Synthetic Studies Relevant to Biosynthetic Research on Vitamin B_{12}. Part 1. Syntheses of *C*-Methylated Chlorins Based on 1-Pyrrolines (3,4-Dihydropyrroles).[1]

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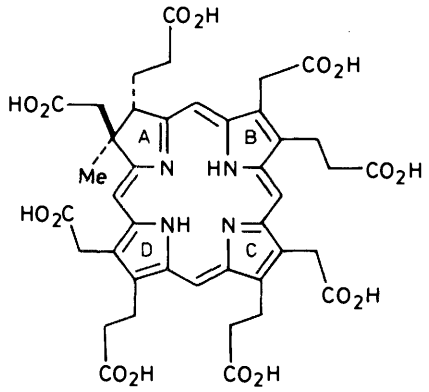
Two routes are explored for the synthesis of chlorins geminally substituted in the reduced ring; both involve cyclisations of 1-pyrroline (3,4-dihydropyrrole) systems promoted by copper(II) salts. In the preferred synthesis, a pyrrolomethyl-1-pyrroline is combined with a 5-bromo-5′-bromomethylpyrromethene; though not high yielding, this approach involves few steps from readily prepared building blocks.

Introduction to the Series of Papers.—Extensive experiments involving isotopic labelling and spectroscopy have yielded much information about the early and middle stages of the biosynthetic pathway to vitamin B_{12}.[2] One result of this work was to focus intense interest on several novel pigments which are either biosynthetic intermediates for vitamin B_{12} or are derived from the true intermediates by simple dehydrogenation steps. Three families of macrocyclic pigments were represented by those which had been found to be related to vitamin B_{12}, *viz.* chlorins,[2] isobacteriochlorins[2] and most recently, pyrrocorphins.[3] Looking to the future, it is clearly essential to obtain workable quantities of the natural pigments for studies of their chemistry and to allow experiments which probe into the unknown part of the B_{12}-pathway; supplies of simpler analogues of the natural pigments will also be invaluable. However, the amounts of the natural materials which are available from the B_{12}-producing micro-organisms range from small (milligrams) to minute (micrograms). Accordingly, work has been undertaken on the total synthesis of chlorins, isobacteriochlorins and pyrrocorphins with the eventual aim of providing good supplies of all the natural pigments. This Series of papers will describe the chemistry involved and we start with the chlorins.

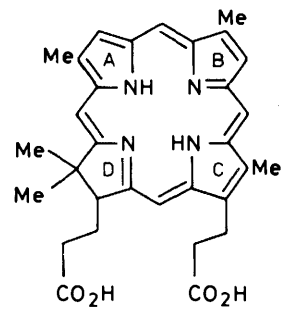
Faktor-I and Bonellin. A very scarce chlorin isolated from the B_{12}-producer *Clostridium tetanomorphum*[4] was called Faktor-I and was shown[5] to have structure (**1**) which is geminally substituted (*C*-methylated) in the reduced ring-A at C-2. Faktor-I differs in this respect from chlorophylls *a* and *b*; these latter pigments carry two hydrogen atoms on their reduced ring-D. Another *C*-methylated chlorin appeared as bonellin[6] (**2**), the green pigment of *Bonellia viridis*, which shows geminal substitution at C-18 of the reduced ring-D.

Although numerous syntheses of chlorins have been reported, especially of substances related to the chlorophylls, there was no rational synthetic route available at the outset of our work capable of yielding unsymmetrical *C*-methylated chlorins such as structures (**1**) and (**2**).

Synthesis of C-Methylated Chlorins.—The synthetic plan involved the combination of an A-D fragment with a B-C portion [see (**1**) and (**2**)] and for the initial studies, the pyrroline (**3**) was chosen for the A-D unit. A general route to pyrrolines[7] makes use of the Michael addition of a nitroalkane to an enone. Accordingly, the readily available aldehydes (**4a**) and (**4b**) were condensed with nitromethane to give the *E*-nitrovinylpyrroles (**5a**) and (**5b**). Borohydride reduction of these products then afforded the nitroethylpyrroles (**6a**) and (**6b**) in excellent yields. Several bases were examined for the Michael reaction including



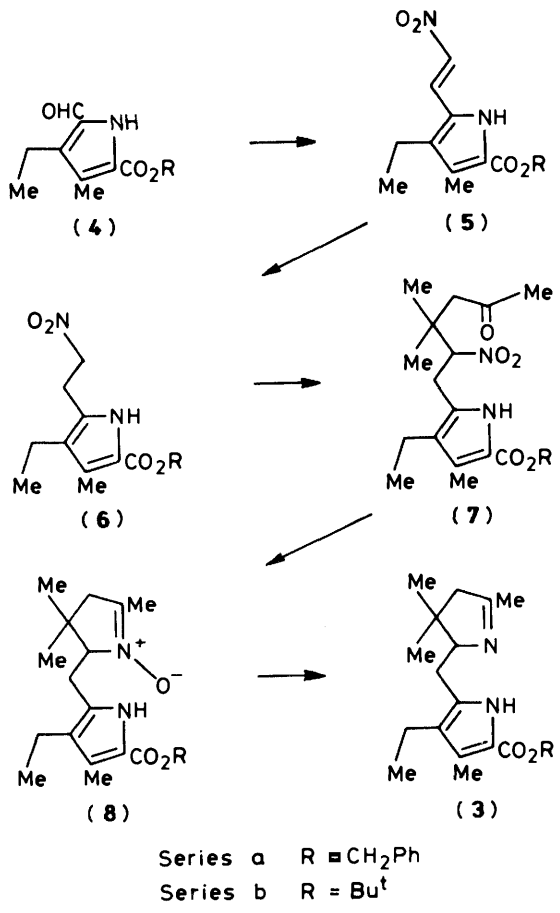
(**1**)



(**2**)

piperidine, benzyltrimethylammonium hydroxide and diazabicyclononane (DBN). Of these, DBN was the most satisfactory in the benzyl series giving the adduct (**7a**) in 73% yield. Fluoride ion,[8] as tetrabutylammonium fluoride (TBAF), was the best catalyst for the t-butyl series to yield the nitro-ketone (**7b**) in 88% yield; one equivalent of TBAF was required.

The most effective method for cyclisation of the nitro ketones (**7a**) and (**7b**) was mild reduction with zinc and acetic acid which gave the pyrroline *N*-oxide (**8a**) in high yield. This product was resistant to deoxygenation with triphenylphosphine or trimethyl phosphite but on treatment with buffered titanium(III) chloride[9] it afforded the desired pyrroline (**3a**) in 75% yield; to our knowledge, this appears to be the first use of titanium(III) for conversion of a nitrone into an imine. The procedure could be shortened by directly treating the filtered reaction mixture with titanium(III) chloride after the zinc step. In this way, the pyrrolines (**3a**) and (**3b**) were obtained in 96% and 88% yields, respectively, from the nitro-ketones (**7a**) and (**7b**). With a viable



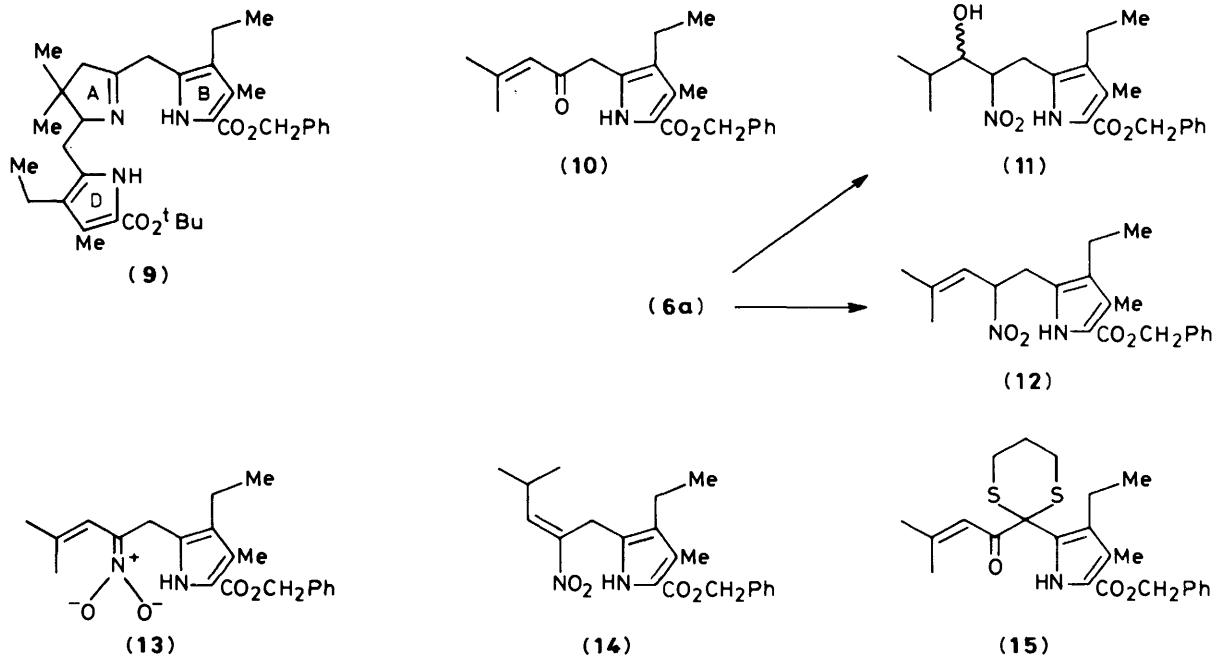
Scheme 1.

route thus available for construction of the A-D fragment, we sought to extend the approach to build a tricyclic D-A-B component (**9**).

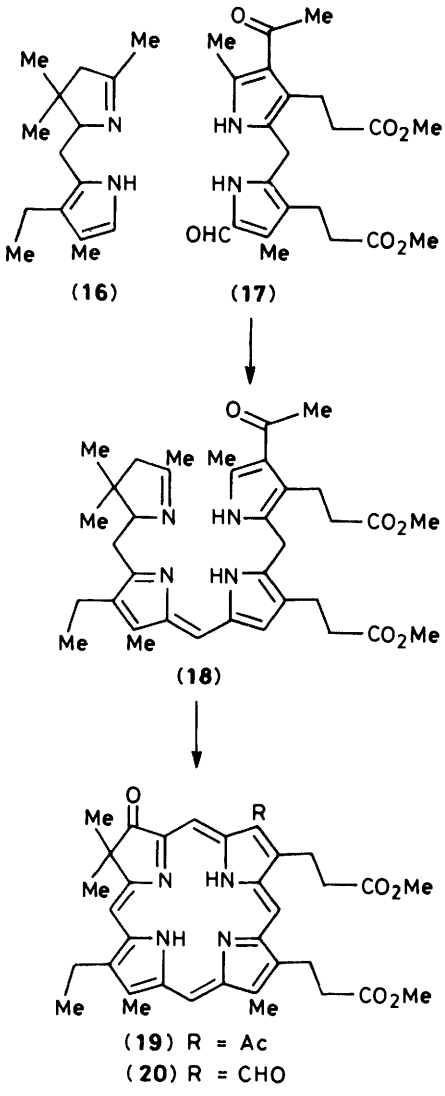
Approaches to a D-A-B *Component.*—A route similar to that of the foregoing section was envisaged in which ring A of the pyrroline (**9**) was to be built *via* Michael addition of the nitroethylpyrrole (**6b**) to the enone (**10**). Few methods are known for preparing such pyrrolylmethyl ketones (**10**) so a nitroalkane intermediate was employed as shown in Scheme 2. The nitroethylpyrrole (**6a**) reacted with 2-methylpropanal in the presence of triethylamine to give the nitro alcohols (**11**) as an inseparable mixture of diastereoisomers. When one equivalent of DBN was used, however, dehydration occurred to give the unexpected non-conjugated nitroalkene (**12**). This presumably arises as the kinetic product of protonation of the allylnitronate anion (**13**) generated from the elimination product. Conversion of the alcohols (**11**) into their *O*-methanesulphonates in the presence of base [10] caused elimination to afford the conjugated nitroalkene (**14**). This was assigned the *E*-configuration from the chemical shift of its vinylic proton which, at δ6.94, had undergone a larger downfield shift than would be expected [11] for the *Z*-isomer.

For conversion of a *C*-nitro group into a ketone, McMurry generated the nitronate anion prior to adding the titanium(III) reagent.[9] In the present case, both nitroalkenes (**12**) and (**14**) should give the same anion (**13**). In accord with this, treatment of each nitroalkene with t-butoxide and then with buffered titanium(III) chloride gave the same enone (**10**) though the yield from alkene (**12**) (59%) was considerably better than from the isomer (**14**) (24%). All attempts to add the nitroethyl-pyrrole (**6b**) or nitromethane Michael-fashion to the enone (**10**) led to its decomposition with none of the desired adduct being isolated. Since the base sensitivity and apparent lack of reactivity of the enone (**10**) could possibly have been due to the acidity of the $-CO-CH_2-$ system, this was blocked by conversion into the dithiane (**15**) using propane-1,3-dithiotosylate.[12] Although the enone (**15**) was considerably more stable, no adduct could be obtained using the pyrrole (**6b**) under any conditions so this route to a D-A-B component was not further pursued.

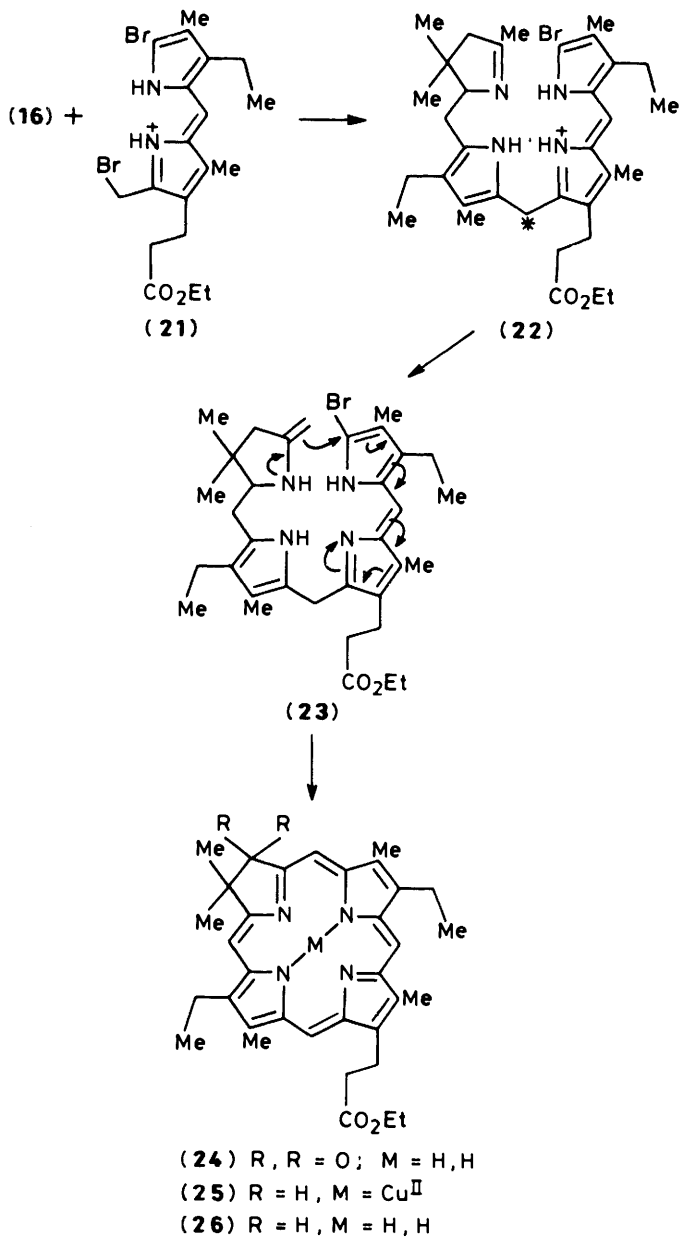
Cyclisations Promoted by Cu^{II}.—Ring-closure promoted by copper(II) are commonly used for the synthesis of porphyrins [13]



Scheme 2.



Scheme 3.



Scheme 4.

so we wished to explore the analogous ring-closure of the seco-system (**18**) (Scheme 3). The pyrrole ring of pyrroline (**3b**) was deprotected by treatment with trifluoroacetic acid (TFA) and the product (**16**) was condensed with the available pyrromethane (**17**).[14] Without isolating the seco-system (**18**), it was cyclised by heating with copper(II) chloride[13] in dimethylformamide to yield, after demetallation of the initial products, two macrocyclic pigments in *ca.* 2:1 ratio. The major pigment was found by u.v.-visible, mass and n.m.r. spectroscopy to be the oxo-chlorin (**19**). The n.m.r. spectrum of the minor product showed loss of the acetyl residue and the sum of all the spectroscopic evidence led to structure (**20**); though initially a surprising result, a survey of the literature showed that related reactions have been observed previously.[15] The formation of oxochlorins in the foregoing sequence and the low yield of product (2—3% overall) led to a study of the alternative approach below.

This second route envisaged ring-closure of a bromopyrromethene system (**22**) *via* its enamine tautomer (**23**) using a metal-ion template as illustrated (Scheme 4). The required system (**22**) was built by alkylation of the same A-D component (**16**), used above, with the readily prepared 5-bromo-5′-bromomethylpyrromethene (**21**).[16] The reaction could be followed by n.m.r. focussing on the disappearance of the signal for the pyrrolic α-hydrogen of component (**16**) and on the change in the signal for the 5′-methylene group of component (**21**). The latter signal moved upfield and became an AB-quartet, δ 4.19, as the alkylation was completed; this chemical shift is as expected for the asterisked CH_2 of seco-system (**22**), as judged from observations on tripyrrenes.[17] The hydrogens at the asterisked CH_2 are diastereotopic because of the pyrroline ring; in addition, the molecule (**22**) may be non-planar.

The initial experiments on ring-closure of the seco-system (**22**) using copper(II) acetate were monitored by u.v.-visible spectroscopy which showed first the formation of a copper complex of the seco-system [(**23**) or tautomer] and later the appearance of the copper complex of a macrocycle. The latter was demetallated to yield the oxochlorin (**24**), *ca.* 5% overall. Closer monitoring of the reaction revealed that the desired chlorin (**25**) was probably being formed and was subsequently

undergoing oxidation. Accordingly, the reaction was repeated in an oxygen-free glove box to yield the desired chlorin as its copper complex (**25**); of various solvents tested for the ring-closure, acetonitrile was best and gave a 6.8% overall yield. Attempted demetallation of (**25**) by the standard TFA–sulphuric acid method caused decomposition of the chlorin so alternative methods were developed.[18] Treatment of the complex (**25**) with TFA saturated with hydrogen sulphide afforded a 71% yield of the chlorin (**26**).

The second method above is worthy of consideration for synthesis of *C*-methylated unsymmetrical chlorins for though the yield over the two steps from the building blocks (**15**) and (**21**) is low, it compares not unfavourably with what could be expected from a less convergent multistage synthesis. The advantages of the method are its simplicity and brevity starting with readily prepared materials and it affords chlorins where all the *meso*-positions are unsubstituted.

A different synthesis of a *C*-methylated chlorin was carried out by Montforts in parallel with the foregoing work and has been briefly described.[19]

Experimental

General Directions.—Melting points were determined on a Kofler hot-stage apparatus and are uncorrected; electronic spectra were recorded with a Pye Unicam SP8-100 spectrophotometer and refer to solutions in dichloromethane unless otherwise stated; infrared spectra were recorded on a Perkin-Elmer 297 or 157G instrument for solutions in chloroform. ^{1}H N.m.r. spectra were run using Varian EM-360, HA-100D, EM-390, CFT-20 or XL-100 spectrometers, operating at 60, 100, 90, 80 and 100 MHz, respectively, with tetramethylsilane or the solvent peak as standard; unless otherwise stated solutions were in $CDCl_3$ and chemical-shift values are quoted on a δ scale relative to tetramethylsilane as δ = 0. Mass spectra were obtained on an A.E.I. MS30 machine fitted with a DS50 data system, A.E.I. MS902, or A.E.I.-Kratos MS50 machine. Field desorption (F.D.) spectra were run on the latter instrument.

Analytical thin-layer chromatography was performed on commercial Merck plates coated with silica gel GF_{254} (0.25 mm). Preparative-layer chromatography was carried out on 20 × 20 cm plates of 1 mm thickness, coated with the same silica gel, or on Merck type 11845 plates (0.25 mm), with a concentration zone and without fluorescent indicator. Column chromatography at atmospheric pressure was carried out on Merck Kieselgel 60 (63—200 μm), the same adsorbent (40—63 μm) being used for flash chromatography. Merck Kieselgel H60, referred to as 'silica H' was employed for 'short, fat columns' run under a moderate pressure of compressed air. Alumina was Woelm Grade I, neutral.

Organic solutions which had been in contact with water were dried over anhydrous sodium sulphate prior to evaporation, which was carried out at 30 Torr in a Büchi rotary evaporator. All solvents were redistilled, chloroform and dichloromethane being kept in the dark after distillation from anhydrous potassium carbonate. Light petroleum refers to the fraction boiling between 40 and 60 °C, and ether to diethyl ether.

Benzyl 4-Ethyl-3-methyl-5-(2-nitrovinyl)pyrrole-2-carboxylate (**5a**).—To a solution of benzyl 4-ethyl-5-formyl-3-methylpyrrole-2-carboxylate (**4a**)[16] (12.5 g, 45 mmol) in methanol (50 ml) containing potassium acetate (4.50 g, 48 mmol) and methylamine hydrochloride (3.06 g, 45 mmol) was added nitromethane (5.49 g, 90 mmol) and trimethyl orthoformate (7.5 ml, 68 mmol). The mixture was heated under reflux for 1 h and the solid was collected from the cooled solution and washed with a little cold methanol. It was dissolved in dichloromethane (150 ml), and the solution washed with water (80 ml); the aqueous layer was back-extracted with dichloromethane (2 × 100 ml). The combined organic layers were passed down a short alumina column, continuing elution with ether. The residue from evaporation crystallised from methanol to give the yellow *nitrovinylpyrrole* (10.3 g, 73%), m.p. 172—174 °C (Found: C, 64.95; H, 5.9; N, 8.9. $C_{17}H_{18}N_2O_4$ requires C, 64.95; H, 5.8; N, 8.9%); $\lambda_{max.}$ 264 and 386 nm; $\nu_{max.}$ 3 440, 3 320, 1 680br, 1 625, 1 450, and 1 330 cm^{-1}; *m/z* 314 (10% M^+), 202 (10), 117 (11), and 91 (100, $C_7H_7^+$); δ 1.14 (3 H, t, *J* 7.5 Hz, CH_2CH_3), 2.29 (3 H, s, $ArCH_3$) 2.60 (2 H, q, *J* 7.5 Hz, CH_2CH_3), 5.44 (2 H, s, CH_2Ph), 7.38 (5 H, m, C_6H_5), 7.69 (1H, d, *J* 13 Hz, O_2NCH=CH) 7.96 (1 H, d, *J* 13 Hz, O_2NCH=CH), and 10.10 (1 H, br, NH).

t-Butyl 4-Ethyl-3-methyl-5-(2-nitrovinyl)pyrrole-2-carboxylate (**5b**).—To a solution of t-butyl 4-ethyl-5-formyl-3-methylpyrrole-2-carboxylate (**4b**)[16] (4.74 g, 20 mmol) in methanol (20 ml) containing sodium acetate (1.73 g, 21 mmol) and methylamine hydrochloride (1.38 g, 20.5 mmol) was added nitromethane (2.44 g, 40 mmol). The solution was stirred at 20 °C for 3 h, then diluted with water (100 ml) and extracted with dichloromethane (100 ml, 3 × 50 ml). The product crystallised from methanol to give the yellow *nitrovinylpyrrole* (3.48 g, 61.8%), m.p. 55—62 °C (Found: C, 59.95; H, 7.2; N, 10.2. $C_{14}H_{20}N_2O_4$ requires C, 60.0; H, 7.2; N, 10.0%); $\lambda_{max.}$ 254 and 388 nm; $\nu_{max.}$ 3 610, 3 440, 1 690s, 1 620, 1 530, and 1 350 cm^{-1}; *m/z* 280 (28%, M^+), 224 [55, $M - (CH_3)_2C{=}CH_2$], 163 (100), and 135 (44); δ 1.13 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.58 [9 H, s, $C(CH_3)_3$], 2.26 [3 H, s, $ArCH_3$], 2.59 (2 H, q, *J* 7 Hz, CH_2CH_3), 7.42 (1 H, d, *J* 13 Hz, O_2NCH=CH), 7.92 (1 H, d, *J* 13 Hz, O_2NCH=CH), and 9.55 (1 H, br, NH).

Benzyl 4-Ethyl-3-methyl-5-(2-nitroethyl)pyrrole-2-carboxylate (**6a**).—To a vigorously stirred solution of the nitrovinylpyrrole (**5a**) (1.55 g, 5 mmol) in DMF (15 ml) and methanol (100 ml) was added solid sodium borohydride, as rapidly as possible, until a stable pale yellow solution was formed. Concentrated hydrochloric acid was added rapidly at 0 °C to bring the solution to pH 1 (*ca.* 6 ml). Water (150 ml) was added and the precipitate collected, washed with water, and crystallised from methanol–water to afford the *nitroethylpyrrole* (1.47 g, 93%), m.p. 155—157 °C (Found: C, 64.2; H, 6.4; N, 8.75. $C_{17}H_{20}N_2O_4$ requires C, 64.5; H, 6.4; N, 8.9%); $\lambda_{max.}$ 277 nm; $\nu_{max.}$ 3 790w, 3 440, 1 680s, 1 600m, 1 550s cm^{-1}; *m/z* 316 (72%, M^+), 269 (54, $M - HNO_2$), and 91 (100, $C_7H_7^+$); δ 1.08 (3 H, t, *J* 7 Hz, CH_2CH_3), 2.29 (3 H, s, $ArCH_3$), 2.40 (2 H, q, *J* 7 Hz, CH_2CH_3), 3.28 (2 H, t, *J* 7 Hz, $CH_2CH_2NO_2$), 4.53 (2 H, t, *J* 7 Hz, $CH_2CH_2NO_2$), 5.32 (2 H, s, CH_2Ph), 7.36 (5 H, m, C_6H_5), and 9.38 (1 H, br, NH).

t-Butyl 4-Ethyl-3-methyl-5-(2-nitroethyl)pyrrole-2-carboxylate (**6b**).—A solution of the nitrovinylpyrrole (**5b**) (3.6 g, 12.9 mmol) in DMF (20 ml) and methanol (150 ml) was treated as above to give the *nitroethylpyrrole* (3.30 g, 91%), m.p. 127—128 °C (Found: C, 59.5; H, 7.7; N, 9.9. $C_{14}H_{22}N_2O_4$ requires C, 59.55; H, 7.85; N, 9.9%); $\lambda_{max.}$ 273 nm; $\nu_{max.}$ 3 610, 3 440, and 1 680s cm^{-1}; *m/z* 282 (28%, M^+), 226 [20, $M - (CH_3)_2C{=}CH_2$], 210 (65), 179 (100), and 165 (50); δ 1.04 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.53 [9 H, s, $C(CH_3)_3$], 2.22 (3 H, s, $ArCH_3$), 2.37 (2 H, q, *J* 7 Hz, CH_2CH_3), 3.25 (2 H, t, *J* 7 Hz, $CH_2CH_2NO_2$), 4.49 (2 H, t, *J* 7 Hz, $CH_2CH_2NO_2$), and 8.86 (1 H, br, NH).

Benzyl 4-Ethyl-5-(3,3-dimethyl-2-nitro-5-oxohexyl)-3-methylpyrrole-2-carboxylate (**7a**).—To a stirred solution of the nitroethylpyrrole (**6a**) (320 mg, 1 mmol) in DMF (1.5 ml) under nitrogen was added DBN (0.12 ml, 1 mmol). The solution was heated to 80 °C and after 30 min 4-methylpent-3-en-2-one (98 mg, 1 mmol) was added. Heating was continued for 22 h, and the mixture evaporated, finally at 0.1 mmHg. The residue in

dichloromethane (15 ml) was washed with 2M-hydrochloric acid (2 × 15 ml), and the aqueous layer back-extracted with dichloromethane (15 ml). The residue from the combined organic layers was chromatographed on a silica H column (6 g), using dichloromethane–light petroleum (1:1) as eluant, later changing to 2:1. The product was crystallised from dichloromethane–hexane to give the *nitro ketone* (298 mg, 74%), m.p. 136—137 °C (Found: C, 66.8; H, 7.4; N, 6.6. $C_{23}H_{30}N_2O_5$ requires C, 66.6; H, 7.3; N, 6.8%); $\lambda_{max.}$ 277 nm; $\nu_{max.}$ 3 440m, 1 690s, br, 1 545, and 1 360 cm^{-1}; *m/z* 414 (10%, M^+), 367 (23, $M - HNO_2$), 310 (27), 258 (27), 202 (35), 135 (70), and 91 (100, $C_7H_7^+$); δ 1.07 (3 H, t, *J* 8 Hz, CH_2CH_3), 1.11 and 1.24 [each 3 H, s, $C(CH_3)_2$], 2.12 (3 H, s, $COCH_3$), 2.25 (3 H, s, $ArCH_3$), 2.36 (2 H, q, *J* 8 Hz, CH_2CH_3), 2.49 (2 H, ABq, *J* 17 Hz, CH_2COCH_3), 2.94 (1 H, dd, *J* 3, 15 Hz CH_2CHNO_2), 3.27 (1 H, dd, *J* 11, 15 Hz, CH_2CHNO_2), 5.13 (1 H, dd, *J* 3, 11 Hz, $CHNO_2$), 5.26 (2 H, s, CH_2Ph), 7.34 (5 H, m, C_6H_5), and 8.81 (1 H, br, NH).

t-Butyl 4-*Ethyl*-5-(3,3-*dimethyl*-2-*nitro*-5-*oxohexyl*)-3-*methylpyrrole*-2-*carboxylate* (**7b**).—A solution of tetrabutylammonium fluoride trihydrate (1.26 g, 4 mmol) in DMF (40 ml) containing Type 3A molecular sieve (2 g) was stirred under argon for 30 min. The nitroethylpyrrole (**6b**) (1.13 g, 4 mmol) and 4-methylpent-3-en-2-one (2.2 g, 22 mmol) were added and stirring at 20 °C was continued for 2 h. The solution was diluted to 150 ml with ether, filtered, and then washed with hydrochloric acid (2M; 80 ml), saturated sodium hydrogen carbonate solution (80 ml), and brine (50 ml). The organic layer was evaporated, finally at 0.1 mmHg, and the residue crystallised from dichloromethane–hexane to give the *nitro ketone* (1.34 g, 88.2%), m.p. 136.5—137 °C (Found: C, 62.9; H, 8.5; N, 7.2; $C_{20}H_{32}N_2O_5$ requires C, 63.1; H, 8.5; N, 7.4%); $\lambda_{max.}$ 274 nm; $\nu_{max.}$ 3 610m, 3 440m, 1 715s, 1 680s, and 1 370 cm^{-1}; *m/z* 380 (14%, M^+), 277 (50), 220 (100), and 166 (39); δ 1.06 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.13 and 1.26 [each 3 H, s, $C(CH_3)_2$], 1.54 [9 H, s, $C(CH_3)_3$], 2.14 (3 H, s, $COCH_3$), 2.21 (3 H, s, $ArCH_3$), 2.36 (2 H, q, J 7 Hz, CH_2CH_3), 2.51 (2 H, ABq, *J* 17 Hz, CH_2CO), 2.96 (1 H, dd, *J* 3, 15 Hz, CH_2CHNO_2), 3.28 (1 H, dd, *J* 11, 15 Hz, CH_2CHNO_2), 5.11 (1 H, dd, *J* 3, 11 Hz, $CHNO_2$), and 8.56 (1 H, br, NH).

5-(5-*Benzyloxycarbonyl*-3-*ethyl*-4-*methylpyrrol*-2-*ylmethyl*)-3,4-*dihydro*-2,4,4-*trimethylpyrrole* 1-*Oxide* (**8a**).—To a vigorously stirred solution of the nitro ketone (**7a**) (80 mg, 0.2 mmol) in glacial acetic acid (3 ml) was added zinc dust (400 mg). After 30 min the solution was filtered through Celite and most of the solvent evaporated. The residue in dichloromethane (20 ml) was washed with aqueous sodium carbonate (20%; 10 ml). Evaporation and trituration with ether yielded the *pyrrole* N-*oxide* (71 mg, 96%), m.p. 120—121 °C (Found: C, 72.0; H, 7.9; N, 7.3. $C_{23}H_{30}N_2O_3$ requires C, 72.2; H, 7.9; N, 7.3%); $\lambda_{max.}$ (rel. int.) 241 (67) and 282 nm (100); $\nu_{max.}$ 3 240br, 1 685s, 1 610m, and 1 570w cm^{-1}; *m/z* 382 (46%, M^+), 365 (38, $M-OH$), 310 (100), 257 (69), 256 (58, M − pyrroline ring), and 202 (80); δ 1.06 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.07, 1.20 [each 3 H, s, $C(CH_3)_2$], 2.07 (3 H, br s, $N{=}CCH_3$), 2.31 (3 H, s, $ArCH_3$), 2.41 (2 H, q, *J* 7 Hz, CH_2CH_3) (obscures signal due to $H{=}CCH_2$), 2.92 (2 H, d, *J* 5 Hz, CH_2CHNO), 3.86 (1 H, m, $CHNO$), 5.30 (2 H, ABq, 12 Hz, CH_2Ph), and 7.20—7.50 (5 H, m, C_6H_5); δ(CD_3OD) 1.02, 1.08 [each 3 H, s, $C(CH_3)_2$], 1.06 (3 H, t, *J* 7 Hz, CH_2CH_3), 2.02 (3 H, d, *J* 1.5 Hz, $N{=}CCH_3$), 2.24 (3 H, s, $ArCH_3$), 2.35 (2 H, q, *J* 7 Hz, CH_2CH_3), 2.46 (2 H, br s, $N{=}CCH_2$), 2.98 (2 H, 2 × dd, *J* 5, 6, 15 Hz, CH_2CHNO), 3.95 (1 H, m, CHNO), 5.24 (2 H, s, CH_2Ph), and 7.22—7.40 (5 H, m, C_6H_5).

5-(5-*Benzyloxycarbonyl*-3-*ethyl*-4-*methylpyrrol*-2-*ylmethyl*)-3,4-*dihydro*-2,4,4-*trimethylpyrrole* (**3a**).—*Method A.* Under nitrogen, a vigorously stirred solution of the foregoing pyrroline *N*-oxide (**8a**) (50 mg, 0.13 mmol) in THF (1 ml) was treated with buffered titanium(III) chloride solution (0.65 ml, 0.26 mmol). After 3 h more, titanium(III) chloride solution (0.65 ml) was added, followed by a similar portion after a further 3 h. After a total of 19 h, the precipitate was removed by filtration through Celite and washed with dichloromethane. The filtrate was extracted with dichloromethane (3 × 10 ml), then the combined organic layers were washed with aqueous sodium carbonate (5%; 20 ml) and brine (20 ml). The solution was passed through a silica H column (2 g), and elution continued with ether. Evaporation of the eluate gave the pure *pyrroline* as a gum (36 mg, 75%) (Found: M^+, 366.2310. $C_{23}H_{30}N_2O_2$ requires M^+, 366.2313); $\lambda_{max.}$ 285 nm; $\nu_{max.}$ 3 320v br, 1 690 (s with shoulder at 1 655), and 1 500 cm^{-1}; *m/z* 366 (26%, M^+), 300 (10), 256 (48, M − pyrroline ring), 203 (72), and 151 (100); δ 0.95, 1.13 [each 3 H, s, $C(CH_3)_2$], 1.06 (3 H, t, *J* 7 Hz, CH_2CH_3), 2.01 (3 H, d, *J* 2 Hz, $N{=}CCH_3$), 2.32 (5 H, s, $ArCH_3$ + $N{=}CCH_2$), 2.41 (2 H, q, *J* 7 Hz, CH_2CH_3), 2.44 (1 H, dd, *J* 10, 15 Hz, CH_2CHN), 2.74 (1 H, dd, 3.5, 15 Hz, CH_2CHN), 3.61 (1 H, ddd, *J* 2, 3.5, 10 Hz, CHN=C), 5.27 (2 H, s, CH_2Ph), and 7.20—7.50 (5 H, m, C_6H_5). Irradiating the signal at δ 3.61 causes signals at δ 2.01, 2.44, and 2.74 to collapse to s, d, *J* 15 Hz, and d, *J* 15 Hz respectively.

Method B. A stirred solution of the nitro ketone (**7a**) (160 mg, 0.40 mmol) in glacial acetic acid (2 ml) was treated with zinc dust (800 mg). After 30 min, the zinc was removed by filtration through Celite. The filtrate was concentrated (to 2 ml) and ammonium acetate (0.6 g) added. The flask was purged with nitrogen and commercial titanium(III) chloride solution (15%; 1.6 ml, 1.6 mmol) was added. After being stirred for 15 h, the mixture was filtered through Celite, the filter cake washed with ether, and the filtrate evaporated at 50 °C. The residue in ether (30 ml) was washed with aqueous ammonia (1M; 2 × 25 ml), and the aqueous layers extracted with more ether (15 ml). Evaporation of the combined organic layers afforded the *pyrroline* (139 mg, 95%), identical with that obtained by Method A.

5-(3-*Ethyl*-4-*methyl*-5-*t-butoxycarbonylpyrrol*-2-*ylmethyl*)-3,4-*dihydro*-2,4,4-*trimethylpyrrole* (**3b**).—This compound was prepared from the nitro ketone (**7b**) (700 mg, 1.83 mmol), according to Method B above. The gum obtained was dissolved in warm methanol (15 ml) and treated with a solution of dry picric acid (440 mg, 1.92 mmol) in methanol (5 ml) to give the *pyrroline picrate monomethanolate* (914 mg, 88.4%), m.p. 131—133.5 °C (Found: C, 54.4; H, 6.5; N, 12.1. $C_{27}H_{39}N_5O_{10}$ requires C, 54.6; H, 6.6; N, 11.8%); all the spectroscopic data refer to the free base (Found: M^+, 332.2467. $C_{20}H_{32}N_2O_2$ requires M^+, 332.2464); $\lambda_{max.}$ 282 nm; $\nu_{max.}$ 3 615, 3 340br, and 1 680s cm^{-1}; *m/z* 332 (8%, M^+), 274 [2, $M - (CH_3)_2C{=}CH_2$], 222 (7, M − pyrroline ring), 166 (100), and 110 (78); δ 0.95, 1.12 [each 3 H, s, $C(CH_3)_2$], 1.04 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.56 [9 H, s, $C(CH_3)_3$], 2.05 (3 H, d, *J* 2 Hz, $N{=}CCH_3$), 2.27 (3 H, s, $ArCH_3$), 2.40 (2 H, q, *J* 7 Hz, CH_2CH_3), 2.41 (2 H, ABq, *J* 7 Hz, $N{=}CCH_2$), 2.46 (1 H, dd, *J* 10, 15 Hz, $CH_2CHN{=}C$), 2.73 (1 H, dd, *J* 3, 15 Hz, $CH_2CHN{=}C$), 3.61 (1 H, ddd, *J* 2, 3, 10 Hz, CHN=C), and 10.16 (1 H, br, NH).

Benzyl 4-*Ethyl*-3-*methyl*-5-(3-*hydroxy*-4-*methyl*-2-*nitropentyl*)*pyrrole*-2-*carboxylate* (**11**).—To a solution of the nitroethylpyrrole (**6a**) (1 g, 3.16 mmol) in DMF (8 ml) containing triethylamine (320 mg, 3.16 mmol), under argon, was added 2-methylpropanal (3 ml, 34 mmol). The solution was allowed to stand at 20 °C in the dark for 4 days, after which the solvent was removed (45 °C/1 mmHg). The residue in dichloromethane (70 ml) was washed with hydrochloric acid (2M; 2 × 50 ml) and the aqueous layer back-extracted with dichloromethane (50 ml).

The residue from evaporation of the combined organic layers was crystallised from chloroform to give the *nitro alcohol* (460 mg), m.p. 150.5—154.5 °C. A second crop was obtained from chloroform (286 mg), m.p. 158—162 °C, and a third crop from methanol (245 mg), m.p. 119—123 °C, remelting at 155—159 °C after cooling. Overall yield 991 mg (80.8%) as a mixture of diastereoisomers (Found: C, 65.0; H, 7.4; N, 7.2%; M^+, 388.2000. $C_{21}H_{28}N_2O_5$ requires C, 64.9; H, 7.3; N, 7.2%; M^+, 388.1998); $\lambda_{max.}$ (MeOH) 205 and 279 nm; $\nu_{max.}$ 3 700w, 3 580w, 3 450m, 1 690br, s, 1 550, and 1 450 cm^{-1}; *m/z* 388 (7%, M^+), 316 [7, $M - (CH_3)_2CHCHO$], 298 (7), 269 (4), 256 [4, $M - (CH_3)_2CHCH(OH)CH(NO_2)$] and 91 (100, $C_7H_7^+$); δ [$(CD_3)_2SO$] 0.98 [9 H, m, $CH_2CH_3 + (CH_3)_2CH$], 1.76 [1 H, m, $(CH_3)_2CH$], 2.19 (3 H, s, $ArCH_3$), 2.32 (2 H, q, *J* 7 Hz, CH_2CH_3), 2.94, 3.26 (each 1 H, m, O_2NCHCH_2), 3.61 (1 H, dd, *J* 5, 7 Hz, CHOH), 3.93 (1 H, br, OH), 5.08 (1 H, m, $CHNO_2$), 5.27 (2 H, s, CH_2Ph), 7.37 (5 H, m, C_6H_5), and 11.22 (1 H, br, NH).

Benzyl 4-*Ethyl*-3-*methyl*-5-(4-*methyl*-2-*nitropent*-3-*enyl*)-*pyrrole*-2-*carboxylate* (**12**).—A stirred solution, under nitrogen, of the nitroethylpyrrole (**6a**) (800 mg, 2.53 mmol) in DMF (6 ml) containing DBN (0.31 ml, 2.6 mmol) and 2-methylpropanal (2.4 ml, 25 mmol) was warmed to 35 °C for 16 h. The solvent was removed (45 °C/1 mmHg), and the residue in ether (50 ml) washed with hydrochloric acid (2M; 3 × 30 ml) and brine (30 ml). The ethereal solution was concentrated and the residual DMF evaporated as an azeotrope with methanol (2 × 10 ml). The residue was purified by column chromatography on silica H (34 g), with dichloromethane–light petroleum (1:3) as eluant and the product crystallised from methanol–water (722 mg, 77.2%), m.p. 90.5—91.5 °C (Found: C, 67.9; H, 7.1; N, 7.5%; M^+, 370.1888. $C_{21}H_{26}N_2O_4$ requires C, 68.1; H, 7.1; N, 7.6%; M^+, 370.1893); $\lambda_{max.}$(MeOH) 205 and 280 nm; $\nu_{max.}$ 3 440m, 3 300w, 1 670s, and 1 550br cm^{-1}; *m/z* 370 (4%, M^+), 324 (10), 256 (21, $M - Me_2C{=}CHCHNO_2$), and 91 (100, $C_7H_7^+$); δ 1.08 (3 H, t, *J* 7.5 Hz, CH_2CH_3), 1.64 (3 H, s, $CH_3C{=}CH$ *anti* to NO_2), 1.74 (3 H, s, $CH_3C{=}CH$ *syn* to NO_2), 2.30 (3 H, s, $ArCH_3$), 2.41 (2 H, q, *J* 7.5 Hz, CH_2CH_3), 3.09 (1 H, dd, *J* 7 , 15 Hz, O_2NCHCH_2), 3.40 (1 H, dd, *J* 7, 15 Hz, O_2NCHCH_2), 5.31 (2 H, s, CH_2Ph), 5.35 (1 H, m, O_2NCH), 5.37 [1 H, d, *J* 7 Hz, $(CH_3)_2C{=}CH$], 7.38 (5 H, m, C_6H_5), and 9.39 (1 H, br, NH). Irradiating the signal at δ 5.35 caused the signals at δ 3.09 and 3.40 to collapse to doublets (*J* 15 Hz).

Benzyl 4-*Ethyl*-3-*methyl*-5-(4-*methyl*-2-*nitropent*-2E-*enyl*)-*pyrrole*-2-*carboxylate* (**14**).— Methanesulphonyl chloride (70 mg, 0.61 mmol) was added rapidly to a stirred solution of the foregoing nitro alcohol (**11**) (211 mg, 0.544 mmol) in dichloromethane (3 ml), at 0 °C. After 10 min, triethylamine (0.3 ml) was added dropwise over 2 min and the solution allowed to stand at 20 °C for 1 h. Dichloromethane (25 ml) was added and the solution washed with water (20 ml), hydrochloric acid (1M; 15 ml), and brine (15 ml). The residue from the organic layer was purified by p.l.c. with dichloromethane as eluant: the more polar component was unchanged nitro alcohol (20 mg); the major component was crystallised from dichloromethane–hexane to give the *conjugated nitroalkene* (133 mg, 71.5% based on unrecovered starting material), m.p. 97.5—100.5 °C (Found: M^+, 370.1884. $C_{21}H_{26}N_2O_4$ requires M^+, 370.1893); $\lambda_{max.}$(MeOH) 207 and 278 nm; $\nu_{max.}$ 3 700w, 3 460m, 1 690s, 1 600w, and 1 580w cm^{-1}; *m/z* 370 (95%, M^+), 323 (100, $M - HNO_2$), 280 (30), and 261 (88); δ 1.01 (3 H, t, *J* 7.5 Hz, CH_2CH_3), 1.07 [6 H, d, *J* 7 Hz, $(CH_3)_2CH$], 2.24 (3 H, s, $ArCH_3$), 2.39 (2 H, q, *J* 7.5 Hz, CH_2CH_3), 2.64 [1 H, symmetrical m, $(CH_3)_2CH$], 3.83 [2 H, s, $CH{=}C(NO_2)CH_2$], 5.22 (2 H, s, CH_2Ph), 6.94 [1 H, d, *J* 11 Hz, $CH{=}C(NO_2)$], 7.28 (5 H, m, C_6H_5), and 8.83 (1 H, br, NH).

Benzyl 4-*Ethyl*-3-*methyl*-5-(4-*methyl*-2-*oxopent*-3-*enyl*)-*pyrrole*-2-*carboxylate* (**10**).—*Method A.* A solution of the unconjugated nitroalkene (**12**) (807 mg, 2.18 mmol) in dry THF (60 ml) and t-butyl alcohol (1 ml) was stirred with resublimed potassium t-butoxide (490 mg, 4.4 mmol) for 25 min. The flask was flushed with nitrogen and buffered titanium(III) chloride solution (21.7 ml, 8.7 mmol) added rapidly. After 1 h, ether (150 ml) was added and the mixture filtered through Celite. The filtrate was washed with water (150 ml). The aqueous layer was filtered again through Celite, then extracted with more ether (2 × 100 ml). The product from the combined organic layers was chromatographed in silica (5 g), eluting with dichloromethane–ether (95:5) to give the *enone* (438 mg, 59%) from ether–hexane, m.p. 90—92 °C (Found: C, 74.1; H, 7.6; N, 4.0%; M^+, 339.1826. $C_{21}H_{25}NO_3$ requires: C, 74.3; H, 7.4; N, 4.1%; M^+, 339.1834); $\lambda_{max.}$(MeOH) (rel. int.) 206 (78), 241 (82), and 283 nm (100); $\nu_{max.}$ 3 460m, 1 690s, and 1 440m cm^{-1}; *m/z* 339 (15%, M^+), 256 [43, $M - (CH_3)_2C{=}CHC{=}O$], 166 (9), 91 (100, $C_7H_7^+$), and 83 (49); δ 1.04 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.89 (3 H, d, *J* 2 Hz, $CH_3C{=}CH$ *anti* to C=O), 2.16 (3 H, d, *J* 1.5 Hz, $CH_3C{=}CH$ *syn* to C=O), 2.30 (3 H, s, $ArCH_3$), 2.39 (2 H, q, *J* 7 Hz, CH_2CH_3), 3.63 (2 H, s, $CH_2C{=}O$), 5.29 (2 H, s, CH_2Ph), 6.07 [1 H, br s, $(CH_3)_2C{=}CH$], 7.37 (5 H, m, C_6H_5), and 9.25 (1 H, br, NH).

Method B. A solution of the conjugated nitroalkene (**14**) (50 g, 0.14 mmol) in THF (6 ml) containing resublimed potassium t-butoxide (30 mg, 0.28 mmol) was stirred for 15 min. The flask was flushed with nitrogen and buffered titanium(III) chloride solution (1.3 ml, 0.56 mmol) added rapidly. The mixture was stirred vigorously for 20 min, then ether (20 ml) and water (20 ml) were added and the mixture filtered through Celite. The aqueous layer was separated, filtered again, and extracted with more ether (2 × 25 ml). The residue from evaporation of the organic layers was purified by p.l.c., with dichloromethane–ether (95:5) as eluant, to give two major bands. The band with higher R_F was the desired enone (11 mg, 24%), identical with that obtained by method A. The more polar band (15 mg, 31%) is thought to be *benzyl* 4-*ethyl*-3-*methyl*-5-(2-*hydroxyimino*-4-*methylpentyl*)*pyrrole*-2-*carboxylate*, on the basis of its mass spectrum. The n.m.r. data is consistent with this, and indicates the presence of both isomers of the oxime (Found: M^+, 356.2079. $C_{21}H_{28}N_2O_3$ requires M^+, 356.2100); *m/z* 357 (53%, $M + 1$), 356 (8, M^+), 256 [87, $M - (CH_3)_2CHCH_2C{=}NOH$], and 91 (100, $C_7H_7^+$); δ 0.74 [*ca.* 3 H, d, *J* 7 Hz, $(CH_3)_2CH$, one isomer], 1.06 (3 H, t, *J* 7.5 Hz, CH_2CH_3), 1.08 [*ca.* 3 H, d, *J* 9 Hz, $(CH_3)_2CH$, other isomer], 2.15 [1 H, m, $(CH_3)_2CH$], 2.28 (3 H, s, $ArCH_3$), 2.37 [2 H, q, *J* 7.5 Hz, CH_2CH_3 (obscures signal due to $(CH_3)_2CHCH_2$)], 3.21 (1 H, br, OH), 3.65 (*ca.* 0.8 H, $ArCH_2C{=}NOH$, one isomer), 3.73 (*ca.* 1.2 H, s, $ArCH_2C{=}NOH$, other isomer), 5.29 (2 H, s, CH_2Ph), 7.36 (5 H, m, C_6H_5), and 9.10 (1 H, br, NH).

Benzyl 4-*Ethyl*-3-*methyl*-5-[2-(3-*methyl*-1-*oxobut*-2-*enyl*)-1,3-*dithian*-2-*yl*]*pyrrole*-2-*carboxylate* (**15**).—A solution of the foregoing pyrrole enone (**10**) (215 mg, 0.634 mmol), propane-1,3-dithiotosylate[12] (251 mg, 0.603 mmol) and potassium acetate (211 mg, 2.16 mmol) in t-butyl alcohol (15 ml) was heated to reflux, under nitrogen for 6.5 h. Most of the solvent was evaporated, and the residue was partitioned between dichloromethane (50 ml) and water (40 ml). The organic layer was washed with saturated aqueous sodium hydrogen carbonate (2 × 30 ml) and evaporated. Purification of the residue by column chromatography on silica H (7 g) with dichloromethane–light petroleum (1:1) afforded the desired *dithianylpyrrole* (214 mg, 76.2%) (Found: M^+, 443.1572. $C_{24}H_{29}NO_3S_2$ requires *M*, 443.1589); $\lambda_{max.}$(MeOH) 205, 253sh and 280 nm; $\nu_{max.}$ 3 430, 2 980, 1 680s, 1 610m and 1 435m cm^{-1}; *m/z* 443 (0.2%, M^+) and 360 [100, $M - (CH_3)_2C{=}CHC{=}O$]; δ

0.97 (3 H, t, *J* 7.5 Hz, CH_2CH_3), 1.82 (3 H, d, *J* 1 Hz, CH_3C=CH *anti* to C=O), 1.93 (2 H, m, $SCH_2CH_2CH_2S$), 2.19 (3 H, d, *J* 1 Hz, CH_3C=CH *syn* to C=O), 2.26 (3 H, s, $ArCH_3$), 2.35 (2 H, q, *J* 7.5 Hz, CH_2CH_3), 2.65 (2 H, m, $SCH_2CH_2CH_2S$ *anti* to pyrrole), 3.10 (2 H, m, $SCH_2CH_2CH_2S$, *syn* to pyrrole), 5.32 (2 H, s, CH_2Ph), 5.96 [1 H, br s, $(CH_3)_2C$=CH], 7.38 (5 H, m, C_6H_5), and 9.15 (1 H, br, NH).

7-*Acetyl*-18-*ethyl*-8,12-*bis*(2-*methoxycarbonylethyl*)-2,2,13,17-*tetramethyl*-3-*oxochlorin* (**19**) *and* 18-*Ethyl*-7-*formyl*-8,12-*bis*(2-*methoxycarbonylethyl*)-2,2,13,17-*tetramethyl*-3-*oxochlorin* (**20**).—The pyrrolylmethylpyrroline (**3b**) (29 mg, 87 μmol) was dissolved in TFA (3 ml) at 20 °C. After 10 min, the solvent was evaporated and the residue in dichloromethane (10 ml) washed with aqueous sodium hydrogen carbonate (5%, 5 ml). The organic layer was evaporated and a solution of 4-acetyl-3,3′-bis(2-methoxycarbonylethyl)-5,4′-dimethyl-5′-formylpyrro methane (**17**)[14] (36.3 mg, 87 μmol) in dichloromethane (5 ml) added, followed by a solution of toluene-*p*-sulphonic acid (76 mg) in methanol (1.3 ml). When the absorption at 496 nm reached maximum intensity (5 min), the mixture was poured into water (10 ml) and extracted with dichloromethane (3 × 10 ml). The combined organic layers were washed with aqueous sodium hydrogen carbonate (5%, 10 ml) and evaporated. A stirred solution of the residue in DMF (5 ml) containing hydrated copper(II) chloride (0.30 g, 1.7 mmol) was heated to 85 °C; absorptions at 408 and 622 nm were observed, which reached maximum intensity after 2 h. The solvent was removed at 0.1 mmHg and the residue partitioned between dichloromethane (20 ml) and water (20 ml). The aqueous layer was extracted with more dichloromethane (20 ml) and the combined organic layers passed through a silica column (3 g), eluting with chloroform until no more green material was obtained. The residue after evaporation of the eluate was treated with TFA (3 ml) and sulphuric acid (18M; 3 ml). After 15 min the solution was poured into ice–water (80 ml) and the chlorins extracted into dichloromethane (5 × 40 ml). The combined organic layers were washed with aqueous ammonia (1M; 50 ml) and water (50 ml), and then evaporated. The mixture was separated by p.l.c. using chloroform and a continuous elution technique. The most intense green band (red fluorescence under long wavelength u.v.), was extracted and rechromatographed using chloroform–dichloromethane (1:1) as eluant with a continuous elution technique to give two components. The major, more polar band gave the 7-*acetyl*-3-*oxochlorin* (**19**) (*ca.* 1 mg) (Found: M^+, 624.2926. $C_{36}H_{40}N_4O_6$ requires M^+, 624.2947); $\lambda_{max.}$(rel. int.) 410 (100), 507 (11.5), 540 (6.4), 587 (5.7), and 643 nm (22.4); *m/z* 624 (100%, M^+) and 551 (15, $M - CH_2CO_2CH_3$); *m/z* (F.D.) 624; δ 1.78 (3 H, t, *J* 7.5 Hz, CH_2CH_3), 2.04 [6 H, s, $C(CH_3)_2$], 3.18 (2 H, t, *J* 7.7 Hz) and 3.29 (2 H, t, *J* 7.3 Hz) (2 × $CH_2CH_2CO_2CH_3$), 3.38, 3.50, 3.51, 3.61, and 3.65 (each 3 H, s, 13-CH_3, 17-CH_3, CH_3C=O, 2 × CO_2CH_3), 3.90 (2 H, q, *J* 7.6 Hz, CH_2CH_3), 4.18 (2 H, t, *J* 7.7 Hz) and 4.59 (2 H, t, *J* 7.3 Hz) (2 × $CH_2CH_2CO_2CH_3$), 8.92 (1 H, s, 20-H), and 9.59, 10.00, and 10.05 (each 1 H, s, 5-H, 10-H, 15-H).

The less polar band yielded the 7-*formyl*-3-*oxochlorin* (**20**) (*ca.* 0.5 mg) (Found: M^+, 610.2806. $C_{35}H_{38}N_4O_6$ requires M^+, 610.2791); $\lambda_{max.}$(rel. int.) 414 (100), 508 (12.1), 540 (4.7), 590 (6.1), and 645 nm (21.6); *m/z* 610 (100%, M^+) and 537 (15, $M - CH_2CO_2CH_3$); *m/z* (F.D.) 610; δ 1.77 (3 H, t, *J* 7.6 Hz, CH_2CH_3), 2.03 [6 H, s, $C(CH_3)_2$], 3.18 and 3.29 (each 2 H, t, *J* 7.7 Hz, 2 × $CH_2CH_2CO_2CH_3$), 3.36, 3.47, 3.55, and 3.66 (each 3 H, s, 13-CH_3, 17-CH_3, 2 × CO_2CH_3), 3.87 (2 H, q, *J* 7.6 Hz, CH_2CH_3), 4.11 and 4.67 (each 2 H, t, *J* 7.7 Hz, 2 × $CH_2CH_2CO_2CH_3$), 8.84 (1 H, s, 20-H), 9.50, 9.99, and 10.09 (each 1 H, s, 5-H, 10-H, 15-H, and 11.73 (1 H, s, HC=O).

8,18-*Diethyl*-13-(2-*ethoxycarbonylethyl*)-2,2,7,12,17-*pentamethyl*-3-*oxochlorin* (**24**).—A solution of the pyrroline picrate (**3b**) (20.0 mg, 33.7 μmol), in chloroform (1 ml) was passed through a 20 × 5 mm column of basic alumina, eluting with more chloroform. The residue from evaporation of the eluate was treated with TFA (1 ml) at 20 °C for 6 min; the mixture was then evaporated and the residue in dichloromethane (15 ml) washed with saturated aqueous sodium hydrogen carbonate (2 × 8 ml). Evaporation yielded the α-free pyrrole (**16**) δ 0.96 and 1.12 [each 3 H, s, $C(CH_3)_2$], 1.10 (3 H, t, *J* 7.5 Hz, CH_2CH_3), 2.03 (3 H, d, *J* 2 Hz, N=CCH_3), 2.06 (3 H, d, *J* 1 Hz, $ArCH_3$), 2.33 (2 H, br s, N=CCH_2), 2.41 (1 H, dd, *J* 12, 16 Hz, CH_2CHN=C), 2.43 (2 H, q, *J* 7.5 Hz, CH_2CH_3), 2.74 (1 H, dd, *J* 4, 16 Hz, CH_2CHN=C), 3.59 (1 H, br d, *J* 12 Hz, CHN=C), 6.43 (1 H, br s, ArH), and 9.35 (1 H, br, NH). To a stirred solution of the α-free pyrrole in dichloromethane (0.5 ml) under argon was added a solution of 5-bromo-5′-bromomethyl-4,3′-dimethyl-4′-(2-ethoxycarbonylethyl)-3-ethylpyrromethene hydrobromide (**21**)[16] (19.8 mg, 36.1 μmol) in the same solvent (1 ml). After 40 min, the red solution was evaporated to give the 2,3-dihydro-*c*-bilene (**22**), $\lambda_{max.}$ 494 nm; δ 1.10 and 1.24 [each 3 H, s, $C(CH_3)_2$], 0.9—1.3 (broad signal containing 2 × ring CH_2CH_3, $CO_2CH_2CH_3$), 1.98, 2.05, and 2.30 (each 3 H, s, 3 × ring CH_3), 2.5—3.0 (broad signal due to most of the other protons), 4.11 (2 H, q, *J* 7.3 Hz, $CO_2CH_2CH_3$), 4.15 and 4.40 (each 1 H, d, *J* 14 Hz, 10-H_2), and 7.10 (1 H, s, 15-H). To a stirred solution of the dihydrobilene (**22**) in methanol (5 ml) under argon was added a slurry of hydrated copper(II) acetate (147 mg, 0.67 mmol) in glacial acetic acid (1.5 ml) to give a deep green solution, $\lambda_{max.}$ 508 nm. The mixture was heated to 60 °C for 17 h in the dark, by which time the peak at 508 nm had been replaced by peaks at 406 and 612 nm. The cooled reaction mixture was diluted with dichloromethane (20 ml), washed with saturated aqueous sodium hydrogen carbonate (3 × 10 ml), and evaporated. Purification of the residue by p.l.c., using dichloromethane–ether (96:4) as eluant gave the *oxochlorin copper complex* (1.0 mg, 5.0%) as the major green band, $\lambda_{max.}$(rel. int.) 412 (100), 565 (5.8), and 612 nm (21.6).

This complex in TFA (0.5 ml) and sulphuric acid (18M; 0.5 ml) was allowed to stand at 20 °C, under argon, for 15 min, then partitioned between ice–water (15 ml) and dichloromethane (10 ml). The aqueous layer was extracted with more dichloromethane (3 × 10 ml) and the combined organic layers were washed with aqueous ammonia (1M; 2 × 10 ml). Purification of the residue by p.l.c. with dichloromethane as eluant gave the oxochlorin as a brown-green band, *ca.* 0.8 mg (4.5%) (Found: M^+, 552.3100. $C_{34}H_{40}N_4O_3$ requires M^+, 552.3100); $\lambda_{max.}$(rel. int.) 404 (100), 506 (5.3), 545 (7.8), 582 (3.7), and 639 nm (20.1); (in CH_2Cl_2 + 5% TFA) 400 (104), 416 (106), 566 (9.6), and 617 nm (17.4); $\nu_{max.}$ 3 700w, 3 340, 1 710s, and 1 600m cm^{-1}; *m/z* 552 (100%, M^+), 465 (16, $M - CH_2CO_2Et$), and 368 (32); δ 1.21 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$), 1.82 (6 H, t, *J* 7.5 Hz, 2 × ring CH_2CH_3), 2.08 [6 H, s, $C(CH_3)_2$], 3.18 (2 H, t, *J* 7 Hz, $CH_2CH_2CO_2Et$), 3.49, 3.57, and 3.61 (each 3 H, s, 3 × ring CH_3), 3.95—4.2 (6 H, m, 2 × ring CH_2CH_3, $CH_2CH_2CO_2Et$), 4.19 (2 H, q, *J* 7 Hz, $CO_2CH_2CH_3$), 9.13 (1 H, s, 20-H), and 9.83, 9.84, and 9.92 (each 1 H, s, 5-H, 10-H, 15-H).

8,18-*Diethyl*-13-(2-*ethoxycarbonylethyl*)-2,2,7,12,17-*pentamethylchlorin* (**26**).—The 2,3-dihydro-*c*-bilene (**22**) was prepared as above, from the pyrroline picrate (**3b**) (40 mg, 67.4 μmol) and the pyrromethene hydrobromide (**21**) (39.4 mg, 71.2 μmol). The resulting red glass was transferred to an argon-filled glove box and was dissolved in degassed acetonitrile (2 ml). To this was added a slurry of hydrated copper(II) acetate (310 mg, 1.43 mmol), in the same solvent (18 ml) and the mixture stirred and heated under reflux in the dark. The visible spectrum of the mixture before heating showed peaks at 356, 396, 514, and 608

nm, in decreasing order of intensity. Heating was continued for 9.5 h, by which time the peaks at 356 and 514 nm had disappeared. The reaction mixture was partitioned between dichloromethane (20 ml) and water (15 ml). The aqueous layer was extracted with dichloromethane (4 × 5 ml) and the combined organic layers washed with saturated aqueous sodium hydrogen carbonate (20 ml), filtered through sodium sulphate, and evaporated. The green residue was separated by p.l.c. using dichloromethane–ether (95:5). The least polar component (blue) was further purified by p.l.c., using dichloromethane as eluant, to yield the chlorin copper complex (2.8 mg, 6.9%). The yield was estimated spectrophotometrically, assuming $\varepsilon_{mM} = 158$:[20] $\lambda_{max.}$(rel. int.) 396 (100), 492 (3.0), 528 (2.6), 560 (4.5), and 608 nm (23.1); *m/z* 601 (54%, M^{+} ^{65}Cu), 599 (100, M^{+} ^{63}Cu) 514 (4), and 512 (10) (both $M - CH_2CO_2Et$). The combined chlorin copper complex from similar preparations (5.00 mg, 8.33 μmol) in TFA (6 ml) was saturated with hydrogen sulphide gas and the green solution stirred for 18 h at 20 °C. The resulting deep blue solution was filtered through Celite, washing with TFA, then concentrated (to 3 ml) and partitioned between ice–water (40 ml) and dichloromethane (30 ml). The aqueous layer was extracted with more dichloromethane (3 × 10 ml), and the combined organic layers were washed with water (20 ml), aqueous ammonia (2M; 30 ml), and brine (30 ml). The residue from evaporation was purified by p.l.c. on a Merck plate which had been pre-treated with ammonia gas, eluting with dichloromethane–hexane (1:1). The blue-green band was the metal-free *chlorin* (3.2 mg, 71%). The yield was measured spectrophotometrically, assuming ε_{mM}(389 nm) = 220[20] (Found: M^{+}, 538.3319. $C_{34}H_{42}N_4O_2$ requires *M*, 538.3308); $\lambda_{max.}$(rel. int.) 389 (100), 488 (5.7), 493 (5.8), 586 (1.9), and 640 (23.6); (in CH_2Cl_2 + 5% TFA) 399 (109), 516 (4.2), 579 (4.4), and 629 nm (17.9); $\nu_{max.}$ 3 690, 3 600w, 3 340, 1 720s, and 1 610s cm^{-1}; *m/z* 538 (100%, M^{+}); δ 1.24 (3 H, t, *J* 6.5 Hz, $CO_2CH_2CH_3$), 1.78 (6 H, t, *J* 7 Hz, 2 × ring CH_2CH_3), 2.06 [6 H, s, $C(CH_3)_2$], 3.17 (2 H, t, *J* 8 Hz, $CH_2CH_2CO_2Et$), 3.43, 3.45, and 3.55 (each 3 H, s, 3 × ring CH_3), 3.80—4.20 (6 H, m, 2 × ring CH_2CH_3, $CH_2CH_2CO_2Et$), 4.21 (2 H, q, *J* 6.5 Hz, $CO_2CH_2CH_3$), 4.64 (2 H, s, 3-H_2), 8.80 (1 H, s, 20-H), 8.91 (1 H, s, 5-H), and 9.70 (2 H, s, 10-H, 15-H). Irradiating at δ 4.64 caused the signal at δ 8.91 to increase in intensity.

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