Synthetic Studies Relevant to Biosynthetic Research on Vitamin B_{12}. Part 6.[1,2] Synthesis of Chlorins by a Photochemical Approach

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A rational synthetic route to *C*-methylated chlorins has been developed in which a seco-chlorin is constructed and then cyclised photochemically by an 18π-electrocyclic process. The conditions of the synthesis are mild and are compatible with the base-sensitive side-chains of the known naturally occurring *C*-methylated chlorins.

Research into the chemistry of the natural chlorins (for example, the chlorophylls) has been given added impetus by the discovery of *C*-methylated chlorins, the most important of these being Faktor I (**1**)[3-6] and bonellin (**2**).[7-10] The latter is the green pigment of the marine echiuran worm *Bonellia viridis* and is of particular interest because of its masculinising effect on *B. viridis* larvae[11] and its anti-tumour activity.[12] The former, Faktor I, isolated from the vitamin B_{12}-producer *Clostridium tetanomorphum*.[3,6] is derived by air oxidation from the mono-*C*-methylated intermediate on the biosynthetic pathway from uroporphyrinogen III to vitamin B_{12}.

The first two papers in this Series[13,14] described the development of the first rational synthetic routes to simple *C*-methylated chlorins, which could be used, in principle, for the construction of the natural products (**1**) and (**2**). However, it seemed likely that the rather vigorous conditions employed for the final cyclisations to give the chlorin macrocycle would prove incompatible with the delicate acetate residues of Faktor I (**1**). Nevertheless, this work provided valuable experience of constructing bicyclic species containing both reduced and pyrrolic rings, and also guided our researches towards schemes in which the substrates for the final cyclisation step were at the same oxidation level as the target macrocycles. Montforts' synthesis of a *C*-methylated chlorin[15] also utilised an approach in which the final cyclisation step was performed at a constant oxidation level.

More recent papers[16] described the development of a route to the isobacteriochlorin macrocycles (**3**) and (**4**), involving first the building of the seco-systems (**5**) and (**6**), which were then cyclised photochemically. This approach was fully compatible with the reactive acetate and propionate side-chains present in the macrocycle (**4**). The illustrated forms of the seco-systems (**5**) and (**6**) are the supposed reacting tautomers which possess an 18π-electron conjugated chromophore. Comparison of the seco-isobacteriochlorin (**5**), for example, with the two possible seco-chlorin systems, (**7**) and (**8**), reveals that, despite the presence of an additional double bond in either ring A or B, the length of the π-system remains unchanged. Therefore the required ring-closure leading to chlorins is again an 18π-electrocyclic reaction, for which the symmetry-allowed processes are either (*a*) photochemically antarafacial (conrotatory), or (*b*) thermally suprafacial (disrotatory). For reasons discussed earlier,[16] it was expected that the favoured mode of cyclisation would be the antarafacial closure of a helical seco-macrocycle under photochemical conditions.

Bearing in mind that the ultimate synthetic target was to be Faktor I itself (**1**), the immediate aim was to synthesize the chlorin (**9**), in which the B, C, and D rings carry the same substituents as the natural product. Also, position 2 of ring A in structure (**9**) is quaternary [*cf.* Faktor I (**1**)] although simply carrying two methyl groups.

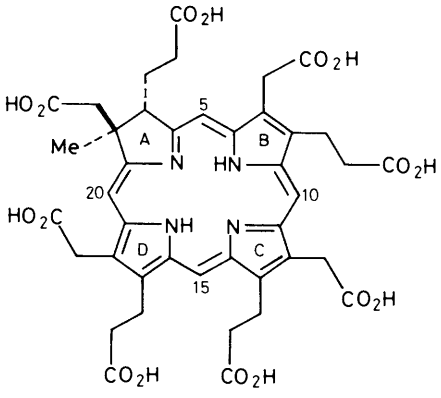
In contrast to the isobacteriochlorins, the chlorin macrocycle may be disconnected between either the A and B or A and D rings to yield appropriate seco-macrocyclic precursors. So that the methodology developed for the synthesis of the isobacteriochlorins involving construction of an A-D building block could be utilised in the present study, a strategy based on a disconnection between the A and B rings was selected. Of the two possible seco-systems resulting from an A/B disconnection, [see the seco-chlorins (**7**) and (**8**)], that in which the carbon destined to become C-5 of the chlorin was carried as a methyl group on the reduced A ring (**10**) appeared the more readily accessible. A further retrosynthetic disconnection between the C and D rings leads to the previously described[16] 'western' bicyclic imine (**11**) and the 'eastern' formyl imidate (**12**) (Scheme 1). The alternative approach in which the formyl group destined to become C-15 of the chlorin (**9**) is carried on the western component was considered to be a less viable option.

Construction of the required eastern portion (**12**) depended on preparation of the bicyclic lactam (**13**) which was planned to be made by base-catalysed condensation of a pyrrol-2(5*H*)-one *e.g.* (**16**) with a 2-formylpyrrole.[17] Rapid access to the pyrrolone (**16**) was offered by the report[18] that 5-bromopyrrole-2-carboxylic esters could be hydrolysed to give, surprisingly, a mixture of regioisomeric pyrrol-2-ones. The required bromo pyrrole (**15**) was prepared in good yield by brominative decarboxylation of the carboxylic acid (**14**)[19] and by studying several different hydrolytic conditions, the most satisfactory was found to be methanolic sulphuric acid. However, the required pyrrolone (**16**) could be obtained only in 13% yield, together with 18% of its regioisomer (**17**). Base-catalysed condensation of the pyrrolone (**16**) with the readily available formylpyrrole (**18**)[16] using Gossauer's procedure,[17,20] followed by re-esterification with diazomethane, gave a low yield of the required bicyclic lactam (**13**) (Scheme 2). However, this route was superseded by the expeditious method described below.

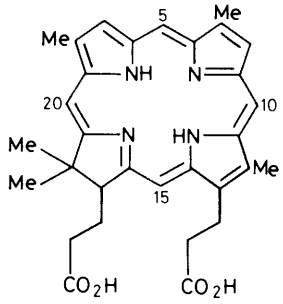
The substantially greater electrophilicity of the pyrromethene (dipyrrin)* system, relative to that of pyrrole, suggested that an analogous hydrolysis of a 5-bromo pyrromethene might proceed under neutral or basic conditions to give a bicyclic lactam directly, *cf.* ref. 21. Indeed, we were encouraged by a recent preparation of the biliverdin system which made use of very similar transformations[22] to those envisaged above.

Bromopyrromethenes are available by the action of bromine on dipyrromethanes and when acetate residues are present in the molecule, formic acid is the preferred solvent.[23] The necessary conditions were worked out using the available dipyrromethane[24] (**20**). This was treated with 2 mol equiv. of

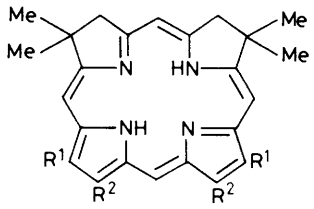
* Although pyrromethene nomenclature is used here, the systematic dipyrrin nomenclature is used throughout the Experimental section.



(1)

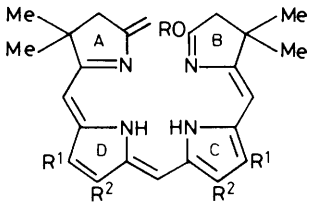


(2)



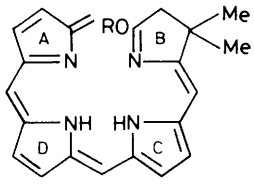
(3) $R^1 = R^2 = Me$

(4) $R^1 = A^{Me}$, $R^2 = P^{Me}$

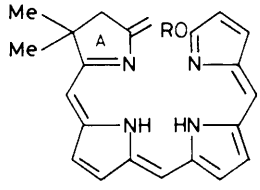


(5) $R^1 = R^2 = Me$

(6) $R^1 = A^{Me}$, $R^2 = P^{Me}$



(7)



(8)

$A^{Me} = CH_2CO_2Me$

$P^{Me} = CH_2CH_2CO_2Me$

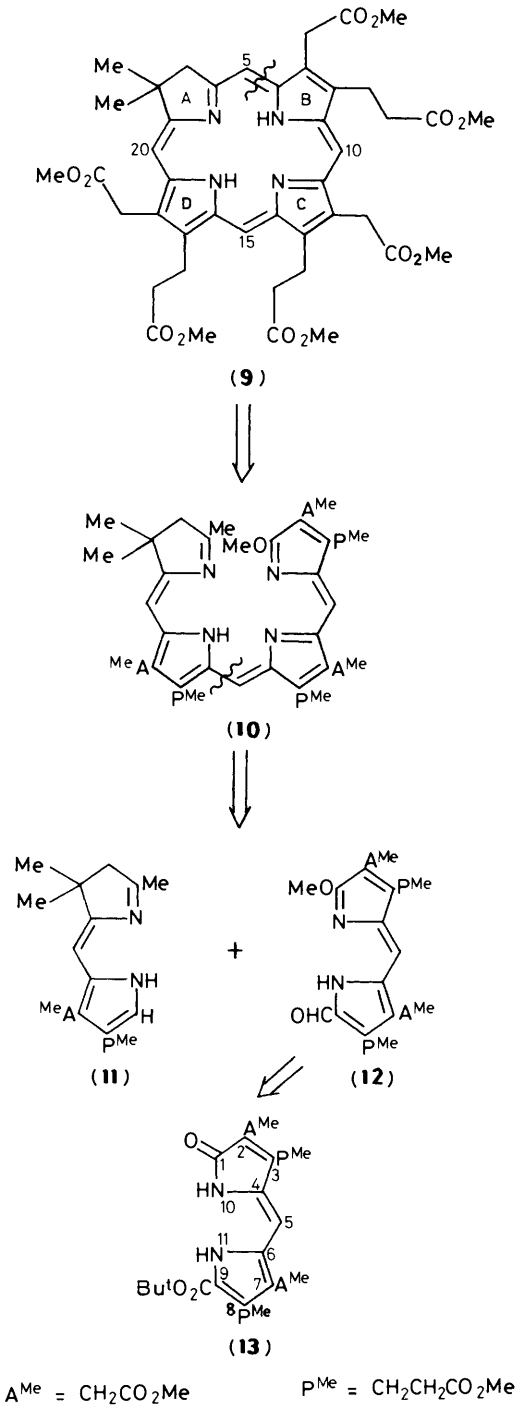
bromine in dry formic acid buffered with sodium formate; the latter was necessary to preserve the *t*-butyl ester which otherwise would have been cleaved by the hydrogen bromide formed in the reaction. An aqueous work-up then afforded the bicyclic lactam (**21**) in 50% yield. The product (**21**) was assigned the *Z*-configuration on the basis of a large bathochromic shift in its u.v./visible absorption maximum on the addition of Zn^{II} ions.[25]

Preparation of the appropriate dipyrromethane (**25**) to yield the bicyclic lactam (**13**) was as follows. Condensation of the acetoxymethylpyrrole (**22**) with the α-free pyrrole (**23**) using toluene-*p*-sulphonic acid in dichloromethane afforded an 81% yield of the differentially protected dipyrromethane (**24**). Subsequent hydrogenolysis gave the monocarboxylic acid (**25**) in 97% yield. Bromination and hydrolysis as above then afforded the bicyclic lactam (**13**) in 51% yield. Deprotection, decarboxylation, and formylation, using the orthoformate method,[26] yielded the formyl lactam (**26**), which was then converted, in 59% yield, into the imidate (**12**) by treatment with Meerwein's reagent and Hunig's base (Scheme 3).[25] The required *O*-methylated product (**12**) was accompanied by up to 30% of the separable *N*-methyl formyl lactam (**27**). Unlike the systems (**12**), (**13**), (**21**), and (**26**), the *N*-methylated product (**27**) showed no bathochromic shift of its u.v./visible absorption maximum in the presence of zinc acetate, consistent with its inability to form a zinc chelate.

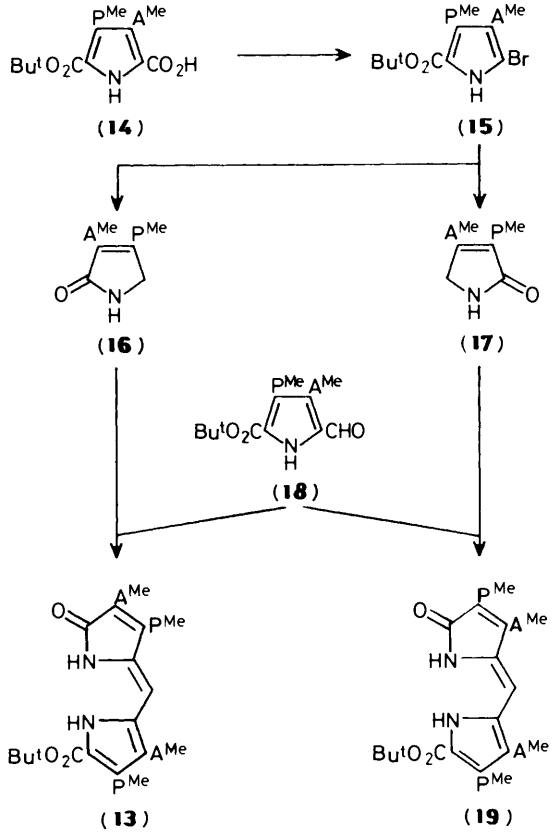
The bicyclic lactam (**13**) prepared by the above route was identical with the product prepared earlier in low yield by condensation of the components (**16**) and (**18**). This correlation established the structure of the pyrrolone used as being (**16**) and accordingly its isomer has structure (**17**) thus providing evidence previously lacking. For completeness, the pyrrolone (**17**) was condensed with the aldehyde (**18**) to afford the bicyclic lactam (**19**) (Scheme 3).

With both building blocks (**12**) and (**28**)[16] available, we turned to the problem of forming the seco-chlorin (**10**). Treatment of the t-butyl ester (**28**) with trifluoroacetic acid generated the unstable α-free pyrrole (**11**) which was condensed directly with the aldehyde (**12**). Under the conditions used for the work on isobacteriochlorins,[16] involving trifluoroacetic acid–methanol containing trimethyl orthoformate, the condensation was inefficient; the seco-compound (**10**) was always accompanied by the tetrapyrrolic dimer (**30**), formed by condensation of two molecules of (**11**) with the orthoformate. However, it was found that, in contrast to the isobacteriochlorin series, the imidate function of system (**12**) was relatively stable to hydrolysis, so that the orthformate could safely be omitted. The best conditions involved treatment of a mixture of the starting materials (**28**) and (**12**) with trifluoroacetic acid; by generating the α-free pyrrole (**11**) *in situ*, the amount of trifluoracetylated material (**29**) formed was reduced. Adjustment of the protonation state of the seco-system (**10**) followed by irradiation then smoothly yielded the chlorin (**9**) (Scheme 4).

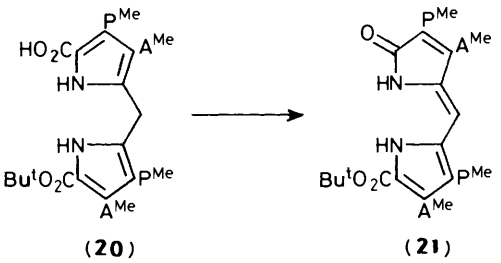
We found from the early cyclisation experiments performed in flasks fitted with septum caps that destruction of pigment was occurring during prolonged irradiation. Trace amounts of oxygenated chlorins were detected as by-products indicating that photo-oxidation was involved both of the product chlorin (**9**) and of its seco-precursor (**10**). Photo-oxidation was avoided by working in a rigorously degassed solution in a sealed-tube. Also, it was found that the photocyclisation could be achieved by irradiation at the long-wavelength absorption (580—680 nm) of the seco-chlorin (**10**). Therefore, the sample was irradiated through a filter of aqueous sodium dichromate, having effectively zero transmittance below 540 nm; the rate of ring-closure was barely affected. Under these conditions, the chlorin (**9**) could be obtained in 54% overall yield from the formyl imidate (**12**).



Scheme 1



Scheme 2

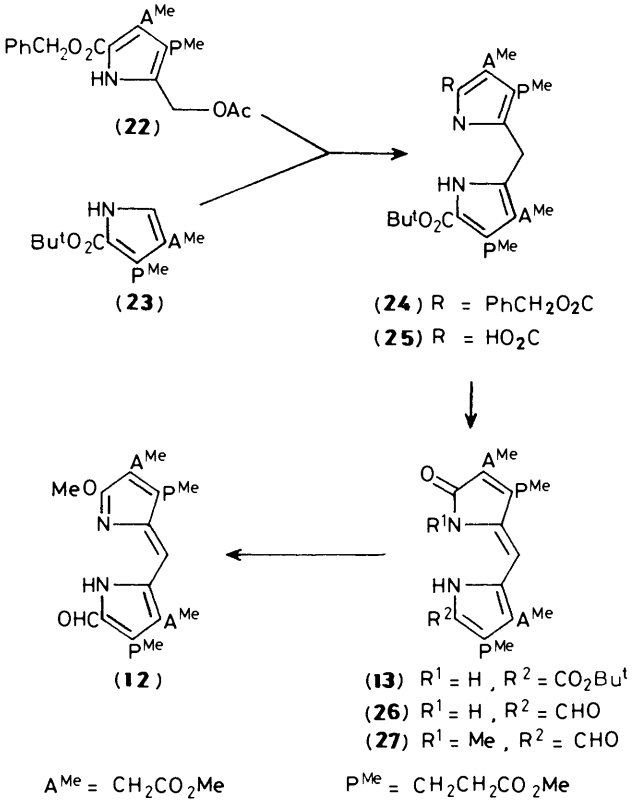


Metal-templated Cyclisations.—In neither the current work nor in the synthetic studies on isobacteriochlorins[16] were any corrinoid pigments detected. In principle, these corrinoids might arise from the seco-system (**10**) by a 16π-electron electrocyclic process and this aspect is fully discussed in ref. 16. Similar 16π-cyclisations have been extensively studied by Eschenmoser's group,[27] including ring-closures which make use of metal templates. It was therefore of interest to make a brief exploration of the effect of metal ions on the cyclisation of the seco-chlorin (**10**) to give the chlorin (**9**).

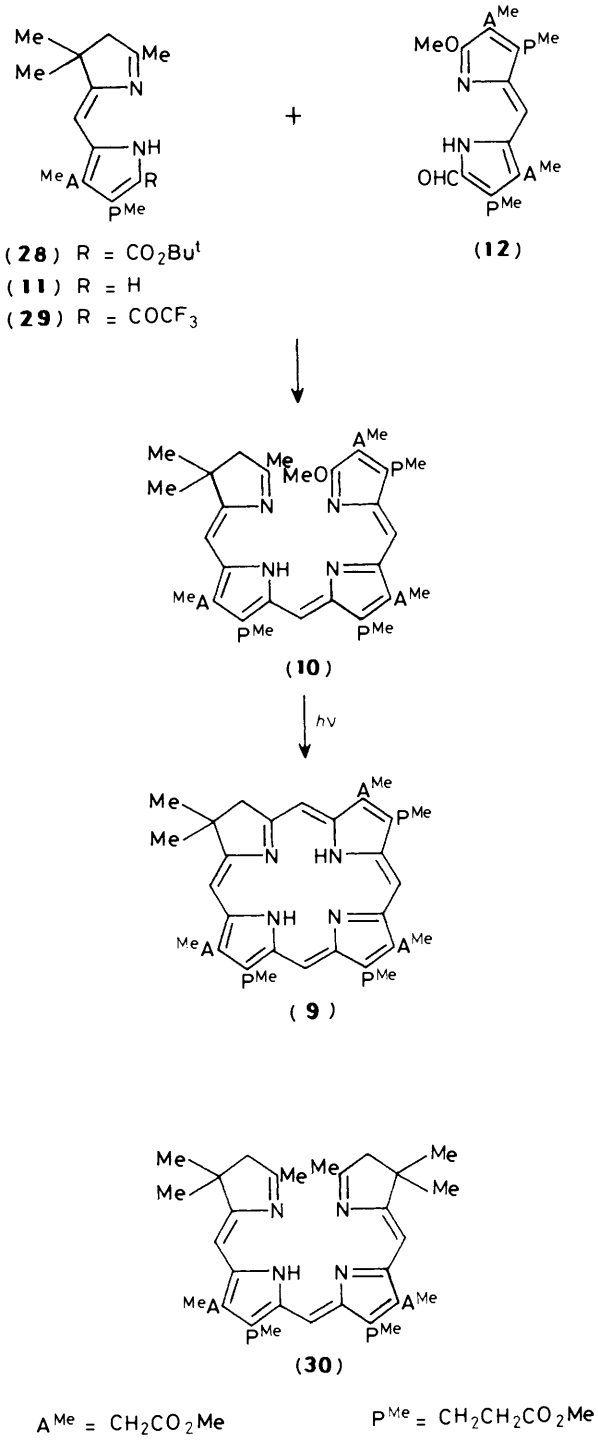
Irradiation of the zinc(II) complex of the seco-chlorin (**10**) as above led to the formation of the chlorin zinc complex, which could either be isolated or demetallated with acid during work-up to give the metal-free macrocycle (**9**) in yields comparable to similar untemplated photocyclisations. Use of copper(II) as the template ion caused rapid decomposition of the seco-compound (**10**) during irradiation and only a trace of the chlorin copper complex could be detected; in neither case was any detectable quantity of corrinoid pigment formed. Further studies are warranted to ascertain how metal templates affect the cyclisation which yields chlorins [*e.g.* (**9**)].

An Alternative Disconnection Strategy.—In planning the foregoing synthesis of the chlorin (**9**), it seemed probable that disconnection of the seco-chlorin (**10**) to give the aldehyde (**33**) and the imidate (**32**) would be less successful than the strategy described above. However, we wished to be sure and so the bicyclic lactam (**13**) was treated with trifluoroacetic acid to afford the α-free bicyclic lactam (**31**) in 83% yield and from it the corresponding imidate (**32**) was obtained in 87% yield (Scheme 5); no significant amount of *N*-methylated by-product was formed.

Formylation of the 'western' A-D component (**11**) proved



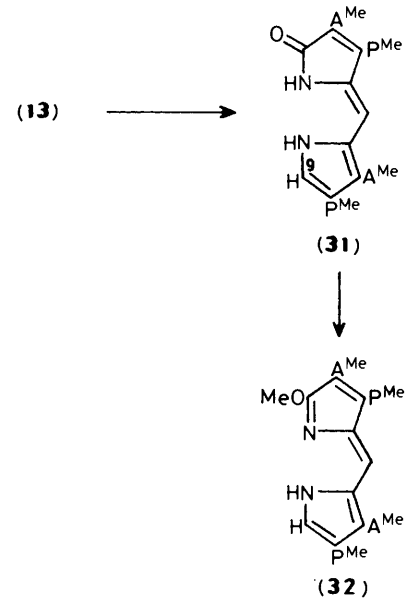
Scheme 3



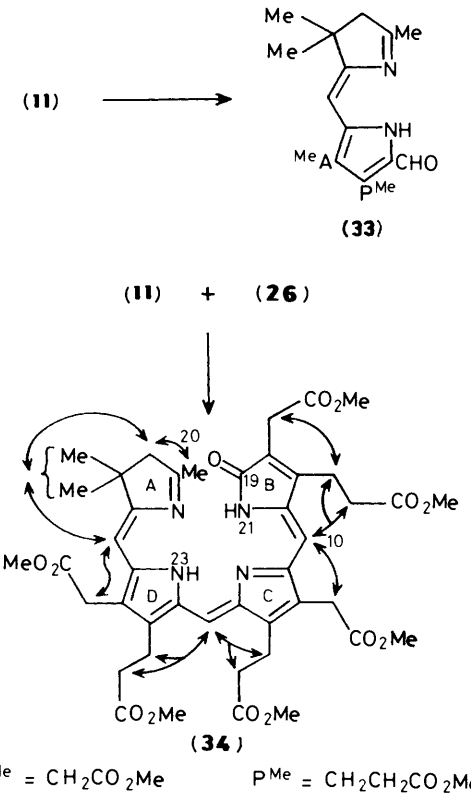
Scheme 4

more difficult. Using the standard orthoformate method,[26] the main products were the coupled product (**30**), together with the trifluoroacetyl derivative (**29**). By performing the reaction at high dilution, formation of the former by-product could be suppressed and the required formylpyrrole (**33**) was isolated in up to 25% yield. It was unstable and was used immediately without full characterisation for direct condensation with the imidate (**32**). However, the characteristic chromophore of the seco-system (**10**) did not appear, thus confirming our initial predictions.

Conformational Studies on a Seco-chlorin.—In accord with the findings for the isobacteriochlorin photocyclisations,[16] it was shown that transformation of the seco-system (**10**) into the chlorin (**9**) occurs only on irradiation; no reaction takes place in the dark. The symmetry-imposed requirement for this photochemical cyclisation step to be antarafacial demands a pseudo-helical transition state. Several biliverdins or biliverdin imidates [which are related in structure to compound (**10**)] have been shown to adopt helical conformations in the crystalline state.[28] In order to obtain similar evidence in the present series, we turned away from the labile seco-imidate (**10**) to the corresponding tetracyclic lactam (**34**). Acid-catalysed condensation of the imine (**11**) and the formyl lactam (**26**) afforded an excellent yield of the seco-lactam (**34**) which was fully characterised and was crystalline. An *X*-ray structure determination by Dr. W. B. Cruse[29] is illustrated in the Figure. These show that in the crystalline state, the lactam (**34**) assumes the all-*syn* conformation and is indeed helical with the individual five-membered rings, including their α-CH groups essentially planar. The distortion of the molecule from planarity is evenly distributed among the 3 methine bridges; the angles between adjacent five-membered ring-planes (defined by the least-squares plane through each ring and its α-CH group) are 10.0, 17.2, and 14.4° for the A and D, D and C, and C and B rings, respectively. The two hydrogen atoms bonded to nitrogen were revealed by a difference map to be bonded exclusively to N-21 and N-23. Therefore, the seco-lactam (**34**) occurs in the crystal as a single tautomeric form (as shown). This assignment is supported by the observed distribution of bond lengths, which further indicates that the π-conjugation extends over the whole chromophore; ring D appears to be a fully delocalised system. The distance between the incipient cyclisation centres [*cf.* compound (**10**), *i.e.* C-20 (the 1-methyl substituent)] on ring A

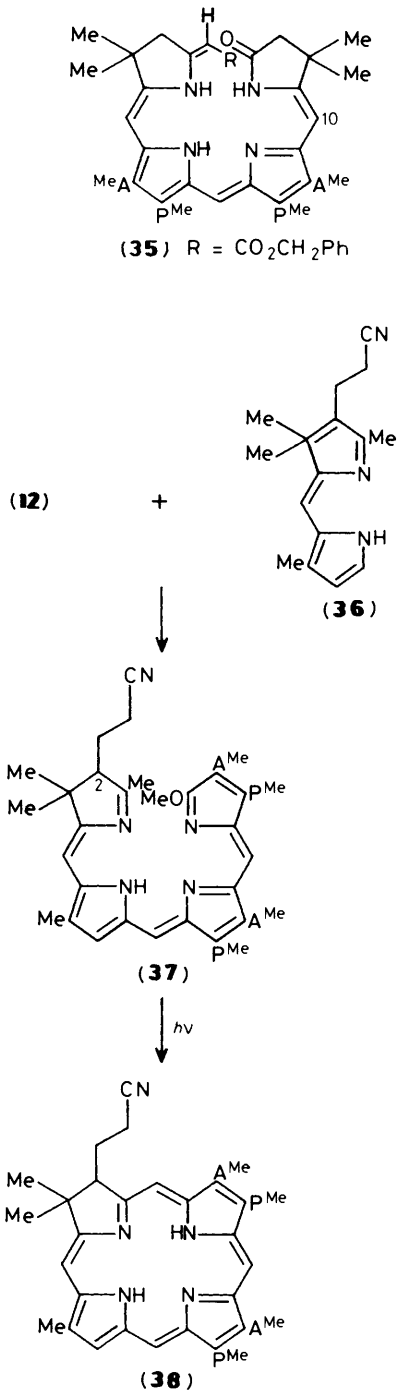


Scheme 5



and C-19 on ring B, is 3.485 Å which is little more than twice the value for the van der Waals' radius of a trigonal carbon.

It is very probable that the helical conformation of the seco-lactam (**34**) in the crystal also holds good in solution. This was demonstrated to be true for the closely related seco-lactam (**35**) which was helical in the crystal and where a nuclear Overhauser enhancement was obtained[30] in solution between the methylene group of the benzyl ester and the methine proton at C-10. This case is a favourable one for n.O.e studies because the benzyl group 'reaches' far across the molecule. Perhaps not surprisingly, a similar n.O.e. study, kindly carried out by Dr. F. J. Leeper, did not reveal any significant interaction between the C-20 methyl group and the protons on and around ring-B and at C-10. However, good n.O.e.'s were observed between the sites connected by arrows on structure (**34**).



Scheme 6

Synthesis of Further Chlorins by Photocyclisation.—Before embarking on syntheses of the two natural products (**1**) and (**2**), we planned first to make a comparative study of simpler systems containing many of the relevant structural features. Condensation of the bicyclic A-D fragment[31] (**36**) with the aldehyde (**12**) afforded the protonated seco-chlorin (**37**). Irradiation of this resulted in a poor conversion (7% yield) into the product chlorin

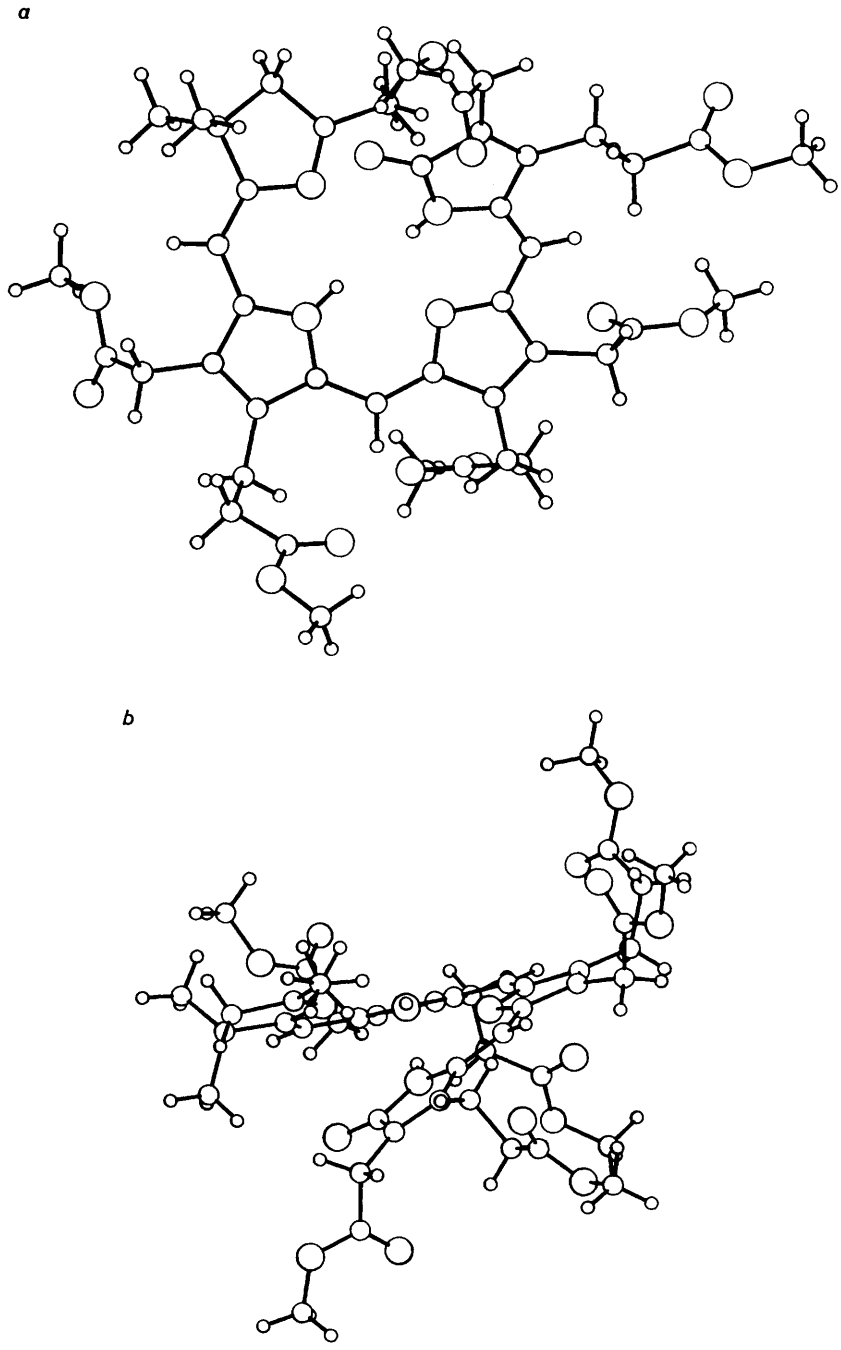
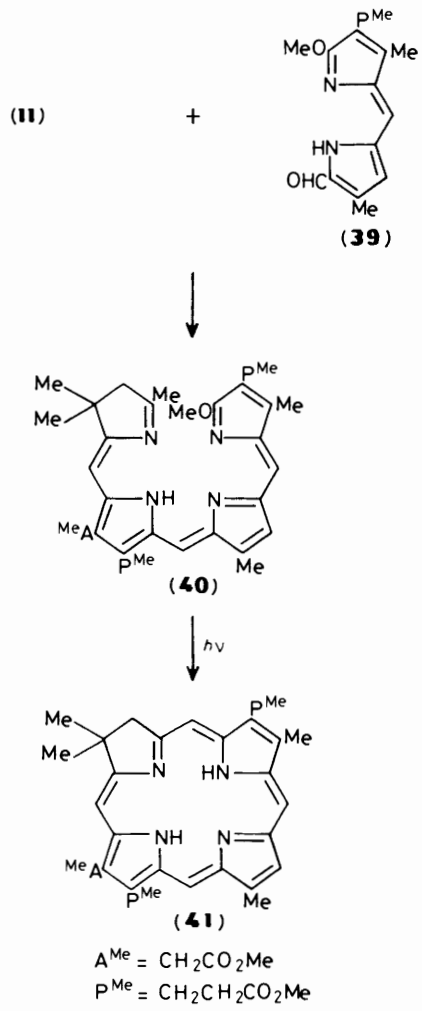


Figure. Structure of the seco-lactam (**34**) determined by *X*-ray analysis: *a*, viewed from above the molecule; *b*, viewed from the side

(**38**) (Scheme 6) even after 3 days and a substantial amount of the seco-chlorin (**37**) was recovered. In contrast photocylisation of the seco-chlorin (**40**), formed by condensation of pyrrole (**11**) with the aldehyde[31] (**39**), proceeded quickly and in good yield under the standard conditions to give the chlorin (**41**) (Scheme 7). This result was initially worrying because it was possible that the much slower cyclisation rate for system (**37**) was due to increased steric congestion at the cyclisation centre caused by the presence of the C-2 cyanoethyl substituent.

However, it was observed that the seco-system (**37**) was significantly more basic than the analogous one (**10**) so that treatment with Hunig's base failed to deprotonate the seco-chlorin (**37**); a similar problem will be described in the following paper.[31] By replacing Hunig's base with the more powerful base 1,8-bis(dimethylamino)napthalene, the extent of the protonation of the seco-chromophore was greatly reduced and the rate of photocyclisation was considerably improved. Although there still remained the possibility that steric factors were affecting the cyclisation rate, these results suggested that a more important factor was the extent to which the seco-chromophore is protonated whilst being irradiated.

With a mild, high-yielding route to *C*-methylated chlorins now available together with a good fund of knowledge concerning the photochemical ring-closure, the stage was set for the synthesis of the natural pigments, Faktor I (**1**) and bonellin (**2**). This work is described in the following two papers.



Scheme 7

Experimental

For general directions, see ref. 13. In addition, ^{1}H n.m.r. spectra were recorded on Varian EM 360 (A), EM 390 (B) and Bruker WH 250 (C) and WH 400 (D) spectrometers. For spectra run on A and B, tetramethylsilane or the residual proton signal from the solvent were used as standards whereas for C and D, the solvent signal was used. Unless stated otherwise, solutions for n.m.r. were in $CDCl_3$ and, for u.v.–visible spectroscopy, in methanol.

t-Butyl 5-Bromo-3-(2-methoxycarbonylethyl)-4-methoxycarbonylmethylpyrrole-2-carboxylate (**15**).—A solution of bromine (2.6 g) in dry methanol (30 ml) was added dropwise during 1.5 h to a vigorously stirred mixture of 2-t-butoxycarbonyl-3-(2-methoxycarbonylethyl)-4-methoxycarbonylmethylpyrrole-5-carboxylic acid[19] (**14**) (5.54 g) and sodium hydrogen carbonate (8.4 g) in dry methanol (85 ml) at 18 °C. After a further 0.5 h, the mixture was diluted with water (150 ml) and dichloromethane (125 ml), the organic layer was separated, and the aqueous layer extracted with dichloromethane (2 × 120 ml, 2 × 70 ml). The combined organic extracts were washed with saturated brine (50 ml) and evaporated to give the *bromo pyrrole* (**15**) (4.89 g, 80.6%), m.p. 132.5—133.5 °C (from dichloromethane–ether–hexane) (Found: C, 47.5; H, 5.4; Br, 19.6; N, 3.45. $C_{16}H_{22}BrNO_6$ requires C, 47.5; H, 5.5; Br, 19.8; N, 3.5%); $\nu_{max.}$ 3 445, 3 255br, 1 738, and 1 683 cm^{-1}; δ(B) 1.48 (9 H, s, Me_3C), 2.50 (2 H, t, *J* 8 Hz, $CH_2CH_2CO_2$) 2.95 (2 H, t, *J* 8 Hz, $CH_2CH_2CO_2$), 3.44 (2 H, s, CH_2CO_2) 3.60 and 3.63 (each 3 H, s, 2 × CO_2Me), and 9.17 (1 H, br s, NH); *m/z* 403/405 (32/34%, M^+), 347/349 (20/22, $M - C_4H_8$), 344/346 (8/8, $M - CO_2Me$), and 315/317 (97/100, 347/349 − MeOH); *M** 301 (405 ⟶ 349), 299 (403 ⟶ 347), 288 (349 ⟶ 317), and 286 (347 ⟶ 315.)

4-(2-Methoxycarbonylethyl)-3-methoxycarbonylmethylpyrrol-2(5H)-one (**16**) *and 3-(2-Methoxycarbonylethyl)-4-methoxycarbonylmethylpyrrol-2(5H)-one* (**17**).—The foregoing bromo pyrrole (**15**) (0.2 g), was heated under reflux in a solution of sulphuric acid in methanol (1M; 5.25 ml) for 1.25 h. The mixture was then diluted with water (5 ml), extracted with dichloromethane (3 × 10 ml), and the material obtained from the combined extracts was fractionated by p.l.c. (1 mm layer, eluted with 1:9 methanol–dichloromethane) to give two products. The slower band gave 4-(2-*methoxycarbonylethyl*)-3-*methoxycarbonylmethylpyrrol*-2(5H)-*one* (**16**) (16 mg, 13.4%), m.p. 100.5—102.5 °C (from dichloromethane–ether) (Found: C, 54.8; H, 6.2; N, 5.8. $C_{11}H_{15}NO_5$ requires C, 54.8; H, 6.3; N, 5.9%); $\nu_{max.}$ 3 690, 3 460, 1 738, 1 695, and 1 604 cm^{-1}; δ(C, CD_2Cl_2) 2.52 (2 H, t, *J* 7.5 Hz, CH_2CH_2), 2.70 (2 H, t, *J* 7.5 Hz, CH_2CH_2), 3.29 (2 H, s, CH_2CO_2), 3.65 and 3.66 (each 3 H, s, 2 × CO_2Me), 3.90 (2 H, s, CH_2N), and 6.74 (1 H, br s, NH); *m/z* 241 (3%, M^+), 210 (21, M − MeO), 209 (11, M − MeOH), 181 (68, $M - HCO_2Me$), 121 (22), and 108 (100, $C_6H_6NO^+$); R_F 0.5 (10% MeOH–CH_2Cl_2).

The faster band gave the isomeric 3-(2-*methoxycarbonylethyl*)-4-*methoxycarbonylmethylpyrrol*-2(5H)-*one* (**17**) (21 mg, 17.6%), m.p. 102.5—104.5 °C (from dichloromethane–hexane) (Found: C, 54.7; H, 6.3; N, 5.9; $C_{11}H_{15}NO_5$ requires C, 54.8; H, 6.3; N, 5.9%); $\nu_{max.}$ 3 463, 1 738, 1 693, and 1 605w cm^{-1}; δ(C, CD_2Cl_2) 2.53 (4 H, s, $CH_2CH_2CO_2$), 3.46 (2 H, s, CH_2CO_2), 3.61 and 3.68 (each 3 H, s, 2 × CO_2Me), 3.95 (2 H, s, CH_2N), and 6.62 (1 H, br s, NH); *m/z* 241 (9%, M^+), 210 (49, M − MeO), 209 (100, M − MeOH), 181 (15, $M - HCO_2Me$), 167 (68, $M - MeCO_2Me$), 122 (20), and 108 (50, $C_6H_6NO^+$); R_F 0.6 (10% MeOH–CH_2Cl_2).

t-Butyl 1,10-Dihydro-2,7,-bis(2-methoxycarbonylethyl)-3,8-bis(methoxycarbonylmethyl)-1-oxodipyrrin-9-carboxylate (**21**).—Bromine (0.53 g) in formic acid (3 ml) was added to the dipyrromethane[32] (**20**) (0.91 g) and sodium formate (0.4 g) in dry formic acid (1.8 ml) at 0 °C under argon. After the mixture had been stirred for 15 min at 0 °C, it was warmed to 18 °C over 5 min and mixed with dichloromethane (15 ml), iced water (10 ml), and then saturated brine (20 ml). The organic layer was separated, the aqueous layer extracted with dichloromethane (3 × 50 ml), and the combined organic solutions were washed with saturated aqueous sodium hydrogen carbonate (30 ml), and the washings back-extracted with dichloromethane (25 ml, 20 ml). The product from evaporation of all the dichloromethane solutions was washed with ether and the insoluble yellow solid was recrystallised from dichloromethane–ether to yield the *title compound* (**21**) (0.43 g, 49.7%), m.p. 188—190.5 °C (Found: C, 58.0; H, 6.1; N, 4.7. $C_{28}H_{36}N_2O_{11}$ requires C, 58.3; H, 6.3; N, 4.9%); $\nu_{max.}$ 3 430, 3 333, 1 738, and 1 694 cm^{-1}; $\lambda_{max.}$ 404sh, 386, 259, and 253infl nm; $\lambda_{max.}$[$Zn(OAc)_2$]440, 420sh, 272sh, and 264 nm; δ(C, CD_2Cl_2) 1.51 (9 H, s, Me_3C), 2.46 (2 H, t, *J* 7.5 Hz, 7′-$CH_2CH_2CO_2$), 2.61 (2 H, t, *J* 7.0 Hz, 2-$CH_2CH_2CO_2$), 2.76 (2 H, t, *J* 7.0 Hz, 2-$CH_2CH_2CO_2$), 2.82 (2H, t, *J* 7.5 Hz, 7-$CH_2CH_2CO_2$), 3.60, 3.61, 3.66, 3.67, and 3.69 (4 × 3 H and 1 × 2 H, s, 4 × CO_2Me and 3-CH_2CO_2), 3.78 (2H, s, 8-CH_2CO_2), 6.13 (1 H, s, C=CH), and 9.81 and 9.84 (each 1 H, br s, 2 × NH); *m/z* 576 (29%, M^+), 545 (7, M − MeO), 520 (100, $M - C_4H_8$), 489 (13, 520 − MeO), 476 (17, $M - CO_2 - C_4H_8$), 461 (8, 520 − CO_2Me), and 460 (10, 520 −

HCO_2Me); *M** 469.5 (576 ⟶ 520), 460 (520 ⟶ 489), and 407 (520 ⟶ 460, 520 ⟶ 461).

1-Benzyl 9-t-Butyl 5,10-Dihydro-3,8-bis(2-methoxycarbonylethyl)-2,7-bis(methoxycarbonylmethyl)dipyrrin-1,9-dicarboxylate (**24**).—Toluene-*p*-sulphonic acid monohydrate (231 mg) was added to a solution of the pyrrole[19] (**23**) (3.9 g) and the acetoxymethylpyrrole[33] (**22**) (5.18 g) in dichloromethane (100 ml) and the mixture was stirred at 18 °C under nitrogen for 2 h. The solution was washed with saturated aqueous sodium hydrogen carbonate (50 ml), and the residue from the organic layer filtered through a column of alumina (10 g; eluted with dichloromethane). The product from the eluate was chromatographed on silica H (10 g), eluting with 0—33% ether in dichloromethane; recrystallisation from dichloromethane–ether–hexane gave the *title compound* (**24**) (6.74 g, 80.6%), m.p. 92—95 °C (lit.,[34] 98—100 °C); $\nu_{max.}$ 3 340br, 1 730, and 1 693 cm^{-1}; δ(B) 1.50 (9 H, s, Me_3C), 2.40—3.10 (8 H, m, 2 × $CH_2CH_2CO_2$), 3.56 (2 H, s, CH_2CO_2), 3.61, 3.65, 3.67, and 3.74 (each 3 H, s, 4 × CO_2Me), 3.83 (2 H, s, CH_2CO_2), 3.94 (2 H, s, methane CH_2), 5.26 (2 H, s, $PhCH_2$), 7.37 (5 H, s, Ph), and 9.58 and 10.01 (each 1 H, br s, 2 × NH); *m/z* (e.i.) 696 (3%, M^+), 639 (20, $M - C_4H_9$), 605 (7, $M - PhCH_2$), 596 (51, $M - CO_2 - C_4H_8$), 549 (43, 605 − C_4H_8), 506 (75, 596 − PhCH), 505 (100, 596 − $PhCH_2$), 461 (58), and 459 (75); *M** 428 (596 ⟶ 506, 596 ⟶ 505).

t-Butyl 1,10-Dihydro-3,8-bis(2-methoxycarbonylethyl)-2,7-bis(methoxycarbonylmethyl)-1-oxodipyrrin-9-carboxylate (**13**).—(*a*) The foregoing dipyrromethane (**24**) was converted as earlier[34] into the corresponding carboxylic acid (**25**). The acid (**25**) (601 mg) and sodium formate (272 mg) were stirred together in dry formic acid (1.2 ml) at 0 °C under argon during the addition of a solution of bromine in formic acid (1M; 2 ml). After the mixture had been stirred for 15 min at 0 °C, it was warmed to 18 °C over 5 min, then diluted with dichloromethane (10 ml), ice-water (5 ml), and saturated brine (15 ml). The organic layer was separated and the aqueous layer extracted with dichloromethane (3 × 30 ml). The combined organic solutions were washed with saturated aqueous sodium hydrogen carbonate (20 ml), and the washings were back-extracted with dichloromethane (2 × 15 ml). The product from the combined organic solutions was washed with ether to give a yellow solid which by recrystallisation from dichloromethane–ether gave the *title compound* (**13**) (290 mg, 50.8%). This was identical to the fully characterised sample from (*b*).

(*b*) A solution of the pyrrol-2-one (**16**) (25 mg) and the formylpyrrole (**18**) (36 mg) in methanol (1 ml) was mixed with aqueous sodium hydroxide (4M; 0.2 ml) and stirred under nitrogen for 24 h. The mixture was diluted with water (1.2 ml), acidified to pH 3 with hydrochloric acid (10M), and evaporated at <0.3 Torr. The residue in methanol (10 ml) was adjusted to pH 3 with hydrochloric acid (10M), treated with an excess of ethereal diazomethane and kept for 0.5 h. The residue from evaporation was partitioned between water and dichloromethane (3 × 20 ml) and the residue from the combined organic solutions was purified by p.l.c. (0.25 mm layer, eluted with 1:9 methanol–dichloromethane) to give the *title compound* (**13**), m.p. and mixed m.p. 173—176.5 °C (Found: C, 58.4; H, 6.35; N, 4.8. $C_{28}H_{36}N_2O_{11}$ requires C, 58.3; H, 6.23; N, 4.9%); $\nu_{max.}$ 3 313br, 1 735, and 1 698 cm^{-1}; $\lambda_{max.}$ 400sh, 386, and 259 nm; $\lambda_{max.}$[$Zn(OAc)_2$] 442, 422sh, and 267 nm; δ(D, CD_2Cl_2) 1.55 (9 H, s, Me_3C), 2.53 (2 H, t, *J* 8.0 Hz, 8-$CH_2CH_2CO_2$), 2.58 (2 H, t, *J* 7.7 Hz, 3-$CH_2CH_2CO_2$), 2.85 (2 H, t, *J* 7.7 Hz, 3-$CH_2CH_2CO_2$), 2.97 (2 H, t, *J* 8.0 Hz, 8-$CH_2CH_2CO_2$), 3.53 and 3.58 (each 2 H, s, 2 × CH_2CO_2), 3.64 (6 H, s, 2 × CO_2Me), 3.64 and 3.67 (each 3 H, s, 2 × CO_2Me), 6.10 (1 H, s, C=CH), and 9.67 (2 H, br s, 2 × N*H*); *m/z* 576 (29%, M^+), 520 (100, $M - C_4H_8$), 489 (27, $M - C_4H_8$ − MeO), 488 (30, $M - C_4H_8$ − MeOH), 476 (11, $M - C_4H_8 - CO_2$), 460 (22), 428 (19), and 401 (60).

t-Butyl 1,10-Dihydro-2,8-bis(2-methoxycarbonylethyl)-3,7-bis(methoxycarbonylmethyl)-1-oxodipyrrin-9-carboxylate (**19**).—A solution of the pyrrol-2-one (**17**) (25.7 mg) and the formylpyrrole (**18**) (36.2 mg) in methanol (1 ml) was treated as above to give the *title compound* (**19**) as a yellow solid (6 mg, 9.8%) (Found: M^+, 576.2323. $C_{28}H_{36}N_2O_{11}$ requires *M*, 576.2319); $\nu_{max.}$ 3 434, 3 330br, 1 737, and 1 700 cm^{-1}; $\lambda_{max.}$ 404sh, 386, and 260 nm; $\lambda_{max.}$[$Zn(OAc)_2$] 444, 426sh, and 269 nm; δ(D, CD_2Cl_2) 1.55 (9 H, s, Me_3C), 2.52 (2 H, t, *J* 8.0 Hz, 2-$CH_2CH_2CO_2$), 2.60 (2 H, t, *J* 6.9 Hz, 8-$CH_2CH_2CO_2$) 2.71 (2 H, t, *J* 6.9 Hz, 8-$CH_2CH_2CO_2$), 2.96 (2 H, t, *J* 8.0 Hz, 2-$CH_2CH_2CO_2$), 3.55 (2 H, s, CH_2CO_2), 3.62, 3.63, 3.64, 3.70, and 3.70 (4 × 3 H and 1 × 2 H, s, 4 × CO_2Me and CH_2CO_2), 5.99 (1 H, s, C=CH), and 8.90 and 9.25 (each 1 H, br s, 2 × N*H*); *m/z* 576 (22%, M^+), 520 (77, $M - C_4H_8$), 489 (9, $M - C_4H_8$ − MeO), 488 (12, $M - C_4H_8$ − MeOH), 383 (31), 256 (20), 230 (43), and 209 (100).

1,10-Dihydro-3,8-bis(2-methoxycarbonylethyl)-2,7-bis(methoxycarbonylmethyl)-1-oxodipyrrin-9-carbaldehyde (**26**).—A solution of the dipyrrin ester (**13**) (0.4 g) in dry TFA (28 ml) was stirred at 50 °C under argon for 1.1 h, then cooled to 0 °C and treated with trimethyl orthoformate (1.2 ml). After a further 20 min at 0 °C, the solution was diluted with water (25 ml) and stirred for 20 min as it warmed to 18 °C. Extraction with dichloromethane (80 ml, 4 × 50 ml) followed by washing of the combined extracts with saturated aqueous sodium hydrogen carbonate (50 ml) gave from the organic solution the *title compound* (**26**) as yellow needles (306 mg, 87.4%), m.p. 206—210 °C (decomp.) (from dichloromethane) (Found: C, 57.3; H, 5.7; N, 5.5. $C_{24}H_{28}N_2O_{10}$ requires C, 57.15; H, 5.6; N, 5.55%); $\nu_{max.}$ 3 340br, 2 850w, 1 738, 1 705, and 1 681 cm^{-1}; $\lambda_{max.}$ 413sh, 394, and 269 nm; $\lambda_{max.}$[$Zn(OAc)_2$] 452, 428, 410infl, 310sh, and 277 nm; δ(C) 2.57—2.71 (4 H, m, 2 × $CH_2CH_2CO_2$), 2.90 (2 H, t, *J* 7.5 Hz, $CH_2CH_2CO_2$), 3.11 (2 H, t, *J* 7.5 Hz, $CH_2CH_2CO_2$), 3.61 and 3.62 (each 2 H, s, 2 × CH_2CO_2), 3.66 and 3.69 (each 3 H, s, 2 × CO_2Me), 3.68 (6 H, s, 2 × CO_2Me), 6.19 (1 H, s, C=CH), 9.78 (1 H, s, CHO), and 10.91 and 10.95 (each 1 H, br s, 2 × NH); *m/z* 504 (63%, M^+), 472 (100, M − MeOH), 445 (13), 444 (15), 443 (12), and 441 (23); *M** 442 (504 ⟶ 472).

1-Methoxy-3,8-bis(2-methoxycarbonylethyl)-2,7-bis(methoxycarbonylmethyl)dipyrrin-9-carbaldehyde (**12**).—A stirred mixture of the foregoing oxodipyrrin carbaldehyde (**26**) (120 mg) and trimethyloxonium tetrafluoroborate (0.7 g) in dichloromethane (17 ml) was treated with Hünig's base (0.83 ml, 0.62 g) at 18 °C under argon. After 20 min, the mixture was diluted with dichloromethane (20 ml), washed with water (2 × 30 ml), and evaporated. The residue by p.l.c. (1 mm layer, eluted with 1:4 methyl acetate–dichloromethane) gave from the faster running yellow band (amber fluorescence under long wavelength u.v. light) the *title compound* (**12**) (72.6 mg, 58.9%), m.p. 98—102 °C (from methyl acetate-hexane) (Found: C, 57.7; H, 5.6; N, 5.4%; M^+, 518.1895. $C_{25}H_{30}N_2O_{10}$ requires C, 57.9; H, 5.8; N, 5.4%; *M*, 518.1900); $\nu_{max.}$ 3 296br, 2 849, 2 740w, 1 738, 1 643, and 1 535 cm^{-1}; $\lambda_{max.}$ 418, 398sh, and 264 nm; $\lambda_{max.}$[$Zn(OAc)_2$] 462, 304, 274sh, and 268 nm; δ(C, CD_2Cl_2) 2.55 and 2.61 (each 2 H, t, *J* 7.6 Hz, 2 × $CH_2CH_2CO_2$), 2.85 and 3.06 (each 2 H, t, *J* 7.6 Hz, 2 × $CH_2CH_2CO_2$), 3.41 (2 H, s, CH_2CO_2), 3.63, 3.64, and 3.67 (total 14 H, each s, 4 × CO_2Me and CH_2CO_2), 4.11 (3 H, s, 1-OMe), 6.53 (1 H, s, C=CH), 9.73 (1 H, s, CHO), and 11. 94 (1 H, br s, NH), *m/z* 518 (99%, M^+); 487 (9, M − MeO), 459 (M − CO_2Me), 445 (35,

$M - CH_2CO_2Me$), 399 (40), 371 (100), 357 (40), and 311 (36).

The slower running pale yellow band yielded the isomeric 1,10-*dihydro*-3,8-*bis*(2-*methoxycarbonylethyl*)-2,7-*bis*(*methoxycarbonylmethyl*)-10-*methyl*-1-*oxodipyrrin*-9-*carbaldehyde* (**27**) (30 mg, 24.3%) m.p. 116.5—118.5 °C (from dichloromethane–hexane) (Found: C, 57.9; H, 5.8; N, 5.6%; M^+, 518.1891. $C_{25}H_{30}N_2O_{10}$ requires C, 57.9; H, 5.8; N, 5.4%; *M*, 518.1900); $\nu_{max.}$ 2 848w, 2 765w, 1 733, 1 710, and 1 647 cm^{-1}; $\lambda_{max.}$ 359, 288, and 266 nm; $\lambda_{max.}$[$Zn(OAc)_2$] 359, 288, and 266 nm; δ(D, CD_2Cl_2) 2.50 (2 H, t, *J* 7.8 Hz, $CH_2CH_2CO_2$), 2.60 (2 H, t, *J* 7.6 Hz, $CH_2CH_2CO_2$), 2.87 (2 H, t, *J* 7.6 Hz, $CH_2CH_2CO_2$), 2.96 (2 H, t, *J* 7.8 Hz, $CH_2CH_2CO_2$), 3.41 and 3.45 (total 5 H, each s, CH_2CO_2 and NMe), 3.63, 3.64, 3.73, and 3.81 (each 3 H, s, 4 × CO_2Me), 3.67 (2 H, s, CH_2CO_2), 5.86 (1 H, s, C=CH), 8.33 (1 H, br s, NH), and 9.76 (1 H, s, CHO); *m*/*z* 518 (100%, M^+), 487 (23, *M* − MeO), and 486 (33, *M* − MeOH).

8,13,17-*Tris*(2-*methoxycarbonylethyl*)-7,12,18-*tris*(*methoxycarbonylmethyl*)-2,2-*dimethylchlorin* (**9**).—(*a*) t-Butyl 2,3-dihydro-8-(2-methoxycarbonylethyl)-7-methoxycarbonylmethyl-1,3,3-trimethyldipyrrin-9-carboxylate[19,16] (**28**) (14.4 mg) and the foregoing oxodipyrrincarbaldehyde (**12**) (9.9 mg) were treated with dry TFA (0.2 ml), 18 °C under argon. After 2.75 h, the red–purple solution was diluted into dry, deoxygenated THF (60 ml) under argon and the resultant deep blue–green solution was then neutralised with dry Hünig's base (0.45 ml). This green solution was transferred, under argon, into a thick-walled glass tube and thoroughly degassed by four cycles of 'freeze-pump-thaw' under high vacuum (<0.3 Torr); the tube was sealed whilst under high vacuum. The solution was irradiated at 20 °C with visible light (tungsten; 1 000 W array; 12 cm) through a solution filter of aqueous sodium dichromate (0.04M; mean path length 6 cm) for 6.2 h, when the solution was green–brown and showed a strong red fluorescence under long wavelength u.v. light.

The solution was then evaporated to *ca.* 5 ml, diluted with dichloromethane (50 ml), washed with saturated aqueous sodium hydrogen carbonate (50 ml) and water (50 ml), then dried, and evaporated. The residue was column chromatographed on silica (5 g) eluting with 0—10% methyl acetate–dichloromethane. Further purification by p.l.c. (2 × 0.25 mm plates, eluted with 3:17 methyl acetate–dichloromethane), gave the *chlorin* (**9**) (8.45 mg by u.v. assay, 54.3%) which crystallised from dichloromethane–methanol as dark needles.

(*b*) The dipyrrin ester (**28**) (5.2 mg), and the oxodipyrrincarbaldehyde (**12**) (4 mg), were treated with dry TFA (0.2 ml) under argon. After 2.5 h, the TFA was removed at high vacuum, and pumping was continued for 0.75 h. A solution of zinc acetate dihydrate (17 mg) in dry methanol (0.5 ml) was added to the residue under argon. The resultant green solution was kept at 18 °C for 1 h, then was diluted with dry, deoxygenated THF (30 ml) under argon and irradiated with visible light (tungsten; 1 000 W array; 12 cm) for 1 h. The solution was then evaporated to *ca.* 2 ml, diluted with dichloromethane (30 ml), and washed with aqueous hydrochloric acid (2.5M; 25 ml) to remove the zinc. The organic layer was washed with saturated aqueous sodium hydrogen carbonate (25 ml) and water (25 ml), dried, and evaporated. The residue was purified as under (*a*) to give the *chlorin* (**9**) [1.46 mg by u.v. assay, 23.3% based on the dipyrrin (**12**)], identical with the product from (*a*), m.p. 172—173 °C (Found: C, 63.4; H, 6.2; N, 6.8. $C_{43}H_{50}N_4O_{12}$ requires C, 63.4; H, 6.2; N, 6.9%); $\nu_{max.}$ 3 344, 1 730, and 1 617 cm^{-1}; $\lambda_{max.}$(MeOAc) 645 (4.79), 616.5 (3.56), 591 (3.60), 543 (3.20), 524 (3.46), 498 (4.10), 491sh (4.06), 391 (5.23), 351infl (4.54), 295sh (4.14), and 281 nm (4.18); δ(D, CD_2Cl_2) −2.33 (2 H, br s, 2 × NH), 2.04 (6 H, s, Me_2C), 3.21—3.32 (6 H, m, 3 × $CH_2CH_2CO_2$), 3.67, 3.67, 3.69, 3.77, 3.78, and 3.79 (each 3 H, s, 6 × CO_2Me), 4.22 (2 H, t, *J* 7.8 Hz, $CH_2CH_2CO_2$), 4.33 and 4.36 (each 2 H, t, *J* 7.7 Hz, 2 × $CH_2CH_2CO_2$), 4.63 (2 H, s, 3-CH_2), 4.90, 4.95, and 4.98 (each 2 H, s, 3 × CH_2CO_2), 8.88 and 8.96 (each 1 H, s, 5-H and 20-H), and 9.79 and 9.82 (each 1 H, s, 10-H and 15-H); *m*/*z* 814 (100%, M^+).

[8,13,17-*Tris*(2-*methoxycarbonylethyl*)-7,12,18-*tris*(*methoxycarbonylmethyl*)-2,2-*dimethylchlorinato*]*zinc*(II).—(*a*) The dipyrrin ester (**28**) (5.4 mg) and the oxodipyrrincarbaldehyde (**12**) (4.3 mg) were treated as in (*b*) above, with modification as described below. After 0.5 h irradiation, the solution was evaporated to *ca.* 2 ml and diluted with dichloromethane (25 ml). The resultant green–blue solution was washed with saturated aqueous sodium hydrogen carbonate (20 ml) and water (20 ml), dried, and evaporated. Preparative t.l.c. (0.25 mm plate, eluted with 1:4 methyl acetate–dichloromethane) gave the *zinc complex* of chlorin (**9**) as a royal blue gum [1.3 mg by u.v. assay, 17.0% based on the dipyrrin (**12**)].

(*b*) A solution of the chlorin (**9**) (6.95 mg, 8.5 μmol) in dichloromethane (4 ml) was stirred with a solution of zinc acetate dihydrate (10 mg) in methanol (6 ml) at 18 °C in the dark for 5.5 h; analytical t.l.c. showed essentially complete conversion into the zinc complex. Dichloromethane (20 ml) was added and the solution was washed with saturated aqueous sodium hydrogen carbonate (20 ml). The blue organic layer was separated and the aqueous layer extracted with more dichloromethane (2 × 10 ml). The combined organic extracts were washed with water (10 ml), dried, and evaporated. The residue by p.l.c. as above gave the *zinc complex* of chlorin (**9**), which crystallised from methyl acetate-hexane (6.2 mg, 82.8%), m.p. 183—185 °C (Found: C, 59.1; H, 5.5; N, 6.5. $C_{43}H_{48}N_4O_{12}Zn$ requires C, 58.8; H, 5.5; N, 6.4%); $\nu_{max.}$ 1 732, 1 628w, and 1 572 cm^{-1}; $\lambda_{max.}$(MeOAc) 615 (4.82), 571 (3.91), 539sh (3.52), 506.5 (3.77), 471sh (3.14), 404 (5.36), 386infl (4.83), 352.5sh (4.34), 292.5sh (4.17), and 281.5 nm (4.17); δ(D, CD_2Cl_2) 1.99 (6 H, s, Me_2C), 3.16—3.29 (6 H, m, 3 × $CH_2CH_2CO_2$), 3.65, 3.67, 3.68, and 3.77 (each 3 H, s, 4 × CO_2Me), 3.78 (6 H, s, 2 × CO_2Me), 4.13—4.23 (6 H, m, 3 × $CH_2CH_2CO_2$), 4.52 (2 H, s, 3-CH_2), 4.77, 4.81, and 4.88 (each 2 H, s, 3 × CH_2CO_2), 8.58 and 8.64 (each 1 H, s, 5-H and 20-H), and 9.56 and 9.61 (each 1 H, s, 10-H and 15-H); *m*/*z* 880 (54%, M^+, ^{68}Zn), 878 (75, M^+, ^{66}Zn), and 876 (100, M^+, ^{64}Zn).

3,8-*Bis*(2-*methoxycarbonylethyl*)-2,7-*bis*(*methoxycarbonylmethyl*)*dipyrrin*-1(10H)-*one* (**31**).—The dipyrrin ester (**13**) (27.4 mg) was stirred with dry TFA (3 ml) under argon at 50 °C for 1 h. The mixture was poured into water (5 ml) and extracted with dichloromethane (6 × 7 ml). The combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate (20 ml), dried, and evaporated. Recrystallisation of the residue from dichloromethane–ether gave the *α-free title compound* (**31**) as yellow needles (18.8 mg, 83%), m.p. 170—179.5 °C (decomp.) (Found: C, 58.3; H, 6.05; N, 5.9%; M^+, 476.1769. $C_{23}H_{28}N_2O_9$ requires C, 58.0; H, 5.9; N, 5.9%; *M*, 476.1794); $\nu_{max.}$ 3 355, 1 732, 1 669, and 1 640 cm^{-1}; $\lambda_{max.}$ 398 nm; $\lambda_{max.}$[$Zn(OAc)_2$] 426infl and 403 nm; δ(C, CD_2Cl_2) 2.56—2.66 (4 H, m, 2 × $CH_2CH_2CO_2$), 2.79 and 2.92 (each 2 H, t, *J* 7.6 Hz, 2 × $CH_2CH_2CO_2$), 3.48 and 3.61 (each 2 H, s, 2 × CH_2CO_2), 3.66 and 3.66 (each 6 H, s, 4 × CO_2Me), 6.32 (1 H, s, C=CH), 6.91 (1 H, d, *J* 2.5 Hz, 9-H), and 10.38 and 11.10 (each 1 H, br, 2 × NH); *m*/*z* 476 (68%, M^-) and 444 (100, *M* − MeOH).

1-*Methoxy*-3,8-*bis*(2-*methoxycarbonylethyl*)-2,7-*bis*(*methoxycarbonylmethyl*)*dipyrrin* (**32**).—A stirred mixture of the foregoing dipyrrinone (**31**) (18.8 mg), and trimethyloxonium tetrafluoroborate (0.14 g), in dichloromethane (3 ml) was treated with Hünig's base (0.12 ml) at 18 °C under argon. After 6 h, the mixture was mixed with dichloromethane (10 ml) and

water (5 ml). The organic layer, after washing with water (5 ml), was dried and evaporated. Purification by p.l.c. (1 mm plate, eluted with 1:4 methyl acetate–dichloromethane) gave the *title compound* (**32**) as yellow needles (16.9 mg, 87.3%), m.p. 95—97 °C (from methyl acetate–hexane) (Found: C, 58.9; H, 6.4; N, 5.8%; M^+, 490.1952. $C_{24}H_{30}N_2O_9$ requires C, 58.8; H, 6.2; N, 5.7%; M, 490.1951); $\nu_{max.}$ 3 325br, 1 733, 1 627, and 1 524 cm^{-1}; $\lambda_{max.}$ 405 nm; $\lambda_{max.}$[$Zn(OAc)_2$] 481 nm; δ(C, CD_2Cl_2) 2.53 and 2.57 (each 2 H, t, J 7.7 Hz, 2 × $CH_2CH_2CO_2$), 2.76 and 2.84 (each 2 H, t, J 7.7 Hz, 2 × $CH_2CH_2CO_2$), 3.38 (2 H, s, CH_2CO_2), 3.60, 3.64, 3.645, and 3.66 (total 14 H, each s, 4 × CO_2Me and CH_2CO_2), 4.03 (3 H, s, 1-OMe), 6.55 (1 H, s, C=CH), 6.83 (1 H, s, 9-H), and 11.23 (1 H, br, NH); *m/z* 490 (100%, M^+), 459 (13, M − MeO), 431 (29, M − CO_2Me), and 417 (19, M − CH_2CO_2Me).

2,3,-*Dihydro*-8,12,17-*tris*(2-*methoxycarbonylethyl*)-7,13,18-*tris*-(*methoxycarbonylmethyl*)-1,3,3-*trimethylbilin*-19(24H)-*one* (**34**).—The oxodipyrrincarbaldehyde (**26**) (11.6 mg) and the dipyrrin ester (**28**) (14.8 mg) were treated with dry TFA (0.2 ml) under argon; formation of the blue pigment was complete after 1.25 h at 18 °C. The mixture was diluted with dichloromethane (25 ml), washed with saturated aqueous sodium hydrogen carbonate (30 ml) and water (25 ml), dried, and evaporated. The residue by p.l.c. (2 × 0.25 mm plates, eluted with 1:4 methyl acetate–dichloromethane) gave the *title compound* (**34**) (15.8 mg, 82.5%), m.p. 127—128.5 °C as blue needles (from ether–hexane) (Found: C, 62.6; H, 6.3; N, 6.7. $C_{43}H_{52}N_4O_{13}$ requires C, 62.0; H, 6.3; N, 6.7%); $\nu_{max.}$ 3 305br, 1 732, 1 691, 1 640w, and 1 593 cm^{-1}; $\lambda_{max.}$(MeOAc) 649 (rel. int. 0.509), 616infl (0.425), 357 (1.0), 344infl (0.928), and 299sh nm (0.488); δ(D, CD_2Cl_2) 1.29 (6 H, s, Me_2C), 1.86 (3 H, s, 1-Me), 2.47 (2 H, s, 2-CH_2), 2.57—2.64 (6 H, m, 3 × $CH_2CH_2CO_2$), 2.86 (2 H, t, J 7.6 Hz, $CH_2CH_2CO_2$), 2.97—3.07 (4 H, m, 2 × $CH_2CH_2CO_2$), 3.38 (2 H, s, CH_2CO_2), 3.61, 3.63, 3.65, 3.66, 3.68, 3.69, and 3.70 (22 H, s, 6 × CO_2Me and 2 × CH_2CO_2), 5.89, 6.20, and 7.07 (each 1 H, s, 5-, 10-, and 15-H), and 9.41 and 12.30 (each 1 H, br s, 2 × NH); *m/z* 833 (100%, $M^+ + 1$).

3-(2-*Cyanoethyl*)-8,13-*bis*(2-*methoxycarbonylethyl*)-7,12-*bis*-(*methoxycarbonylmethyl*)-2,2,18-*trimethylchlorin* (**38**).—The oxodipyrrincarbaldehyde (**12**) (10.3 mg) and 2,3-dihydro-2(2-cyanoethyl)-1,3,3,7-tetramethyldipyrrin (**36**)[31] (7.6 mg) were treated with dry TFA (0.2 ml) at 18 °C under argon whereupon a purple–red colour rapidly developed. After being kept for 1.25 h, the purple–red solution was diluted with dry, de-oxygenated THF (50 ml) under argon and the resulting deep blue–green solution treated with dry Hünig's base (0.45 ml). The solution was transferred under argon into a thick-walled glass tube, degassed by four cycles of 'freeze-pump-thaw' under high vacuum (<0.3 Torr), and the tube sealed at high vacuum. The solution was then irradiated at 20 °C with visible light (tungsten; 1000 W array; 12 cm) through a solution filter of aqueous sodium dichromate (0.04M; mean path length 6 cm) for 68 h.

The solution was then evaporated to *ca.* 5 ml, mixed with dichloromethane (50 ml), washed with saturated aqueous sodium hydrogen carbonate (50 ml) and water (50 ml), dried, and evaporated. The products were chromatographed on silica (5 g) eluting with 0—10% methyl acetate in dichloromethane, and the red fluorescent fractions (long wavelength u.v. light) were collected. A turquoise–blue pigment was obtained by further elution with methyl acetate. The product from the former fractions were purified by p.l.c. first eluting with 8% methyl acetate in dichloromethane (× 3) followed by further p.l.c. using ether to give the *chlorin* (**38**) as a dark green gum [0.97 mg by u.v. assay, 6.8% based on the dipyrrin (**12**)] (Found: M^+, 723.3276. $C_{40}H_{45}N_5O_8$ requires M, 723.3268); $\nu_{max.}$ 3 348, 2 248w, 1 730, and 1 613 cm^{-1}; $\lambda_{max.}$(MeOAc) 642 (rel. int. 0.279), 611sh (0.024), 588 (0.026), 522 (0.020), 496 (0.067), 488 (0.068), 390, (1.0), and 346infl nm (0.186); δ(D) −2.05 (2 H, br s, 2 × NH), 1.79 (3 H, s, 2α-Me), 2.19 (3 H, s, 2β-Me), 2.18—2.44 (3 H, m, 3β-$CH_aH_bCH_2CN$), 2.63 (1 H, m, 3β-$CH_aH_bCH_2CN$), 3.20 (2 H, t, J 8.1 Hz, 13-$CH_2CH_2CO_2$), 3.29 (2 H, t, J 7.7 Hz, 8-$CH_2CH_2CO_2$), 3.54 (3 H, s, 18-Me), 3.68, 3.72, 3.73, and 3.79 (each 3 H, s, 4 × CO_2Me), 4.21 (2 H, t, J 8.1 Hz, 13-$CH_2CH_2CO_2$), 4.38 (2 H, ABqt, J 14.8 and 7.7 Hz, 8-$CH_aH_bCH_2CO_2$), 4.57 (1 H, dd, J 6.7 and 7.2 Hz, 3α-H), 4.90 (2 H, s, 12-CH_2CO_2), 4.95 (1 H, d, J 16.0 Hz, 7-$CH_aH_bCO_2$), 5.02 (1 H, d, J 16.0 Hz, 7-$CH_aH_bCO_2$), 8.80 and 8.98 (each 1 H, s, 5-H and 20-H), 8.95 (1 H, s, 17-H), and 9.67 and 9.88 (each 1 H, s, 10-H and 15-H), *m/z* 723 (100%, M^+); irradiation of the singlet at 1.79 p.p.m. caused an enhancement of the double doublet at 4.57 p.p.m. Irradiation of the singlet at 2.19 p.p.m. caused an enhancement of the multiplet at 2.63 p.p.m. Irradiation of the triplet at 3.29 caused the AB quartet triplet at 4.38 p.p.m. to collapse to an AB quartet. The above turquoise–blue fraction by p.l.c. eluting with methanol–dichloromethane (1:9) gave the seco-system, 2-(2-*cyanoethyl*)-2,3-*dihydro*-19-*methoxy*-12,17-*bis*(2-*methoxycarbonylethyl*)-13,18-*bis*(*methoxycarbonylmethyl*)-1,3,3,7-*tetramethylbilin* (**37**) (9 mg, 59.9%) as a dark blue–green gum (Found: M^+, 755.3540. $C_{41}H_{49}N_5O_9$ requires M, 755.3530); $\nu_{max.}$ 1 735 cm^{-1}; $\lambda_{max.}$(MeOAc) 626, 418, 398, and 301 nm; δ(D, CD_2Cl_2) 1.14 (6 H, s, Me_2C), 1.11—1.30 (2 H, m, CH_2CH_2CN), 2.09 and 2.16 (each 3 H, s, 7-Me and 1-Me), 2.43—2.63 (7 H, m, 2 × $CH_2CH_2CO_2$, CH_2CH_2CN, and 3-H), 2.85 (4 H, m, 2 × $CH_2CH_2CO_2$), 3.41 and 3.62 (each 2 H, s, 2 × CH_2CO_2), 3.64 and 3.645 (each 3 H, s, 2 × CO_2Me), 3.66 (6 H, s, 2 × CO_2Me), 4.10 (3 H, s, 19-OMe), 5.28, 6.15, 6.54, and 7.06 (each 1 H, s, 5-H, 8-H, 10-H, and 15-H), and 11.57 (1 H, br s, NH); *m/z* 755 (100%, M^+).

7,17-*Bis*(2-*methoxycarbonylethyl*)-18-*methoxycarbonylmethyl*-2,2,8,13-*tetramethylchlorin* (**41**).—A solution of the imine (**11**) (7 mg) and the aldehyde[31] (**39**) (5 mg) in TFA (0.1 ml) under argon was kept at 18 °C for 2.25 h. Tetrahydrofuran (30 ml) was then added followed by Hünig's base (0.22 ml) which caused a colour change from blue to green. The solution was irradiated with a 1000 W array of tungsten lamps for 20 min, then evaporated and the residue in dichloromethane (10 ml) was washed with dilute aqueous sodium hydrogen carbonate, dried, and evaporated. The residue was purified by p.l.c. eluting with 1:4 hexane–diethyl ether to give the *chlorin* (**41**) which was eluted with methyl acetate. It crystallised from methanol as dark needles (3.7 mg, 38 %), m.p. 139—140 °C (Found: M^+, 612.2942. $C_{35}H_{40}N_4O_6$ requires M, 612.2947); $\nu_{max.}$($CHCl_3$) 3 325, 2 900, 1 730, 1 610, and 1 160 cm^{-1}; $\lambda_{max.}$(MeOAc) 386, 641, 610, 587, 540, 518, 492, and 484 nm; δ(D, CD_2Cl_2) 9.8 (1 H, s), 9.6 (1 H, s), 8.95 (1 H, s), 8.88 (1 H, s), 8.7 (1 H, br s), 5.0 (2 H, s), 4.65 (2 H, s), 4.35 (2 H, t, J 8 Hz), 4.28 (2 H, t, J 8 Hz), 3.75 (3 H, s), 3.7 (3 H, s), 3.67 (3 H, s), 3.5 (3 H, s), 3.48 (3 H, s), 3.25 (2 H, t, J 8 Hz), 3.17 (2 H, t, J 8 Hz), and 2.03 (6 H, s); *m/z* 612 (M^+).

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