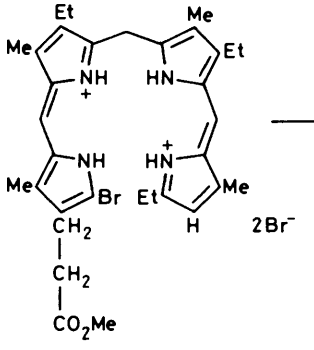
Cyclizations of Terminally Substituted *a,c*-Biladiene Salts to give *meso*-Substituted Porphyrins

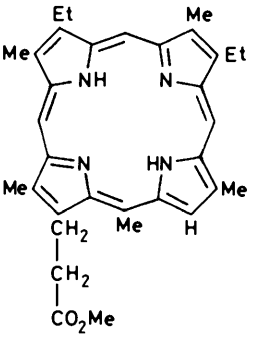
Kevin M. Smith * and Ravindra K. Pandey
Department of Chemistry, University of California, Davis, California 95616

Cyclizations of 1′,8′-disubstituted *a,c*-biladiene salts using copper(II) salts afford the corresponding *meso*-substituted porphyrins (after removal of copper) along with smaller amounts of the corresponding *meso*-unsubstituted analogues. For example, the *a,c*-biladiene salt (**6**) (1′-Me, 8′-Et) affords the corresponding *meso*-methylporphyrin (**10**) as the major product. The diethyl-*a,c*-biladiene (**13**) gave the *meso*-methylporphyrin (**14**). Copper(II) promoted cyclizations of an *a,c*-biladiene (**17**) substituted at the 1′ and 8′ positions with propionic ester groups gives mainly the *meso*-acrylic substituted porphyrin (**18**) after demetallation. The 1′-unsubstituted-8′-propionic ester *a,c*-biladiene salt (**25**), when cyclized using iodine–bromine in hot *o*-dichlorobenzene gives the *meso*-acetic substituted porphyrin (**28**), indicating that such a transformation might provide a viable route for synthesis of chlorophyll-a derivatives.

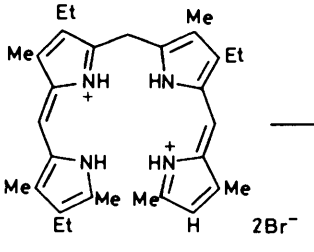
Fischer *et al.*[1] showed that, along with several other porphyrins, a meagre 3.5% yield of a *meso*-methylporphyrin could be obtained by cyclization of a 5-methyl-5′-bromopyrromethene with a 5-ethyl-5′-bromopyrromethene. More than 30 years later, Johnson and co-workers[2] showed that cyclization, in hot *o*-dichlorobenzene, of a 1′-ethyl-8′-bromo-*a,c*-biladiene salt (**1**) gave a 29% yield of the same *meso*-methylporphyrin (**2**), the terminal methyl group of the 1′-ethyl being retained as a *meso*-substituent at the point of cyclization. A similar cyclization of a 1′-(γ-oxobutyrate) substituted *b*-bilene was also a key step in Woodward's chlorophyll synthesis.[3] Copper(II) promoted cyclizations of 1′,8′-dimethyl-*a,c*-biladiene salts (**3**) can, under certain circumstances,[4] afford porphyrins bearing *meso*-methyl (**4**) and *meso*-formyl (**5**) groups. In the present paper we report cyclizations of 1′,8′-dialkyl-*a,c*-biladienes, and show that porphyrins bearing *meso*-substituents of the type necessary for a total synthesis of chlorophyll-a can be obtained.



(**1**)



(**2**)



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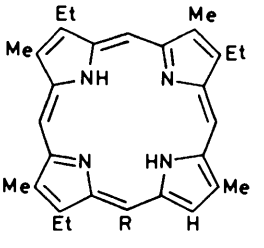
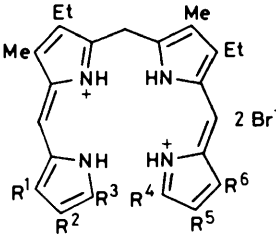
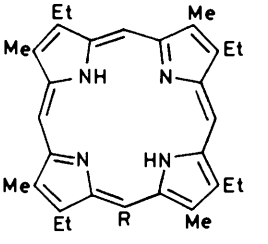


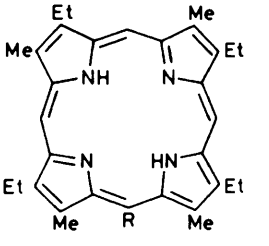
(**4**) R = Me
(**5**) R = CHO



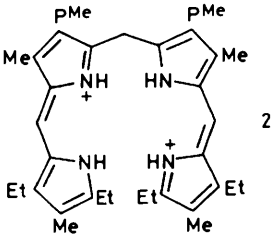
(**6**) $R^1 = R^3 = R^5 = Me$, $R^2 = R^4 = R^6 = Et$
(**7**) $R^1 = R^3 = R^4 = R^6 = Et$, $R^2 = R^5 = Me$
(**8**) $R^1 = R^6 = Me$, $R^2 = R^3 = R^4 = P^{Me}$, $R^5 = H$



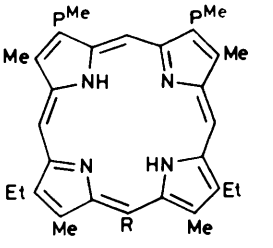
(**9**) R = H
(**10**) R = Me



(**11**) R = Me
(**12**) R = H



(**13**)



(**14**) R = Me
(**15**) R = H

$P^{Me} = CH_2CH_2CO_2Me$

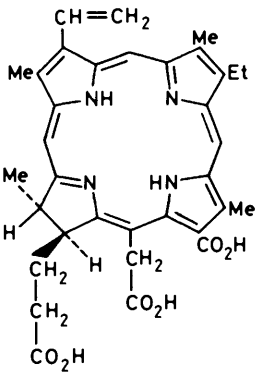
a,c-*Biladiene Cyclizations.*—Copper(II) catalyzed cyclization, followed by removal of copper (10% H_2SO_4 in TFA), of the 1′-methyl-8′-ethyl-*a,c*-biladiene (**6**)* gave, as expected, a mixture of the *meso*-unsubstituted (**9**) (2.5%) and *meso*-methyl (**10**) (20.5%) porphyrins. When the 1′,8′-diethyl-*a,c*-biladiene (**7**) was employed, the *meso*-substituted porphyrin (**11**) (22%), the *meso*-unsubstituted porphyrin (**12**) (1.5%) and some chlorin (spectrophotometry) (<0.5%) were obtained. Likewise, when the related 1′,8′-diethyl-*a,c*-biladiene hydrobromide (**13**) was cyclized, the *meso*-methylporphyrin (**14**) (23%), the corresponding *meso*-unsubstituted porphyrin (**15**) (1.2%), and a mixture of unidentified chlorins were again obtained.

There are several examples of chlorophyll degradation products bearing *meso*-carboxymethyl substituents, the most famous of these being chlorin-e_6 (**16**). In order to obtain a *meso*-methoxycarbonylmethyl-substituted porphyrin using *a,c*-biladiene cyclization, the 1′,8′-bis(2-methoxycarbonylethyl)-*a,c*-biladiene (**17**) was cyclized in dimethylformamide containing copper(II) acetate (145—150 °C, 10 min) to give a 10% yield of the *meso*-acrylic ester porphyrin (**18**), along with a small amount of *meso*-unsubstituted porphyrin (**18a**). We suggest that this porphyrin arises by way of the *meso*-(2-methoxycarbonylethyl)porphyrin (**19**), produced by migration of the whole terminal group,[4] followed by oxidation of the *meso*-propionate group to acrylate. A similar propionate to acrylate oxidation, by way of the intermediate (**20**), was described in Woodward's chlorin-e_6/chlorophyll-a synthesis.[3]

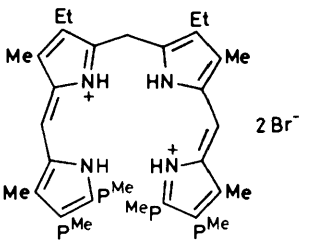
For a chlorophyll-a synthesis, a 6-methoxycarbonylethyl substituent would not be satisfactory; 6-methoxycarbonyl [as in chloroporphyrin-e_6 (**21**)] or 6-unsubstituted [as in (**22**)] would be considerably more useful,† if the corresponding *meso*-acrylates could be obtained. However, cyclization of the *a,c*-biladienes (**23**) or (**24**) gave the *meso*-unsubstituted porphyrin (**26**) in very low yield (<1%), with no *meso*-substituted product, while the 1-unsubstituted *a,c*-biladiene salt (**28**) gave a mixture of porphyrins containing a minor amount of the γ-(2′-methoxycarbonylvinyl)porphyrin (**27**).

In contrast, cyclization of the 1′-unsubstituted 8′-(2-methoxycarbonylethyl)-*a,c*-biladiene hydrobromide (**25**) with bromine–iodine in hot *o*-dichlorobenzene[7] gave a mixture of the *meso*-unsubstituted porphyrin (**28**) (5%) and the *meso*-(methoxycarbonylmethyl)porphyrin (**29**) (12%). We surmise that the initial step in this reaction involves formation of the corresponding 1′-bromo-*a,c*-biladiene analogue (**30**), and that this cyclizes as described by Johnson and co-workers,[2] with a proportion of the *meso*-acetic substituent being eliminated, presumably after porphyrin formation. Woodward[8] has discussed the facile elimination of acetic side chains during porphyrin cyclizations.

a,c-*Biladiene Syntheses.*—All *a,c*-biladiene salts used in this study were prepared using methodology which is now accepted as standard.[9,10] The *a,c*-biladiene (**7**), being symmetrical, was prepared in 79% yield from the pyrromethane (**31**) using 2 mol equiv. of the pyrrolecarbaldehyde (**36**); this pyrrolecarbaldehyde (**36**) was in turn prepared from the pyrrole (**35**) as shown in Scheme 1. Likewise, the *a,c*-biladiene (**17**) was obtained in 80% yield by treatment of the pyrromethane (**32**) with 2 mol equiv. of the pyrrolecarbaldehyde (**37**). The *a,c*-biladiene salt (**13**) was obtained in 86% yield in a similar manner from the pyrromethane (**33**) by treatment with 2 mol equiv. of the pyrrolecarbaldehyde (**36**) (obtained from a standard pyrrole, as shown in Scheme 2).

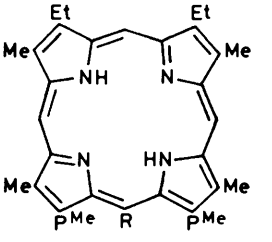


(**16**)

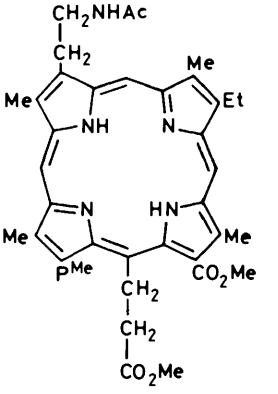


(**17**)

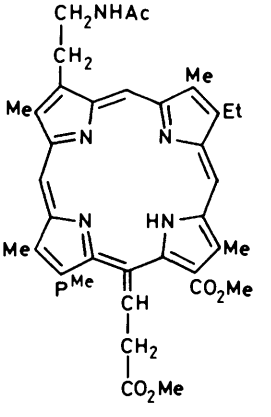
P^{Me} = $CH_2CH_2CO_2Me$



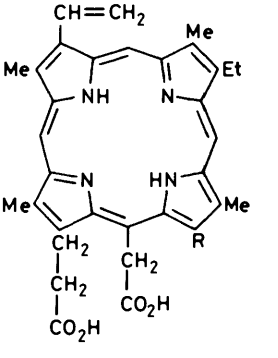
(**18**) R = $CH{=}CHCO_2Me$
(**18a**) R = H



(**19**)



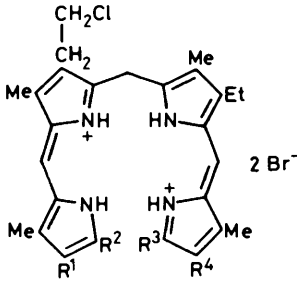
(**20**)



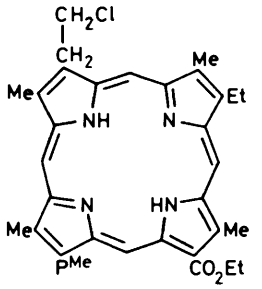
(**21**) R = CO_2H
(**22**) R = H

* *Editor's note.* Throughout, the Fischer form of nomenclature and numbering has been used; this differs from that recommended by the IUPAC authorities for such compounds. As examples of the differences which arise, application of the IUPAC rules of nomenclature to compounds (**6**) and (**39**) would lead to the following names: 2,8,13,17,19-pentaethyl-1,3,7,13,18-pentamethyl-21*H*,24*H*-*ac*-biladiene and 7-chloroethyl-2-ethyl-13,14-bis(2-methoxycarbonylethyl)-3,8,12-trimethyl-5,15-dihydro-16*H*-tripyrrin-1-carboxylic acid 17-hydrobromide, respectively.

† A major problem in any chlorophyll synthesis is the *trans*-reduction of ring D in a porphyrin precursor; Fischer has shown that sodium pentanoate reduction of phyllohemin (bearing a gamma-*meso*-methyl and a 6-unsubstituted position) produces solely the ring D reduced chlorin (*cf.* ref. 6).

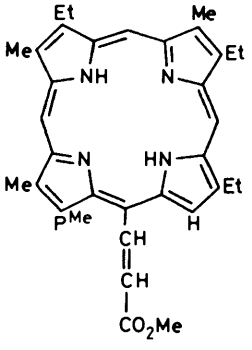


(23) $R^1 = R^2 = R^3 = P^{Me}$, $R^4 = CO_2Et$
(24) $R^1 = R^2 = P^{Me}$, $R^3 = Me$, $R^4 = CO_2Et$
(25) $R^1 = R^2 = R^4 = P^{Me}$, $R^3 = H$

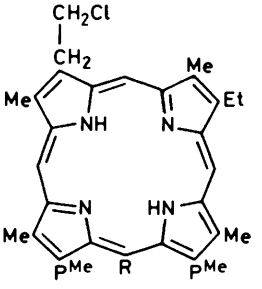


(26)

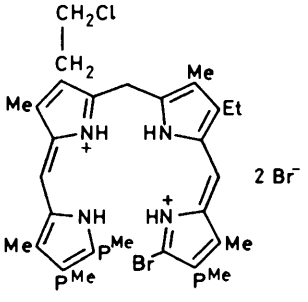
$P^{Me} = CH_2CH_2CO_2Me$



(27)



(28) R = H
(29) R = CH_2CO_2Me

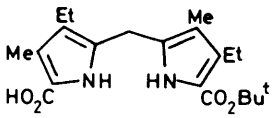


(30)

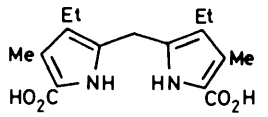
$P^{Me} = CH_2CH_2CO_2Me$

All remaining *a,c*-biladiene hydrobromides were obtained *via* tripyrrenes. Thus, the *a,c*-biladiene (**6**) was obtained in 85% yield by treatment of the tripyrrene hydrobromide (**38**)[11] with the pyrrolecarbaldehyde (**36**).

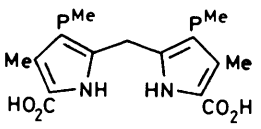
Treatment of the tripyrrene (**44**) with the pyrrolecarbaldehyde (**40**) gave the *a,c*-biladiene (**8**); the pyrrolecarbaldehyde (**40**) was obtained as indicated in Scheme 3, and the tripyrrene hydrobromide (**39**) was obtained by condensation of the pyrrolecarbaldehyde (**37**) with the pyrromethanecarboxylic acid (**34a**). *a,c*-Biladiene dihydrobromide (**23**) was synthesized from the tripyrrene hydrobromide (**39**) by condensation with the pyrrolecarbaldehyde (**41**) (obtained as shown in Scheme 4), and was obtained in 80% yield. The *a,c*-biladiene dihydrobromide (**25**) was prepared along similar lines from the tripyrrene (**39**) and the pyrrolecarbaldehyde (**42**) (prepared



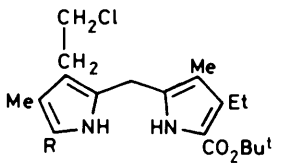
(31)



(32)

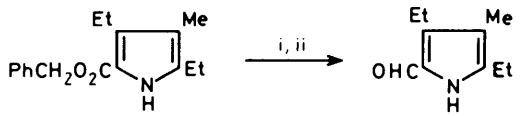


(33)



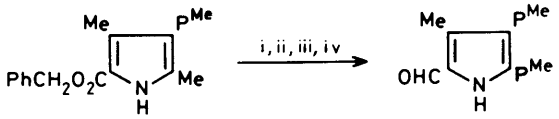
(34) R = CO_2CH_2Ph
(34a) R = CO_2H

$P^{Me} = CH_2CH_2CO_2Me$



(35) (36)

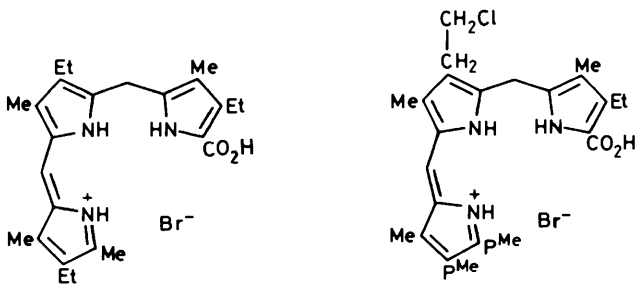
Scheme 1. *Reagents:* i, H_2/Pd-C; ii, $(MeO)_3CH$, TFA



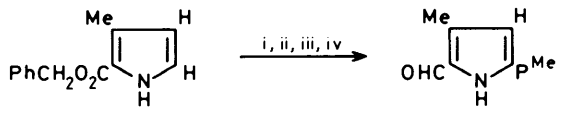
(37)

$P^{Me} = CH_2CH_2CO_2Me$

Scheme 2. *Reagents:* i, $2SO_2Cl_2$, then H_2O; ii, $(EtO)_2P(O)CH_2CO_2Me$/KOH; iii, H_2/Pd-C; iv, $(MeO)_3CH$, TFA



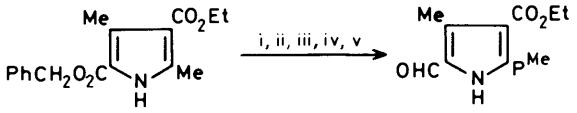
(38) (39)



(40)

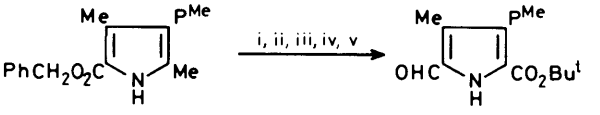
$P^{Me} = CH_2CH_2CO_2Me$

Scheme 3. *Reagents:* i, $POCl_3$/DMF (separate); ii, $(EtO)_2P(O)CH_2CO_2Me$/KOH; iii, H_2/Pd-C; iv, $(MeO)_3CH$, TFA



(41)

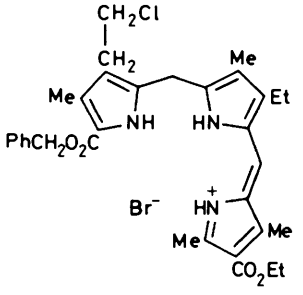
Scheme 4. *Reagents:* i, $2SO_2Cl_2$, then H_2O; ii, $(EtO)_2P(O)CH_2CO_2Me$/KOH; iii, H_2/Pd-C; iv, I_2, KI, $NaHCO_3$; v, PtO_2, H_2



(42)

$P^{Me} = CH_2CH_2CO_2Me$

Scheme 5. *Reagents:* i, $3SO_2Cl_2$, then Bu^tOH; ii, H_2/Pd-C; iii, I_2, KI, $NaHCO_3$; iv, PtO_2, H_2; v, $POCl_3$/DMF



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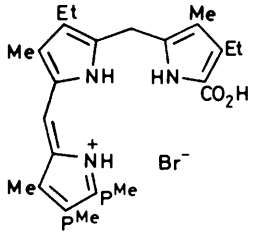

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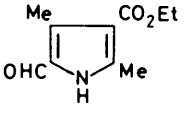

(45)

$P^{Me} = CH_2CH_2CO_2Me$

according to Scheme 5). Treatment of the tripyrrene (**43**) with the pyrrolecarbaldehyde (**37**) gave an 81% yield of the *a,c*-biladiene (**24**). The tripyrrene (**42**) was obtained in 70% yield by treatment of the pyrromethane (**34**) with the pyrrolecarbaldehyde (**45**).

Further experiments designed to develop a simple total synthesis of chlorophyll-a will be reported elsewhere.

Experimental

Melting points were measured on a hot-stage apparatus, and are uncorrected. Silica gel 60 (Merck, 70—230 mesh) or alumina (Merck) were used for column chromatography, and preparative t.l.c. was carried out on 20 × 20 cm glass plates coated with Merck GF 254 silica gel (1 mm thick). Analytical t.l.c. was performed using Merck silica gel 60 F 254 precoated sheets (0.2 mm). Whenever possible, reactions were monitored by t.l.c. and/or spectrophotometry. ^1H N.m.r. spectra were measured in deuteriochloroform solution at 360 MHz using a Nicolet NT-360 spectrometer or at 90 MHz with a Varian EM-390 spectrometer with tetramethylsilane as internal standard. Electronic absorption spectra were measured, in dichloromethane solution, using a Hewlett-Packard 8450A spectrophotometer. Mass spectra were measured on a Finnegan 3200 mass spectrometer (direct insertion probe, 70 eV, 50 μA, source temperature 200—300 °C). Elemental analyses were performed at the Berkeley Microchemical Analysis Laboratory, UC Berkeley.

3,5-*Diethyl*-4-*methylpyrrole*-2-*carbaldehyde* (**36**).—Benzyl 3,5-diethyl-4-methylpyrrole-2-carboxylate[12] (**35**) (5 g) in tetrahydrofuran (THF) (50 ml) containing triethylamine (0.1 ml) was hydrogenated at atmospheric pressure and room temperature over 10% palladized charcoal (500 mg) until uptake of hydrogen ceased. The catalyst was removed by filtration through Celite and the filtrate was evaporated to give the pyrrole-2-carboxylic acid which was treated with trifluoroacetic acid (5 ml) and trimethyl orthoformate (7 ml). The mixture was stirred for 10 min, poured into water (100 ml) and extracted with dichloromethane (2 × 50 ml); the extract was washed with aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (elution with 30% ethyl acetate in cyclohexane), the appropriate eluates being evaporated to afford a residue, which was crystallized from aqueous methanol to give the pyrrolecarbaldehyde (2 g, 66%), m.p. 84—85 °C (Found: C, 72.45; H, 9.0; N, 8.65. $C_{10}H_{15}NO$ requires C, 72.72; H, 9.09; N, 8.48%); δ 9.50 (1 H, s, CHO), 9.40 (1 H, br s, NH), 2.65 (4 H, q, CH_2CH_3), 1.98 (3 H, s, Me), and 1.22 (6 H, t, CH_2CH_3).

Benzyl 4-(2-*Methoxycarbonylethyl*)-5-(2-*methoxycarbonylvinyl*)-3-*methylpyrrole*-2-*carboxylate*.—Benzyl 5-formyl-4-(2-methoxycarbonylethyl)-3-methylpyrrole-2-carboxylate (1.92 g) and diethyl methyl phosphonoacetate (1.97 g) in THF (10 ml) was added to a stirred solution of potassium hydroxide (420 mg) in THF (15 ml) under nitrogen at room temperature. The mixture was stirred for 24 h and then diluted with ether. The ethereal layer was washed with water (3 × 100 ml) dried (Na_2SO_4), and evaporated to dryness. The product was crystallized from dichloromethane–hexane to give white crystals (2.0 g, 92%), m.p. 125—127 °C (Found: C, 65.8; H, 6.25; N, 3.45. $C_{21}H_{23}NO_6$ requires C, 65.44; H, 6.01; N, 3.63%); δ 9.52 (1 H, bs, NH), 7.60, 6.18 (each d, *J* 16 Hz, CH=$CHCO_2Me$), 5.35 (2 H, s, CH_2Ph), 3.65, 3.75 (each 3 H, s, CO_2Me), 2.45, 2.85 (each 2 H, t, CH_2CH_2CO), and 2.30 (3 H, s, Me).

4,5-*Bis*(2-*methoxycarbonylethyl*)-3-*methylpyrrole*-2-*carbaldehyde*.—The foregoing pyrrole (1.5 g) was dissolved in THF (50 ml) and hydrogenated at room temperature and atmospheric pressure over palladized charcoal (150 mg) until uptake of hydrogen ceased. The catalyst was removed by filtration through Celite and the filtrate was evaporated; the residue (pyrrole-2-carboxylic acid) was dissolved in trifluoroacetic acid (3 ml) and after 10 min at room temperature under nitrogen the mixture was cooled to 0 °C before addition of trimethyl orthoformate (5 ml). The mixture was stirred for 10 min, poured into water (100 ml), and extracted with dichloromethane (2 × 50 ml). The extract was washed with aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (elution with 30% ethyl acetate in cyclohexane), the appropriate eluates being evaporated to afford the pyrrolecarbaldehyde (770 mg, 71%) as a viscous oil which failed to crystallize; δ 9.80 (1 H, s, NH), 3.62, 3.65 (each 3 H, s, OMe), 2.32—3.00 (8 H, m, CH_2CH_2CO), and 2.30 (3 H, s, Me).

5-(2-*Methoxycarbonylethyl*)-3-*methylpyrrole*-2-*carbaldehyde* (**40**).—Benzyl 5-(2-methoxycarbonylethyl)-3-methylpyrrole-2-carboxylate[13] (1 g) was hydrogenated, as described above, over

10% palladized charcoal (200 mg) to give the corresponding pyrrole-2-carboxylic acid. This, likewise, was treated with trifluoroacetic acid (3 ml) and trimethyl orthoformate (3 ml) and, after chromatography (silica gel, elution with 30% ethyl acetate in cyclohexane) and crystallization (aqueous methanol) gave 750 mg (65%) of the pyrrolecarbaldehyde, m.p. 76—77 °C (Found: C, 61.65; H, 6.7; N, 7.15. $C_{10}H_{13}NO_3$ requires C, 61.52; H, 6.72; N, 7.16%). δ 10.10 (1 H, br s, NH), 9.52 (1 H, s, CHO), 5.85 (1 H, s, 4-H), 3.65 (3 H, s, OMe), 2.62, 2.90 (each 2 H, t, CH_2CH_2CO), and 2.32 (3 H, s, Me).

Benzyl 4-Ethoxycarbonyl-5-formyl-3-methylpyrrole-2-carboxylate.—Benzyl 4-ethoxycarbonyl-3,5-dimethylpyrrole-2-carboxylate (10 g) in carbon tetrachloride (150 ml) was treated, over a period of 30 min, with a solution of sulphuryl chloride (5.4 ml) in carbon tetrachloride (25 ml). The reaction was monitored by n.m.r. spectroscopy. After the mixture had been stirred for 22 h the solvent was evaporated and the oily residue was dissolved in THF (150 ml) and sodium hydrogen carbonate (12 g) in water (250 ml) was added. The mixture was stirred at room temperature for 24 h. The pale yellow precipitate was filtered off and was chromatographed on a silica gel column, eluting with dichloromethane. The appropriate eluates were collected, evaporated, and the residue crystallized from aqueous methanol to give the product (6.8 g, 65%), m.p. 103—104 °C (Found: C, 64.8; H, 5.35; N, 4.45. $C_{17}H_{17}NO_5$ requires: C, 64.75; H, 5.43; N, 4.44%). δ 10.30 (1 H, s, NH), 7.32 (5 H, s, Ph), 5.30 (2 H, s, CH_2Ph), 4.30 (2 H, q, CH_2CH_3), 2.60 (3 H, s, Me), and 1.35 (3 H, t, CH_2CH_3).

Benzyl 4-Ethoxycarbonyl-5-(2-methoxycarbonylvinyl)-3-methylpyrrole-2-carboxylate.—Crushed potassium hydroxide pellets (1.12 g) were stirred with dry THF (15 ml) under nitrogen. The foregoing pyrrolecarbaldehyde (4.5 g) and diethyl methyl phosphonoacetate (4.5 g) in THF (10 ml) were added to the mixture which was stirred for a further 20 h. The mixture was then diluted with ether (50 ml) and the ethereal layer was washed exhaustively with water, dried (Na_2SO_4), and evaporated to dryness. The residue was crystallized from dichloromethane–hexane to give a white fluffy solid (4.4 g, 90%), m.p. 147—148 °C (Found: C, 64.6; H, 5.6; N, 3.75. $C_{20}H_{21}NO_6$ requires C, 64.68; H, 5.69; N, 3.77%); δ 9.80 (1 H, s, NH), 6.35, 8.30 (each 1 H, d, CH=CH), 5.32 (2 H, s, CH_2Ph), 4.30 (2 H, q, $CO_2CH_2CH_3$), 3.75 (3 H, s, OMe), 2.55 (3 H, s, Me), and 1.35 (3 H, t, $CHCH_3$).

4-Ethoxycarbonyl-5-(2-methoxycarbonylethyl)-3-methylpyrrole-2-carboxylic Acid.—The foregoing pyrrole (4 g) in THF (100 ml) and triethylamine (0.1 ml) was hydrogenated at room temperature and atmospheric pressure with 10% palladized charcoal (400 mg) until uptake of hydrogen ceased. The catalyst was removed by filtration through Celite and the filtrate was evaporated to give a residue which was crystallized from THF–hexane to give a white powder (3 g, 98%), m.p. 150—155 °C (Found: C, 55.5; H, 6.0; N, 4.85. $C_{13}H_{17}NO_6$ requires C, 55.12; H, 6.04; N, 4.94%); δ 4.25 (2 H, q, CH_2CH_3), 3.70 (3 H, s, OMe), 3.30, 2.70 (each 2 H, t, CH_2CH_2CO), 2.60 (3 H, s, Me), and 1.40 (3 H, t, OCH_2CH_3).

Ethyl 2-Iodo-5-(2-methoxycarbonylethyl)-3-methylpyrrole-4-carboxylate.—The foregoing pyrrole (4 g) in methanol (35 ml) was treated with sodium hydrogen carbonate (3.4 g) in water (35 ml) and warmed to 60 °C before addition of a solution of iodine (3.4 g) and potassium iodide (5.5 g) in methanol (45 ml) and water (11 ml) with stirring at a rate such that no permanent colouration developed. Water (40 ml) was then added and the mixture was stirred for a further 1 h. It was then cooled and extracted with dichloromethane (2 × 100 ml) and the extract washed with water (3 × 50 ml), dried (Na_2SO_4), and evaporated to dryness. The residue was chromatographed on silica gel (elution with dichloromethane) the appropriate eluates being collected and evaporated. The resulting residue was crystallized from dichloromethane–hexane to give a white fluffy solid (3.90 g, 76%), m.p. 89—90 °C (Found: C, 39.7; H, 4.5; N, 3.8. $C_{12}H_{16}INO_4$ requires C, 39.47; H, 4.41; N, 3.83%); δ 9.80 (1 H, s, NH), 4.28 (2 H, q, OCH_2CH_3), 3.72 (3 H, s, OMe), 3.26, 2.70 (each 2 H, t, CH_2CH_2CO), 2.26 (3 H, s, Me), and 1.30 (3 H, t, OCH_2CH_3).

Ethyl 5-(2-Methoxycarbonylethyl)-3-methylpyrrole-4-carboxylate—The foregoing iodopyrrole (3.8 g) in methanol (100 ml) containing sodium acetate trihydrate (4 g) and Adams' catalyst (40 mg) was hydrogenated at room temperature and atmospheric pressure until uptake of hydrogen ceased. The catalyst was removed by filtration through Celite and the solvent was evaporated before dilution with dichloromethane (50 ml) and water (50 ml). The organic phase was dried (Na_2SO_4) and evaporated to give a residue which was filtered through a short column of silica gel (elution with dichloromethane). The appropriate eluates were collected and evaporated to give a residue which spontaneously crystallized and was dried *in vacuo*; yield 2.45 g (98%), m.p. 75—77 °C (Found: C, 60.5; H, 7.1; N, 5.75. $C_{12}H_{17}NO_4$ requires C, 60.23; H, 7.16; N, 5.85%); δ 9.78 (1 H, s, NH), 6.40 (1 H, bs, 2-H), 4.30 (2 H, q, OCH_2CH_3), 3.70 (3 H, s, OMe), 3.25 and 2.70 (each 2 H, t, CH_2CH_2CO), 2.28 (3 H, s, Me), and 1.32 (3 H, t, OCH_2CH_3).

Ethyl 2-Formyl-5-(2-methoxycarbonylethyl)-3-methylpyrrole-4-carboxylate (**41**).—The foregoing pyrrole (1 g) in dry dichloromethane (10 ml) was added dropwise, below 0 °C, to the Vilsmeier reagent prepared by mixing phosphoryl chloride (1.2 ml) and dimethylformamide (1.5 ml) in dichloromethane (15 ml). The mixture was stirred at the same temperature for 30 min and then at room temperature for 1 h. It was diluted with dichloromethane (50 ml) and treated with aqueous sodium hydrogen carbonate to maintain the pH at 7, and then stirred at room temperature overnight. The organic layer was separated, washed with water, dried (Na_2SO_4), and evaporated to give a residue which was chromatographed on silica gel (elution with 30% ethyl acetate in cyclohexane). Evaporation of the solvent and crystallization from dichloromethane–hexane gave the pyrrole as a pale yellow solid (900 mg, 81%), m.p. 93—94 °C (Found: C, 58.35; H, 6.35; N, 5.3. $C_{13}H_{17}NO_5$ requires C, 58.41; H, 6.41; N, 5.24%); δ 10.40 (1 H, br s, NH), 4.32 (2 H, q, OCH_2CH_3), 3.70 (3 H, s, OMe), 3.32, 2.75 (each t, CH_2CH_2CO), 2.62 (3 H, s, Me), and 1.40 (3 H, t, OCH_2CH_3).

t-Butyl 5-Formyl-3-(2-methoxycarbonylethyl)-4-methylpyrrole-2-carboxylate, (**42**).—t-Butyl 3-(2-methoxycarbonylethyl)-4-methylpyrrole-2-carboxylate [14] (1 g) in dichloromethane (10 ml) was added to the Vilsmeier reagent [prepared from phosphoryl chloride (0.86 ml) and dimethylformamide (1.0 ml)] in dichloromethane (15 ml) at 0 °C under nitrogen. The mixture was stirred at the same temperature for 1 h and was then worked up as described above to give the title compound (825 mg, 75%) as a viscous oil, δ 9.72 (1 H, s, NH), 9.68 (1 H, br s, NH), 3.60 (3 H, s, OMe), 2.90, 2.42 (each 2 H, t, CH_2CH_2), 2.25 (3 H, s, Me), and 1.55 (9 H, s, Bu^t).

Polypyrroles

3-(2-Chloroethyl)-1-ethyl-6,6′-bis(2-methoxycarbonylethyl-(2,4,5-trimethyltripyrrene-1′-carboxylic Acid, (**39**).—A stirred solution of the pyrromethane–5–carboxylic acid (**34a**) [15] (340 mg) in dichloromethane (40 ml) was treated with the pyrrolecarbaldehyde (**37**) (235 mg) under a nitrogen atmo-

sphere. To this was added toluene-*p*-sulphonic acid (340 mg) in methanol (5 ml) and the mixture was stirred at room temperature for 50 min before spectrophotometry showed the reaction to be complete. The solution was diluted with dichloromethane (100 ml), washed with water (5 × 50 ml), aqueous sodium hydrogen carbonate, and then water again. The organic layer was separated, dried (Na_2SO_4), and evaporated to dryness to give a residue which was taken up in dry dichloromethane (10 ml), treated with dry HBr gas (pipette bubbler) for 5 s, and then rapidly evaporated to dryness. Dry benzene (25 ml) was added as a chaser and then evaporated. Ether (15 ml) was likewise added and rapidly evaporated. The deep red residue was dissolved in dichloromethane (1 ml) and ether was added slowly to induce crystallization of the hydrobromide salt, which was filtered off, washed with cold ether and then air dried; yield 380 mg (70%), m.p. >150 °C (decomp.) (Found: C, 53.55; H, 6.45; N, 6.2. $C_{30}H_{39}BrClN_3O_6$·H_2O requires C, 53.75; H, 6.11; N, 6.25%); $\lambda_{max.}$ 492 nm (ε 48 000); δ 13.35, 13.02, and 10.30 (each 1 H, s, NH), 7.10 (1 H, s, =CH–), 4.40 (2 H, s, CH_2), 3.65, 3.62 (each 3 H, s, OMe), 3.30, 2.90 (each 4 H, m, CH_2CH_2CO), 3.12, 2.52 (each 2 H, t, CH_2CH_2Cl), 2.75 (2 H, q, CH_2CH_3), 2.32, 2.30, and 2.08 (each 3 H, s, Me), and 1.10 (3 H, t, CH_2CH_3).

Benzyl 2-(2-*Chloroethyl*)-6-*ethoxycarbonyl*-4-*ethyl*-1,3,5,6′-*tetramethyltripyrrene*-1′-*carboxylate Hydrobromide*, (**43**) (*with Dr. M. Miura*).—Benzyl 5′-t-butoxycarbonyl-3-(2-chloroethyl)-4-ethyl-3′,4-dimethylpyrromethane-5-carboxylate (**34**) (1.56 g) was stirred in trifluoroacetic acid (5 ml) at room temperature under nitrogen for 5 min before ethyl 5-formyl-2,4-dimethylpyrrole-3-carboxylate (**45**) (477 mg) in methanol (5 ml) was added. The mixture was treated as described above to afford the product (1.44 g, 70%, m.p. >150 °C (decomp.) (Found: C, 60.15; H, 6.0; N, 6.45. $C_{33}H_{39}BrClN_3O_4$ requires C, 60.32; H, 5.98; N, 6.40%); $\lambda_{max.}$ 484 nm (ε 46 500); δ 13.64, 12.24, and 10.70 (each 1 H, s, NH), 7.50 and 7.35 (5 H, m, Ph), 7.20 (1 H, s, =CH), 5.30 (2 H, s, CH_2Ph), 4.40 (2 H, s, CH_2), 4.35 (2 H, q, OCH_2CH_3), 3.42, 2.93 (each 2 H, t, CH_2CH_2Cl), 2.69 (2 H, q, CH_2CH_3), 2.60, 2.27, 2.08, and 1.60 (each 3 H, s, Me), and 1.40 and 1.18 (3 H, t, $CO_2CH_2CH_3$ and CH_2CH_3).

1,3-*Diethyl*-6,6′-*bis*(2-*methoxycarbonylethyl*)-2,4,5-*trimethyltripyrrene*-1′-*carboxylic Acid Hydrobromide*, (**44**).—The pyrromethane-5-carboxylic acid (**31**) (250 mg), pyrrolecarbaldehyde (**37**) (190 mg) and toluene-*p*-sulphonic acid (250 mg) were treated as described above for tripyrrene (**39**) and gave 290 mg (70%) of product, m.p. >150 °C (decomp.) (Found: C, 57.95; H, 6.2; N, 6.55. $C_{30}H_{40}BrN_3O_6$ requires C, 58.25; H, 6.52; N, 6.79%); $\lambda_{max.}$ 485 nm (ε 47 500); δ 13.20, 12.95, and 10.46 (each 1 H, s, NH), 7.10 (1 H, s, =CH–), 4.35 (2 H, s, CH_2), 3.70 (6 H, s, OMe), 2.72, 2.46 (each 2 H, q, CH_2CH_3), 3.30, 3.10, 2.85, and 2.48 (each 2 H, t, CH_2CH_2CO), 2.05 (3 H, s, Me), 2.30 (6 H, s, Me), and 1.08, 0.98 (each 3 H, t, CH_2CH_3).

4,5-*Diethyl*-1,1′,8,8′-*tetrakis*(2-*methoxycarbonylethyl*)-2,3,6,7-*tetramethyl*-a,c-*biladiene Dihydrobromide*, (**17**).—Pyrromethane-5,5′-dicarboxylic acid (**32**)[16] was stirred in trifluoroacetic acid (3 ml) for 10 min under nitrogen before being treated with the pyrrolecarbaldehyde (**37**) (580 mg) in methanol (15 ml) along with 31% HBr in acetic acid (3 ml) and then stirred for 30 min. The mixture was cooled (ice–water bath) and ether was added until *a,c*-biladiene precipitation was complete. The mixture was stirred for a further 30 min after which the product was filtered off, washed with cold ether, and air dried; yield 740 mg (80%), m.p. >300 °C (decomp.) (Found: C, 54.95; H, 6.1; N, 6.2. $C_{43}H_{58}Br_2N_4O_8$·H_2O requires C, 55.12; H, 6.41; N, 5.98%); $\lambda_{max.}$ 454 (ε 23 500) and 530 nm (46 800); δ 13.51, 13.20 (each 2 H, s, NH), 7.10 (2 H, s, =CH–), 5.20 (2 H, s CH_2), 3.71, 3.70 (6 H, each s, OMe), 3.25, 3.10, 2.75, and 2.50 (each m, 20 H, CH_2CH_3 and CH_2CH_2CO), 2.35, 2.25 (6 H, each s, Me), and 0.75 (6 H, t, CH_2CH_3).

1′2,4,6,7,8′-*Hexaethyl*-1,3,5,8-*tetramethyl*-a,c-*biladiene Dihydrobromide*, (**7**).—Treatment of the pyrromethanecarboxylic acid (**31**)[7] (500 mg) and pyrrolecarbaldehyde (**36**) (520 mg) in methanol (10 ml) as described above, using trifluoroacetic acid (4 ml) and 31% HBr in acetic acid (3 ml) afforded the *a,c*-biladiene (845 mg, 79%, m.p. >300 °C (decomp.) (Found: C, 61.1; H, 7.3; N, 8.1. $C_{35}H_{40}Br_2N_4$ requires C, 61.24; H, 7.29; N, 8.16%); $\lambda_{max.}$ 452 (ε 68 000) and 528 nm (66 000); δ 13.32, 13.10 (2 H, each br s, NH), 7.10 (2 H, s, =CH), 5.22 (2 H, s, CH_2), 3.02 (4 H, m, CH_2CH_3), 2.75, 2.72, and 2.50 (each 2 H, q, CH_2CH_3), 2.30, 2.10, 1.98, and 1.65 (each 3 H, s, Me), 1.40 (6 H, t, CH_2CH_3), and 1.25, 1.15, and 0.70 (each 3 H, t, CH_2CH_3).

1′,2,7,8′-*Tetraethyl*-4,5-*bis*(2-*methoxycarbonylethyl*)-1,3,6,8-*tetramethyl*-a,c-*biladiene Dihydrobromide*, (**13**).—This *a,c*-biladiene was likewise prepared from the pyrromethane-5,5′-dicarboxylic acid (**33**)[18] (500 mg) and pyrrolecarbaldehyde (**36**) (390 mg) in methanol (10 ml) in 86% yield (785 mg), m.p. >300 °C (Found: C, 57.95; H, 6.6; N, 6.8. $C_{39}H_{54}Br_2N_4O_4$ requires C, 58.36; H, 6.73; N, 6.98%); $\lambda_{max.}$ 450 (ε 55 000) and 524 nm (53 000); δ 13.50, 13.20 (2 H, each br s, NH), 7.12, 7.10 (each 1 H, s, =CH), 5.25 (2 H, s, CH_2), 2.45 (6 H, s, OMe), 3.10, 2.85, and 2.70 (each m, CH_2CH_3 and CH_2CH_2CO), 2.25, 2.02 (6 H, each s, Me), and 1.40, 1.22 (6 H, each t, CH_2CH_3).

1,4,6,7,8′-*Pentaethyl*-1′,2,3,5,8-*pentamethyl*-a,c-*biladiene Dihydrobromide*, (**6**).—1,3,6-Triethyl-2,4,5,6′-tetramethyltripyrrene-1′-carboxylate hydrobromide (**38**) (630 mg) was stirred in trifluoroacetic acid (5 ml) for 10 min before addition of the pyrrolecarbaldehyde (**36**) (215 mg) in methanol (10 ml) followed by 31% HBr in acetic acid (4 ml). The mixture was stirred for 30 min before dropwise addition of ether to precipitate the product. The precipitate was filtered off, washed with cold ether, and then dried in air; yield 752 mg (85%), m.p. >300 °C (Found: C, 60.95; H, 7.35; N, 8.1. $C_{35}H_{50}Br_2N_4$ requires C, 61.24; H, 7.29; N, 8.16%); $\lambda_{max.}$ 452 (ε 67 000) and 524 nm (65 000); δ 13.32, 13.30 (each 1 H, s, NH), 13.10 (2 H, br s, NH), 7.12 (2 H, s, =CH), 5.20 (2 H, s, CH_2), 3.00 (4 H, m, CH_2CH_3), 2.76, 2.72, and 2.50 (each 2 H, q, CH_2CH_3), 2.70, 2.40, 2.30, 2.26, and 1.95 (each 3 H, s, Me), and 1.40, 1.38, 1.25, 1.15, and 0.67 (each 3H, t, CH_2CH_3).

4-(2-*Chloroethyl*)-8-*ethoxycarbonyl*-6-*ethyl*-1,1′,8′-*tris*(2-*methoxycarbonylethyl*)-2,3,5,7-*tetramethyl*-a,c-*biladiene Dihydrobromide*, (**23**).—This *a,c*-biladiene was likewise prepared from the tripyrrene (**39**) (370 mg) and the pyrrolecarbaldehyde (**41**) (156 mg) in 80% yield (425 mg), m.p. >300 °C (Found: C, 52.15; H, 5.55; N, 6.0. $C_{42}H_{55}Br_2ClN_4O_8$·H_2O requires C, 62.65; H, 5.95; N, 5.85%); $\lambda_{max.}$ 450 (ε 22 000) and 524 nm (60 000); δ 14.10, 13.64, 13.42, and 13.22 (each 1 H, s, NH), 7.41, 7.20 (each 1 H, s, =CH), 5.30 (2 H, s, CH_2), 4.42 (2 H, q, OCH_2CH_3), 3.71, 3.70, and 3.50 (each 3 H, s, OMe), 3.30, 3.25, 3.22, 3.15, 3.02, 3.00, 2.70, and 2.50 (each 2 H, t, CH_2CH_2Cl and CH_2CH_2CO), 2.70, 2.32, 2.30, and 2.00 (each 3 H, s, Me), and 1.20, 1.10 (6 H, t, CH_2CH_3).

4-(2-*Chloroethyl*)-8-*ethoxycarbonyl*-6-*ethyl*-1′,1-*bis*(2-*methoxycarbonylethyl*)-2,3,5,7,8′-*pentamethyl*-a,c-*biladiene Dihydrobromide*, (**24**).—Benzyl 2-(2-chloroethyl)-6-ethoxycarbonyl-4-ethyl-1,3,5,6′-tetramethyltripyrrene-1′-carboxylic acid hydrobromide (**43**) (260 mg) was treated with trifluoroacetic acid and pyrrolecarbaldehyde (**37**) (115 mg) as described above. The reaction yielded 278 mg (81%) of product, m.p. >300 °C (Found: C, 54.3; H, 6.0; N, 6.25. $C_{39}H_{51}Br_2ClN_4O_6$ requires C, 54.02; H, 5.92; N, 6.48%); $\lambda_{max.}$ 450 (ε 44 000) and 522 nm

(60 000); δ 13.80, 13.70, 13.25, and 13.20 (each 1 H, s, NH), 7.31, 7.10 (each 1 H, s, =CH), 5.30 (2 H, s, CH_2), 4.20 (2 H, q, OCH_2CH_3), 3.80 (6 H, s, OMe), 3.00 (2 H, q, OCH_2CH_3), 3.63, 3.60, 3.58, 2,85, 2.70, and 2.50 (each 2 H, t, CH_2CH_2Cl, CH_2CH_2CO), 2.98, 2.75, 2.20, 2.18, and 2.00 (each 3 H, s, Me), and 1.35, 1.12 (each 3 H, t, OCH_2CH_3 and CH_2CH_3).

2,4,5,8-*Tetraethyl*-1,3,6,7,γ-*pentamethylporphyrin*, (**11**).—Copper(II) acetate (2 g) in dimethylformamide (15 ml) was heated to 145 °C before addition of the *a,c*-biladiene dihydrobromide (**7**) (300 mg). The mixture was stirred for 4 min under nitrogen and then poured into water (100 ml) and after cooling extracted with dichloromethane (3 × 75 ml). The organic phases were combined, washed with water (3 × 100 ml), dried (Na_2SO_4), and evaporated to give a residue which was treated with 15% sulphuric acid in trifluoroacetic acid (20 ml) and stirred at room temperature for 1 h under nitrogen; it was then poured into water and extracted with dichloromethane. The extract was washed with aqueous saturated sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated and the residue was chromatographed on alumina (Brockmann Grade III, elution with dichloromethane). Two porphyrins were separated, the least polar (1.5% yield) was identified as 2,4,5,8-tetraethyl-1,3,6,7-tetramethylporphyrin (**12**) (etioporphyrin-III), δ 10.15 (4 H, s, *meso*-H), 4.20 (8 H, q, CH_2CH_3), 3.62 (12 H, s, Me), 1.85 (12 H, t, CH_2CH_3), and −3.75 (2 H, s, NH). The slower running band was crystallized from dichloromethane–hexane to give 47.5 mg (22%), m.p. >300 °C (Found: C, 80.65; H, 8.3; N, 11.35. $C_{33}H_{40}N_4$ requires C, 80.45; H, 8.18; N, 11.37%); $\lambda_{max.}$ 406 (ε 115 000), 504 (15 200), 538 (6200), 574 (6300), and 628 nm (1550); δ 10.02 (2 H, s, *meso*-H), 9.83 (1 H, s, *meso*-H), 4.50 (3 H, s, *meso*-Me), 4.09 (8 H, q, CH_2CH_3), 3.59 (12 H, s, Me), and 1.85 (12 H, t, CH_2CH_3).

2,4,5,7-*Tetraethyl*-1,3,6,8-γ-*pentamethylporphyrin*, (**9**).—The *a,c*-biladiene (**6**) (300 mg) was added to a solution of copper(II) acetate (2.0 g) in dimethylformamide (15 ml) previously heated to 145 °C and stirred for 4 min. After a work-up as described above, chromatography on alumina (Brockmann Grade III, elution with dichloromethane) gave two fractions which were collected separately. The initial fraction yielded a small amount (5.8 mg) of 2,4,5,7-tetraethyl-1,3,5,8-tetramethylporphyrin (**10**) (etioporphyrin-IV); [δ 10.12 (4 H, s, *meso*-H), 4.21 (8 H, q, CH_2CH_3), 3.64 (12 H, s, Me), 1.82 (12 H, t, CH_2CH_3), and −3.74 (2 H, s, NH).] The second fraction (more polar) afforded the title porphyrin (44 mg, 20%), crystallized from dichloromethane–hexane with m.p. >300 °C (Found: C, 79.9; H, 8.1; N, 11.25. $C_{33}H_{40}N_4$ requires C, 80.45; H, 8.18; N, 11.37%); $\lambda_{max.}$ 406 (ε 160 000), 504 (14 500), 538 (5700), 574 (5800), and 628 nm (1500); δ 10.02 (2 H, s, *meso*-H), 9.80 (1 H, s, *meso*-H), 4.58 (3 H, s, *meso*-Me), 4.10 (8 H, m, CH_2CH_3), 3.60 (12 H, s, Me), and 1.85 (12 H, m, CH_2CH_3).

1,4-*Diethyl*-6,7-*bis*(2-*methoxycarbonylethyl*)-2,3,5,8,α-*pentamethylporphyrin*, (**14**).—This porphyrin was likewise prepared from the *a,c*-biladiene (**13**) (350 mg) and copper(II) acetate (3 g) in hot dimethylformamide (20 ml). The residue obtained after the demetallation step was treated with 5% sulphuric acid in methanol (25 ml) and stirred at room temperature overnight; it was then poured into aqueous sodium acetate (100 ml) and extracted with dichloromethane. The extract was washed with aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated and the residue was chromatographed on alumina (Brockmann Grade III, elution with dichloromethane) to give three fractions. The least polar fraction afforded 1,4-diethyl-6,7-bis(2-methoxycarbonylethyl)-2,3,5,8-tetramethylporphyrin (**15**) (mesoporphyrin-XIII dimethyl ester) (5 mg), m.p. 215—216 °C (lit.,[19] m.p. 217 °C); δ 10.15 (4 H, s, *meso*-H), 4.15 (4 H, q, CH_2CH_3), 4.38, 3.30 (each 4 H, t, CH_2CH_2CO), 3.65 (6 H, s, OMe), 3.58, 3.57 (6 H, each s, Me), 1.82 (6 H, t, CH_2CH_3), and −3.75 (2 H, s, NH). Evaporation of the eluates from the second band afforded a green substance which was shown by n.m.r. spectroscopy to be a mixture of chlorins which were not further identified. The most polar fraction afforded the title compound (61 mg, 23%), crystallized from dichloromethane–hexane, m.p. 213—214 °C (Found: C, 72.85; H, 7.25; N, 9.3. $C_{37}H_{44}N_4O_4$ requires C, 73.00; H, 7.29; N, 9.20%); $\lambda_{max.}$ 406 (120 000), 504 (14 000), 538 (5000), 576 (5300), and 628 nm (1000); δ 10.02 (2 H, s, *meso*-H), 9.82 (1 H, s, *meso*-H), 4.50 (3 H, s, *meso*-H), 4.38, 3.30 (4 H, each t, CH_2CH_2CO), 4.10 (4 H, q, CH_2CH_3), 3.62 (6 H, s, OMe), 3.64, 3.60 (6 H, s, Me), 1.82 (6 H, t, CH_2CH_3), and −3.2 (2 H, br s, NH).

2,3-*Diethyl*-6,7-*bis*(2-*methoxycarbonylethyl*)-γ-(2-*methoxycarbonylvinyl*)-1,4,5,8-*tetramethylporphyrin*, (**18**).—This porphyrin was likewise prepared from the *a,c*-biladiene (**17**) (300 mg), and copper(II) acetate (2.5 g) in dimethylformamide (15 ml) at 145 °C. After a work-up as described above, chromatography on alumina (Brockmann Grade III, elution with dichloromethane) gave two fractions. The most mobile fraction afforded the *meso*-unsubstituted porphyrin (**18a**) (mesoporphyrin-III dimethyl ester) (5 mg), m.p. 270—273 °C (lit.,[20] m.p. 270—275 °C, 277—279 °C). The more polar fraction gave the title compound (22 mg, 10%), m.p. 275 °C, crystallized from dichloromethane–hexane (Found: C, 70.05; H, 6.9; N, 7.65. $C_{40}H_{46}N_4O_5 \cdot \frac{1}{2}H_2O$ requires C, 69.78; H, 6.83; N, 8.14%); $\lambda_{max.}$ 404 (150 000), 504, (11 500), 538 (7000), 574 (6300), and 628 nm (2600); δ 10.35, 6.25 (each d, *J* 16 Hz, 1 H, *trans*-CH=CHCO), 10.10 (2 H, s, *meso*-H), 9.85 (1 H, s, *meso*-H), 4.39 (4 H, t, CH_2CH_2CO), 4.16 (4 H, q, CH_2CH_3), 3.87 (3 H, s, $CH{=}CHCO_2Me$), 3.67 (6 H, s, OMe), 3.58 (12 H, s, Me), 3.10 (4 H, t, CH_2CH_2CO), 1.82 (6 H, t, CH_2CH_3), and −3.52 (2 H, s, 2NH); *m/z* (%), 678 (96) and 591 (100).

2-(2-*Chloroethyl*)-4-*ethyl*-6,7-*bis*(2-*methoxycarbonylethyl*)-γ-*methoxycarbonylmethyl*-1,3,5,8-*tetramethylporphyrin*, (**29**).—The tripyrrene (**39**) (360 mg) was treated with trifluoroacetic acid (3 ml) under nitrogen for 10 min before addition of pyrrolecarbaldehyde (**42**) (165 mg) in methanol (10 ml) and 31% HBr in acetic acid. The mixture was stirred for 30 min before ether was added to precipitate the *a,c*-biladiene dihydrobromide (288 mg, 65%) as a red solid, slightly contaminated (spectrophotometry) with some tripyrrene hydrobromide. The product (**25**) (250 mg) was therefore dissolved in *o*-dichlorobenzene (100 ml) along with iodine (202 mg, 5 mol equiv.) and bromine (52 mg, 2 mol equiv.) and the mixture was refluxed for 20 min. It was cooled and passed through a column of alumina [Brockmann Grade III, elution with hexane (to remove *o*-dichlorobenzene) and then with dichloromethane]. The dichloromethane eluates were evaporated and the crude product was separated on preparative silica gel plates (elution with 5% methanol in dichloromethane). Two major bands were isolated; the faster moving of these afforded 2-(2-chloroethyl)-4-ethyl-6,7-bis(2-methoxycarbonylethyl)-1,3,5,8-tetramethylporphyrin (**28**) (15 mg), δ 10.15 (3 H, s, *meso*-H), 9.98 (1 H, s, *meso*-H), 4.75—4.02 (10 H, m, CH_2CH_3 and CH_2CH_2CO and CH_2CH_2Cl), 3.65 (18 H, s, Me, OMe), 3.25 (4 H, t, CH_2CH_2CO), 1.90 (3 H, t, CH_2CH_3), and −3.80 (2 H, br s, NH). The slower moving band gave the title compound which was crystallized from dichloromethane–hexane; yield 24 mg, m.p. 164—166 °C (Found: M^+, 700.303 970. $C_{39}H_{45}ClN_4O_6$ requires *M*, 700.302 76); $\lambda_{max.}$ 408 (ε 120 000), 504 (13 000), 540 (6600), 576 (6000), and 628 nm (2500); *m/z* 700 (100%) and 664 (64); δ 1.10 (2 H, s, *meso*-H), 9.80 (1 H, s, *meso*-H), 6.10 (2 H, bd, CH_2CO), 4.42 and 4.30 (8 H, m, CH_2CH_2Cl and CH_2CH_2CO),

4.10 (2H, q, CH_2CH_3), 3.82, 3.80, and 3.75 (each 3 H, s, OMe), 3.70, 3.45 (each 3 H, s, Me), 3.60 (6 H, s, Me), 3.20 (4 H, t, CH_2CH_2CO), 1.90 (3 H, t, CH_2CH_3), and −3.00 (2 H, br s, NH).

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