H, J = 2.0, 18.0 Hz, CH=CH_2), 8.32 (dd, J = 12.0, 18.0 Hz, 2H, CH=CH_2), 10.15 (s, 2H, 2 × *meso*-H), 10.23 (s, 2H, 2 × *meso*-H); ^{13}C nmr (10% TFA – $CDCl_3$) δ: 11.71, 12.61 (4C, 4 × -CH_3), 16.18 (2C, 2 × CH_2CH_3); 20.07 (2C, 2 × CH_2CH_3), 99.09, 99.48 (4C, 4 × *meso* carbons); 127.59 (2C, 2 × CH=CH_2), 128.23 (2C, 2 × CH=CH_2), 138.34, 138.60, 140.52, 141.54, 142.82, 145.00, (16C, α- and β-pyrrolic carbons); ms (*m/z*): 474 (M^+) 459, 444. Anal. calcd. for $C_{32}H_{34}N_4$: C 80.98, H 7.22, N 11.80; found: C 80.41, H 7.38, N 11.65.

*2,12-Bis(2-acetoxyethyl)-7,17-[(methoxycarbonyl)ethyl]-3,8,13,18-tetramethylporphyrin (**48**)*

The biladiene **44** (370 mg, 0.39 mmol) dissolved in DMSO (25 mL) was treated with pyridine (1.5 mL) and allowed to stand in the dark at room temperature for 6 days. Methanol (15 mL) was added followed by water (6 mL), the solution was cooled to 0°C, and the porphyrin crystals were filtered and washed with methanol. Yield 194 mg (71%); mp 238–240°C; visible spectrum (CH_2Cl_2) λ_{max} (nm) (relative intensities): 400 (25.6), 498 (2.53), 532 (1.79), 568 (1.35), 620 (1.00); ^{1}H nmr ($CDCl_3$) δ: −3.76 (br s, 2H, 2 × NH), 2.09 (s, 6H, 2 × $COCH_3$), 3.29 (t, 4H, 2 × CH_2CO), 3.67, 3.68, 3.69 (3s, 6H each, 2 × OCH_3, 4 × CH_3), 4.36–4.48 (m, 8H, 2 × CH_2CH_2CO, 2 × CH_2CH_2O), 4.89 (t, 4H, 2 × CH_2O), 10.10, 10.15 (2s, 2H each, 2 × *meso*-H); ms (*m/z*): 710 (M^+), 696, 637, 577. Exact mass calcd. for $C_{40}H_{46}N_4O_8$: 710.3316; found: 710.3320.

*2,12-Bis(2-hydroxyethyl)-7,17-bis[(methoxycarbonyl)ethyl]-3,8,13,18-tetramethylporphyrin (**49**)*

The bis(acetoxyethyl)porphyrin **48** (190 mg, 0.27 mmol) was dissolved in 5% H_2SO_4 – methanol (40 mL) and allowed to stand in the dark for 20 h. Dichloromethane (50 mL) and dilute aqueous sodium acetate (100 mL) were added, the organic phase separated, and was washed with 5% aqueous $NaHCO_3$, then with water, and dried ($NaSO_4$). The product was crystallized by the addition of *n*-hexane. Yield 165 mg (99%); mp 253–255°C; visible spectrum (CH_2Cl_2) λ_{max} (nm) (relative intensities): 400 (20.5), 498 (2.19), 532 (1.63), 568 (1.27), 620 (1.00); ^{1}H nmr ($CDCl_3$/TFA) δ: −3.25 (br s, 2H, 2 × NH), 3.18 (t, 4H, 2 × CH_2CO), 3.66, 3.70, 3.74 (3s, 6H each, 2 × OCH_3, 4 × CH_3), 4.48 (t, 4H, 2 × CH_2CH_2CO), 4.56 (t, 4H, 2 × CH_2CH_2OH), 5.05 (t, 4H, 2 × CH_2OH), 10.73, 10.86 (2s, 2H each, 2 × *meso*-H); ms (*ms/z*): 626 (M^+), 595, 564, 553. Exact mass calcd. for $C_{36}H_{42}N_4O_6$: 626.3104; found: 626.3113.

*2,12-Bis(2-chloroethyl)-7,17-bis[(methoxycarbonyl)ethyl]-3,8,13,18-tetramethylporphyrin (**50**)*

The bis(hydroxyethyl)porphyrin **49** (152 mg, 0.24 mmol) was chlorinated as described earlier. The crude reaction mixture was chromatographed on neutral alumina (4% water added), using dichloromethane as eluent. The product was isolated by crystallization from dichloromethane–*n*-hexane. Yield 143 mg (89%); mp 265–267°C; visible spectrum (CH_2Cl_2) λ_{max} (nm) (relative intensities): 400 (26.8), 498 (2.62), 534 (1.87), 568 (1.40), 622 (1.00); ^{1}H nmr ($CDCl_3$/TFA) δ: −3.15 (t, 4H, 2 × CH_2CO), 3.60, 3.67 3.72 (3s, 6H each 2 × OCH_3, 4 × CH_3), 4.17 (t, 4H, CH_2CH_2CO), 4.43 (t, 4H, CH_2CH_2Cl), 4.56 (t, 4H, CH_2Cl), 10.55, 10.74 (2s, 2H each, 2 × *meso*-H), NH protons not observed; ms (*m/z*): 662 (M^+), 628, 613, 589. Exact mass calcd. for $C_{36}H_{40}N_4O_4Cl_2$: 662.2427; found: 662.2429.

*7,17-Bis[(methoxycarbonyl)ethyl]-3,8,13,18-tetramethyl-2,12-divinylporphyrin (**8**d)*

The bis(chloroethyl)porphyrin **50** (143 mg, 0.22 mmol) in pyridine (30 mL) was heated to reflux and treated with 10% aqueous NaOH (5 mL). Heating was continued for 3 h, the reaction mixture was cooled, 25% aqueous acetic acid (50 mL) and water (25 mL) were added, and the solution concentrated *in vacuo*. The precipitated solid was filtered onto a Celite pad, washed with water, and dried in a vacuum desiccator over KOH.

The product was dissolved in 5% H_2SO_4 – methanol (100 mL), the Celite removed by filtration, and the solution allowed to stand overnight. Dichloromethane (100 mL) was added to the above solution, the organic layer was washed with 5% aqueous $NaHCO_3$, then washed and dried (Na_2SO_4). After filtration, the solution was evaporated to dryness, redissolved in dichloromethane, chromatographed on neutral alumina (4% water added), and the product crystallized from *n*-hexane. Yield 101 mg (79%); mp 268–270°C (lit. (4) mp 270–272°C); visible spectrum (CH_2Cl_2) λ_{max} (nm) (relative intensities): 402 (27.6), 506 (2.57), 544 (2.90), 572 (1.89), 630 (1.00); ^{1}H nmr ($CDCl_3$/TFA) δ: −3.75 (br s, 2H, 2 × NH), 3.27 (t, 4H, 2 × CH_2CO), 3.65, 3.68, 3.71 (3t, 6H each, 2 × OCH_3, 4 × CH_3), 6.18 (dd, 2H, J = 2.0, 12.0 Hz, -CH=CH_2), 6.36 (dd, 2H, J = 2.0, 18.0 Hz, -CH=CH_2), 8.28 (dd, J = 12.0, 18.0 Hz, -CH=CH_2), 10.07, 10.17 (2s, 2H each, *meso*-H); ms (*m/z*): 590 (M^+), 531, 517. Exact mass calcd. for $C_{36}H_{38}N_4O_4$: 590.2893; found: 590.2894.

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