Synthetic Studies Relevant to Biosynthetic Research on Vitamin B_{12}. Part 10.[1] Construction of the East and West Building Blocks for Synthesis of Isobacteriochlorins

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Studies with model compounds have led to the development of effective methods for (a) linking the pyrrolic rings to the reduced rings present in the isobacteriochlorin system (*e.g.* **4**) and (b) for introducing the carbon at C-5 required to complete the macrocycle. In the course of this work, many new pyrrolic systems have been prepared and characterised.

Part 12 of this Series (in preparation) describes the synthesis of sirohydrochlorin octamethyl ester **4** by assembling in a controlled way the components illustrated in Scheme 1. That synthesis of a natural isobacteriochlorin was achieved using methods developed by extensive experimentation with simpler model compounds. These studies led to solutions for the two problems which faced us (a) how to join ring A to ring D and also ring B to ring C (Scheme 1) and (b) how to introduce the one-carbon unit which would become C-5 of sirohydrochlorin ester **4**; the C_1-unit for C-15 presents no difficulty. All the model studies on these two topics will be reported in the present paper. The following paper, Part 11, describes how the initially formed east and west building blocks were successfully modified to allow isobacteriochlorins to be synthesized and Part 12 will report the culmination of this work.

Results and Discussion

As shown in Scheme 1, we envisaged coupling the monothioimides **1** and **2** with a phosphorus ylide **3** where X was to be some electron-withdrawing group. Such a group was felt to be necessary to make the phosphorus-bearing centre sufficiently acidic for generation of the anion in the presence of several other ionizable groups. This approach to the coupling step builds on the earlier work of Gossauer[2] but, as will be seen later, there may be a mechanistic difference between his work and ours.

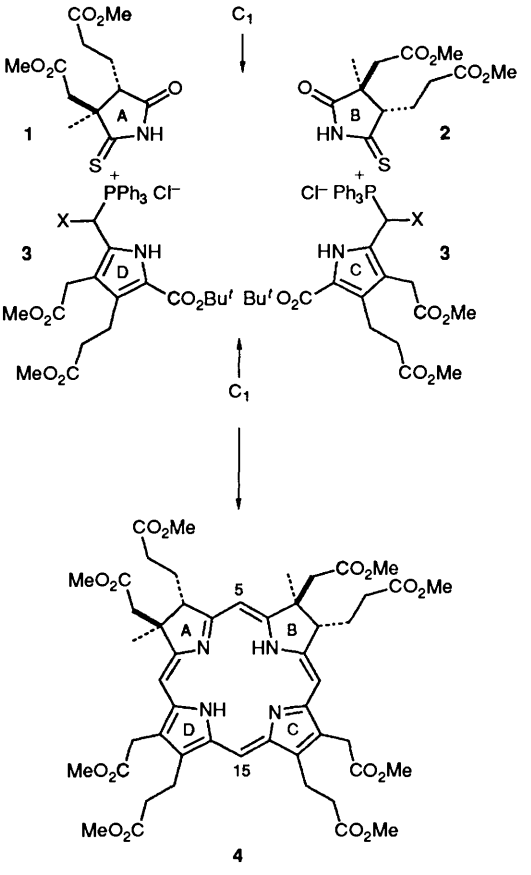
The first step was to explore possible groups X by using mostly the model system **10** as the thioimide component though some early experiments involved the simpler model **9**. The various groups which were studied as candidates for X will be considered in turn.

X = Hydrogen.—Though the argument seemed strong that an electron-withdrawing group X would be needed for the chemistry in Scheme 1, it was important to determine whether X was actually necessary. Clearly if X has to be used, it must be removed at some later stage in the synthesis. The stable phosphonium salt **6** was prepared from the known chloride[1] **5** and when this was converted into the ylide **7** by treatment with sodium hydride in the presence of propanal, the *E*-alkenylpyrrole **8** was formed in 63% yield, Scheme 2. However, replacement of the aldehyde by the monothioimide **9** in this procedure gave no coupled product and the ylide decomposed, a process probably initiated by proton transfer and expulsion of triphenylphosphine as illustrated.

Since the leaving group from the phosphonate **11** is poorer than that from the phosphonium salt **6**, such decomposition should be slower. Accordingly, the reagent **11** was made from the chloride **5** and triethyl phosphite by the Arbuzov process. However, treatment of the phosphonate **11** with base in the presence of either propanal or the monothioimide **9** afforded only starting material.

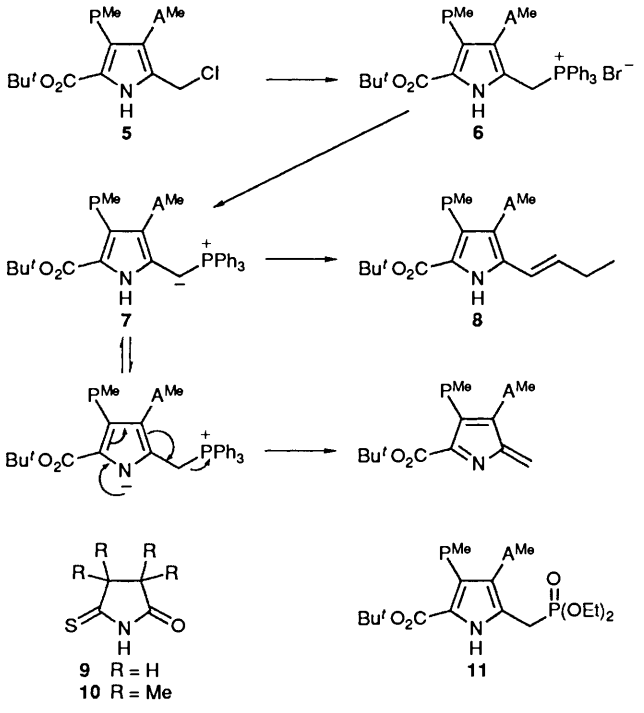
These results convinced us that a group X was indeed required for our work and the following survey was made.

X = Sulfide, Sulfoxide or Sulfone Group.—These groups were attractive because it should be possible subsequently to remove them fairly readily. The sulfide **12**, Scheme 3, was prepared, in 79% yield, by treatment of the chloride **5** with thiophenol and this product could be selectively oxidised by

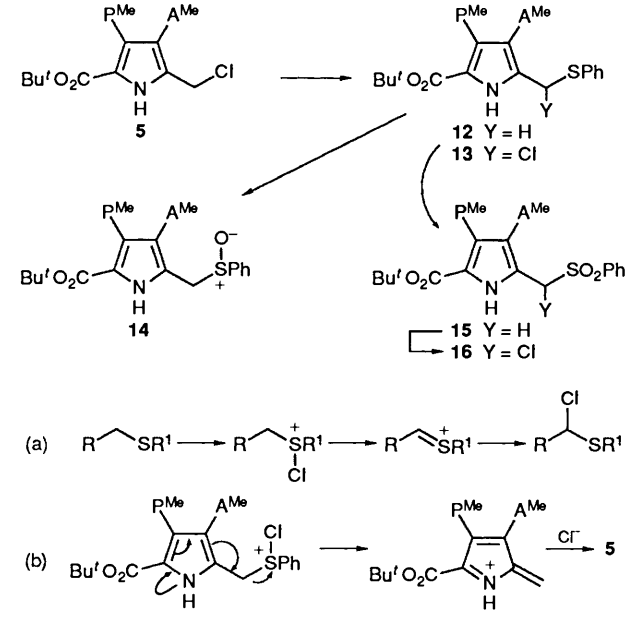


Scheme 1

† Deceased 22 February 1992.
‡ Deceased 24 September 1990.



Scheme 2 $A^{Me} = CH_2CO_2Me$, $P^{Me} = CH_2CH_2CO_2Me$



Scheme 3

sodium metaperiodate to either the sulfoxide **14**, 95% or the sulfone **15**, 93%.

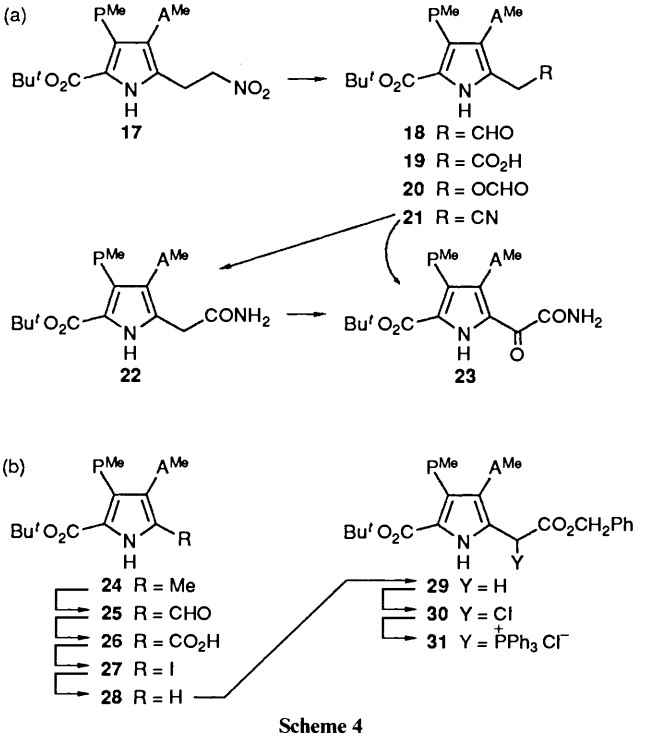
Attempted chlorination of the sulfide **12** with sulfuryl dichloride did not give the halide **13** but yielded the chloromethylpyrrole **5**. This can be understood on the basis that α-chlorination of sulfides with sulfuryl dichloride occurs *via* the Pummerer rearrangement,[3] Scheme 3a. In the present case, the first formed chlorosulfonium species, Scheme 3b, can undergo elimination and the product be trapped by chloride ion to give the observed product **5**. As now expected, attempted chlorination of the sulfoxide **14** gave the same result.

The sulfone **15** cannot be attacked at sulfur and so chlorination in this case gave the required α-chloro derivative **16** which was identified spectroscopically but could not be fully purified because of ready hydrolysis to the corresponding α-formylpyrrole. The chlorine atom of this product **16** could not, however, be displaced by triphenylphosphine, a result in keeping with earlier experience[4] that displacement reactions at the α-centre to a sulfonyl group are difficult for steric reasons.

The foregoing experiments gave the first indications that success in coupling of the pyrrolic and monothioimide units would depend not only on the presence of an anion-stabilising group X but also on this group being a sterically undemanding one such as a cyano group. Our studies with this group are outlined later but first the results from experiments with X as benzyloxycarbonyl will be described.

X = Benzyloxycarbonyl.—This is the group used in Gossauer's work[2] and, for the present studies, the pyrrole **29** was required as starting material for the synthesis of phosphonium salt **31**. Such pyrrolylacetic esters are not readily prepared[5,6] and hence two new routes were explored. Scheme 4a shows the formation of the extremely labile aldehyde **18** by reduction of the nitronate anion, derived from the nitroethyl system[7] **17**, with titanium(III) chloride.[8] Of the wide range of oxidising agents tested for conversion of this aldehyde **18** into the corresponding acid **19**, only *m*-chloroperbenzoic acid (MCPBA) yielded the required material **19** and then only in low yield (9%) together with the isomeric formate **20**, 20%.

Conversion of the nitrile[1] **21** into the acid **19** was then attempted, Scheme 4a, *via* the amide **22**, which was formed in 40% yield using hydroperoxide anion.[9] Manganese dioxide has been used for converting nitriles into amides[10] but, in our case, unwanted oxidation occurred to give a low yield of the keto amide **23**. This same product **23** also resulted in ~20% yield from attempted conversion of the amide **22** into the acid **19** using dinitrogen tetraoxide.[11] Presumably the mechanism involves nitrosation at the reactive α-methylene centre, tautomerism to the oxime and subsequent hydrolysis.



Scheme 4

As a result recourse had to be taken to insertion of the carbene[6] from benzyl diazoacetate into the α-C–H bond of the pyrrole **28**, Scheme 4b; the preparation of this starting pyrrole was greatly improved as follows. Although the pyrrole **24** could be efficiently mono- or di-chlorinated using one or two

equivalents of sulfuryl dichloride with potassium carbonate added, trihalogenation was difficult and after hydrolysis, only ~30% of the acid **26** was obtained. However, hydrolysis of the dihalogenated material gave a high yield of the aldehyde **25**, which was oxidised by neutral permanganate in aqueous acetone[12] to give the crystalline acid **26** in 63% overall yield from the methylpyrrole **24**. The standard high yielding (>90%) transformations **26** ⟶ **27** ⟶ **28** in Scheme 4 then afforded the required pyrrole **28**.

The insertion step, involving treatment of the pyrrole **28** with benzyl diazoacetate and copper powder, was capricious and the highest yield of product **29** was 25% (51% based on consumed starting material); often the yields were lower. However, sufficient material was obtained for chlorination to give the halide **30**, which with triphenylphosphine led to the stable crystalline salt **31**.

The precious nature of this product **31** led us to try the coupling process directly on the optically active monothioimide[13] **2** carrying the 'natural' side-chains but under no conditions could coupling be effected.

A few further experiments were carried out using the available model pyrrole[14] **32** which was converted into the salt **33** by bromination followed by reaction with triphenylphosphine. Prolonged heating of the derived ylide with the monothioimide **10** gave a modest yield (19%) of the desired product **34**; the configuration at the double bond was not assigned.

These results interlocked with those from use of X = sulfone group and they indicated that the X group must be small.

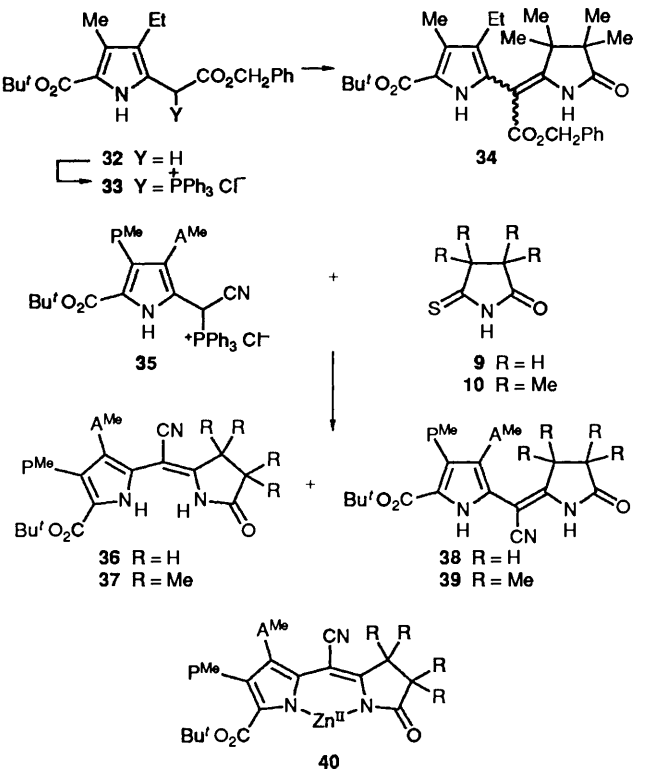
X = Cyano.—To have X as cyano now seemed to be ideal since this group is both small and linear, and also space-filling models indicated that the more favourable double-bond geometry in the desired product **37** should be *E* with the pyrrole and lactam functions *cis*-oriented. This is the required arrangement for formation of the isobacteriochlorin macrocycle.

The ylide derived from the salt[1] **35** by treatment with aqueous sodium carbonate was heated with the monothioimide **9** in *tert*-butyl alcohol to yield, gratifyingly, the coupled products **36** and **38** but in low and variable yield, Scheme 5. Careful study of this reaction showed that addition of a catalytic quantity of potassium *tert*-butoxide to the reaction mixture resulted in a more rapid and higher yielding reaction, the products **36** and **38** now being obtained in ~4:1 ratio, respectively, in a combined yield of 69%. The major product was assigned the *E*-configuration **36** on the basis of the marked bathochromic shift of its UV absorption maximum on addition of zinc(II) ions;[15] the shift results from Zn^{II} chelation, as in complex **40**, which is not possible for the *Z*-isomer **38**.

The best coupling procedure involved deprotonation of the salt **35** *in situ* by addition of 1.5 mole equivalents of potassium *tert*-butoxide to a mixture of the salt **35** and the monothioimide **10** in toluene, followed by heating. The *E*-product **37** was then obtained in 88% yield together with 1% of the *Z*-isomer **39**. Thus a highly effective process for coupling ring A to ring D and ring B to ring C (see Scheme 1) was available.

The above coupling method is a most interesting one, especially the requirement for excess of base, in which it apparently differs from Gossauer's study;[2] its mechanism has been elucidated (by W. G. Whittingham) and these findings will be reported separately.

Although the coupling problem was solved, the consequent one of removing the cyano group from the bicyclic product **37** was proving to be very resistant. This problem was finally overcome (see Part 11) but before that was achieved, we explored the effectiveness of isocyanide as the group X, *e.g.* by using the phosphonium salt **45**. Successful coupling of salt **45** with the monothioimide **10** would yield the model system **46**



Scheme 5

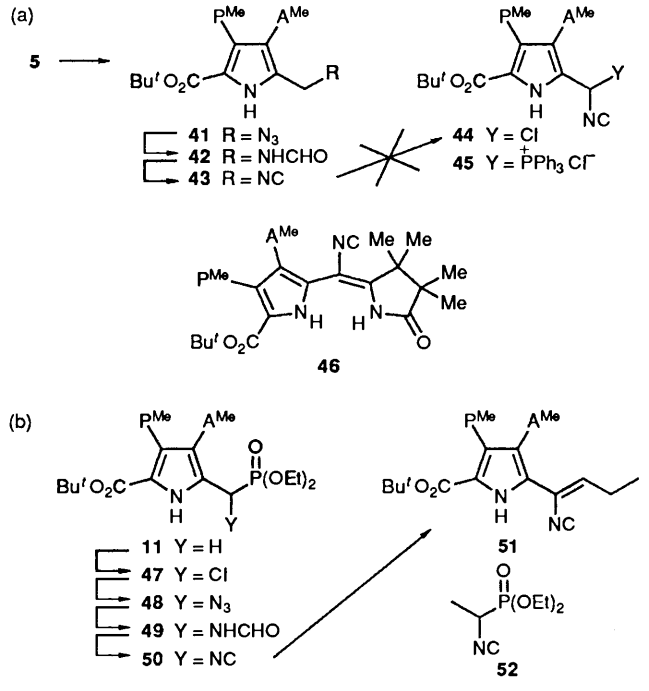
and it was expected that the isocyano residue would be more readily removed than would a cyano group.

X = Isocyano.—The isocyanide **43** required as starting material was prepared by the reaction **41** ⟶ **42** ⟶ **43** as in Scheme 6a but it was not possible to chlorinate this product to form the halide **44**. However, the phosphonate **11** was available (Scheme 2) and was converted into the required isocyanide **50** by the sequence **11** ⟶ **47** ⟶ **48** ⟶ **49** ⟶ **50** as in Scheme 6b. This underwent base-catalysed reaction with propanal to give a low yield (25%) of the olefin **51**. However, none of the desired product **46** could be detected from attempted coupling of the anion from the isocyanide **50** with the monothioimide **10**. It seems that the thioimide system is insufficiently reactive for success of the envisaged chemistry because it was subsequently shown that the monothioimide **10** did not react with the anion derived from the phosphonate **52**, kindly supplied by Professor D. H. R. Barton. This latter anion has been used successfully in reactions with several 17-oxo steroids.[16]

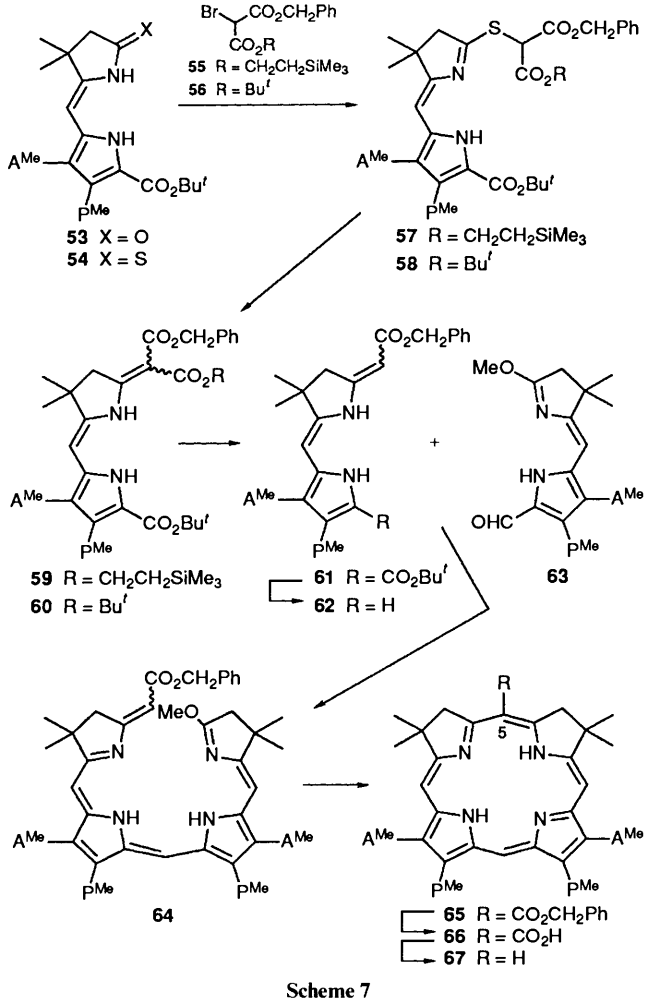
The outcome of all these studies was to focus our efforts on the coupling method where the group X is a cyano group.

The C-5 Problem.—Attention now turned to the second problem, that of introducing the one-carbon unit which was to become C-5 of the isobacteriochlorin macrocycle **4** (Scheme 1). The plan was to study the synthesis of the model isobacteriochlorin[7] **67** by using the known[7] lactam **53** as precursor of both eastern and western parts of the structure, Scheme 7. In this way, we were able to explore various methods to set C-5 in place.

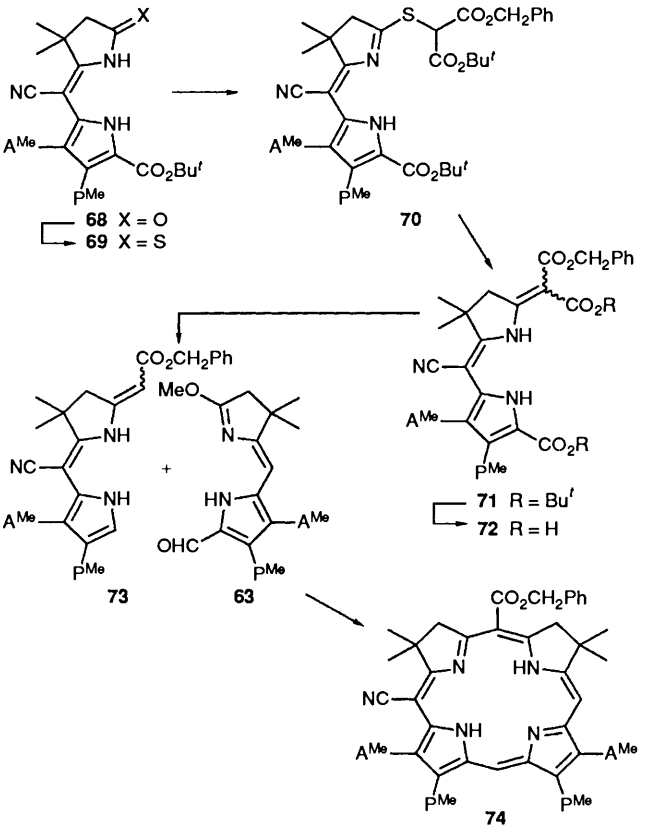
The lactam **53** was first converted into the thiolactam **54** by using Lawesson's reagent[17] and this was used for experiments based on sulfur extrusion[18,19] with the bromo esters **55** and **56** as *S*-alkylating agents, Scheme 7. Details of the preparation of both bromo esters are given in the Experimental section,



Scheme 6



Scheme 7



Scheme 8

synthesis of the former drawing on analogous earlier studies by Rasetti.[19]

The properties of thioimidates in this series were studied in exploratory experiments by converting the thiolactam **54** into its *S*-methyl derivative by using trimethyloxonium tetrafluoroborate and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). It was confirmed by UV and ^{13}C NMR spectroscopy that *S*- not *N*-methylation had occurred and this product was encouragingly stable. In addition, the *S*-benzyloxycarbonylmethyl derivative of thiolactam **54** could readily be prepared by *S*-alkylation using benzyl bromoacetate. This product also was stable to normal handling.

Treatment of the thiolactam **54** with the bromide **55** gave the thioimidate **57**, 81%, which on heating with triphenylphosphine and DBU yielded a mixture of the two geometric isomers **59**, 82%. Removal of the silyl protecting group with fluoride anion afforded the enamines **61** directly due to facile decarboxylation in this step. The yield of enamines **61** was never better than 35%, which was unacceptable for the main synthesis. Nevertheless, the enamines **61** were carried forward so that the later stages could be explored. The first step was treatment of the enamines **61** with trifluoroacetic acid (TFA) to generate the α-free pyrrole **62**, which was a stable system, this being one benefit of the electron-withdrawing benzyloxycarbonyl group. This material condensed smoothly with the known[7] aldehyde **63** and the resultant 18π-electron seco-system **64** was cyclised photochemically[7] to form the isobacteriochlorin **65**. Though the yield of the macrocycle **65** was low, its formation demonstrated that cyclisation was possible with a benzyloxycarbonyl group as part of the conjugated system.

The second bromo ester **56** proved to be a much better choice, for when this was used in the analogous series of steps, **54** → **58** → **60**[20] → **62** → **64** → **65**, Scheme 7, all the yields were good with that for the final cyclisation being 68%. This synthesis has been used to prepare substantial quantities of the isobacteriochlorin **65**. The final steps of removing the 5-benzyloxycarbonyl group to yield the isobacteriochlorin **67**, 62%, involved acid-catalysed cleavage of the benzyl group followed by decarboxylation of the resultant acid **66**. One

approach to insertion of the C-5 carbon, at least in model systems, was thus available.

For reasons which are given in Part 11, it appeared at this stage of our synthetic work that the cyano group present after coupling rings A and D, *e.g.* in the model **37**, might have to be carried forward to the isobacteriochlorin stage. Accordingly, the foregoing approach to C-5 insertion was tested on the thiolactam **69** derived as usual from the known[1] lactam **68**. The sequence **69** ⟶ **70** ⟶ **71** ⟶ **72** ⟶ **73** + **63** ⟶ **74**, Scheme 8, was run to yield the required isobacteriochlorin. The only appreciable difference from the previous series leading to the macrocycle **65** was that the diacid **72** resulting from cleavage of the *tert*-butyl groups from the pyrrole **71** had to be heated with toluene-*p*-sulfonic acid (PTSA) to effect decarboxylation. This was not unexpected in the nitrile series.[1]

Most of the yields in this last sequence were good but two were modest (*e.g.*, 30%). They have not been optimised because our main aim was to determine whether the option of leaving the cyano residue in place to the final stage was available to us; if necessary, it clearly was.

An important observation in the foregoing studies was that photochemical cyclisation of the benzyloxycarbonyl *seco*-system **64** was ~10-fold slower than for the corresponding unsubstituted seco-system[7] (as **64**, H in place of CO_2CH_2Ph). This, taken with the need for two further steps for removal of the 5-benzyloxycarbonyl group from the isobacteriochlorin **65**, led to a search for a way to avoid these disadvantages. The one devised, based on di-*tert*-butyl 2-bromomalonate, was used successfully in the chlorin series[20] and for the synthesis of sirohydrochlorin in Part 12 where this method will be described.

Experimental

General Directions.—Most general directions are as in ref. 21. UV spectra were recorded on solutions in ethanol or methanol unless otherwise stated. Proton NMR spectra were recorded on Varian EM360 (A, 60 MHz), CFT20 (B, 80 MHz), EM390 (C, 90 MHz) and XL100 (D, 100 MHz) spectrometers and on Bruker WM250 (E, 250 MHz) and WH400 (F, 400 MHz) spectrometers; *J*-values are given in Hz. ^{13}C NMR spectra were recorded on the Bruker instruments. Where deuteriochloroform or deuteriodichloromethane were used as solvents, they were passed through an alumina column directly before use. TLC or preparative TLC (PLC) of all tetrapyrrolic compounds was carried out on indicator-free plates made with Merck Kieselgel 60 silica. Organic solutions were dried over magnesium sulfate except that solutions of tetrapyrrolic compounds were dried over analytical grade sodium sulfate. Ether refers to diethyl ether, THF to tetrahydrofuran, and Hünig's base to *N*-ethyldiisopropylamine.

General Directions for Photochemical Cyclisations.—The following procedures were adopted for the photochemical cyclisations, and similar precautions were observed for all other experiments involving tetrapyrrolic compounds. All glassware was thoroughly dried at 120 °C before use. The starting materials were dried at room temperature at 0.1 mmHg for a minimum of 8 h and all reagents and solvents were purified immediately prior to the experiment. THF was distilled under argon from potassium and then had argon bubbled through it for a minimum of 3 h before use. All reactions were carried out under argon and every attempt was made to exclude water and oxygen; except during irradiation, light was also excluded. Solvents and reaction solutions were transferred by gas-tight syringe, or for larger quantities *via* a double ended needle using a small pressure of argon. THF solutions of reactants in thick-walled glass tubes were subjected to a minimum of three cycles of freeze–pump–thaw degassing at 0.1 mmHg prior to being sealed under vacuum. Irradiations were performed using a 1000 W array of tungsten light bulbs with the tubes immersed in 0.4 mol dm^{-3} aq. potassium dichromate and cooled to below 30 °C. All aqueous solutions were prepared from glass-distilled water and AR grade reagents.

tert-*Butyl* 4-*Acetyl*-3-(2-*methoxycarbonylethyl*)-5-*methylpyrrole*-2-*carboxylate*.—To a stirred solution of 1-*tert*-butyl 6-methyl 3-oxohexanedioate (166.6 g, 0.712 mol) in acetic acid (300 cm^3), cooled in ice, was added during 20 min a solution of sodium nitrite (52.3 g, 0.758 mol) in water (95 cm^3). The solution was stored for 16 h and then added during 45 min to a stirred solution of acetylacetone (86 g, 0.86 mol) in acetic acid (300 cm^3) at the same time as a mixture of zinc dust (130 g) and sodium acetate (150 g). The temperature was maintained at 60–70 °C during the addition with cooling if necessary and then the mixture was heated to 60–65 °C for a further 1 h. Ice–water (1 dm^3) was added to precipitate the product, which was filtered off, dissolved in dichloromethane (1 dm^3), filtered, washed with water (2 × 800 cm^3), dried and evaporated. The residue was recrystallised from ether–hexane to give the *title pyrrole* (117 g, 53%), m.p. 92.5–93 °C (Found: C, 62.0; H, 7.45; N, 4.45. $C_{16}H_{23}NO_5$ requires C, 62.1; H, 7.5; N, 4.55%); λ_{max}/nm 232 (100%) and 283 (58); ν_{max}/cm^{-1} 3430, 2960, 1730, 1670sh and 1650; δ_H(A) 1.56 (9 H, s, Bu^t), 2.40 and 2.50 (each 3 H, s, pyrr-Me and COMe), 2.5 and 3.2 (each 2 H, t, *J* 8, $CH_2CH_2CO_2$), 3.58 (3 H, s, OMe) and 9.2 (1 H, br s, NH); *m*/*z* 309 (45%, M^+), 253 (21, $M - C_4H_8$), 222 (6) and 193 (100).

tert-*Butyl* 3-(2-*Methoxycarbonylethyl*)-4-*methoxycarbonylmethyl*-5-*methylpyrrole*-2-*carboxylate* **24**.—To a solution of *tert*-butyl 4-acetyl-3-(2-methoxycarbonylethyl)-5-methylpyrrole-2-carboxylate (70 g, 206 mmol) in methanol (900 cm^3) was added a solution of thallium(III) nitrate (103 g, 232 mmol), conc. nitric acid (34.0 cm^3) and methanol (450 cm^3). The mixture was stirred for 6 h, until TLC indicated complete consumption of starting material, then was filtered through Celite, washing the residue with dichloromethane (400 cm^3). The filtrate was shaken with water (1800 cm^3), the phases were separated, and the aqueous phase was extracted with dichloromethane (3 × 500 cm^3). The combined organic phases were washed with water (500 cm^3), dried and evaporated. Flash chromatography [eluent dichloromethane, then light petroleum–ethyl acetate (2:1)] and recrystallisation gave the triester **24** as needles (52.0 g, 73%), m.p. 125–127 °C (from light petroleum–ethyl acetate; lit.,[22] 126–127 °C) (Found: C, 59.9; H, 7.3; N, 4.0. Calc. for $C_{16}H_{23}NO_5$; C, 60.15; H, 7.4; N, 4.1%); λ_{max}/nm 279; ν_{max}/cm^{-1} 3450, 2970, 1730 and 1675; δ_H(A) 1.53 (9 H, s, Bu^t), 2.17 (3 H, s, pyrr-Me), 2.5 and 2.9 (each 2 H, t, *J* 8, $CH_2CH_2CO_2$), 3.32 (2 H, s, CH_2CO_2), 3.58 (6 H, s, 2 × OMe) and 9.0 (1 H, br s, NH); *m*/*z* 339 (52%, M^+), 283 (35, $M - C_4H_8$), 251 (100), 224 (65), 223 (75) and 192 (60).

[5-tert-*Butoxycarbonyl*-4-(2-*methoxycarbonylethyl*)-3-(*methoxycarbonylmethyl*)*pyrrol*-2-*yl*]*methyltriphenylphosphonium Bromide* **6**.—The methylpyrrole **24** (1.02 g, 3.0 mmol) was stirred with potassium carbonate (4.14 g, 30 mmol) at 0 °C in dichloromethane (30 cm^3) during dropwise addition of sulfuryl dichloride (418 mg, 3.1 mmol). After 10 min at 0 °C and 10 min at 20 °C, the mixture was filtered (Celite). A trial run checked at this stage showed complete formation of the chloromethylpyrrole **5**; δ_H(A) 1.57 (9 H, s, Bu^t), 2.53 (2 H, m, $CH_2CH_2CO_2$), 2.98 (2 H, m, $CH_2CH_2CO_2$), 3.48 (2 H, s, CH_2CO_2), 3.61 (6 H, br s, 2 × OMe), 4.54 (2 H, s, CH_2Cl) and 9.70 (1 H, br s, NH).

The solution of the chloromethylpyrrole **5** was treated with triphenylphosphine (864 mg, 3.3 mmol), kept for 1 h and then evaporated. The residue, in warm water (60 cm^3), was extracted

successively with toluene (20 cm^3 then 10 cm^3) and ether (20 cm^3). The aqueous layer was treated with potassium bromide (4 g) and extracted with dichloromethane (20 cm^3, then 2 × 10 cm^3). The combined dichloromethane extracts were dried, filtered and evaporated and the residue was recrystallised from dichloromethane–methyl acetate to give the *phosphonium salt* **6** (1.41 g, 69%), m.p. 204–206 °C (Found: C, 61.7; H, 5.9; N, 2.3. $C_{35}H_{39}BrNO_6P$ requires: C, 61.8; H, 5.8; N, 2.1%); λ_{max}/nm 268; ν_{max}/cm^{-1} 3170br, 1730, 1690 and 1440; δ_H(A) 1.49 (9 H, s, Bu^t), 2.38–3.31 (4 H, m, $CH_2CH_2CO_2$), 2.96 (2 H, br s, CH_2CO_2), 3.39 and 3.54 (each 3 H, s, OMe), 5.51 (2 H, d, *J* 12, CH_2P) and 7.38–8.01 (15 H, m, PPh_3).

tert-*Butyl* (E)-5-*But*-1-*enyl*-3-(2-*methoxycarbonylethyl*)-4-(*methoxycarbonylmethyl*)*pyrrole*-2-*carboxylate* **8**.—To a suspension of the phosphonium salt **6** (68 mg, 0.1 mmol) in THF (3 cm^3) and propionaldehyde (29 mg, 0.5 mmol) were added aliquots of sodium hydride (50% dispersion in oil; 5 mg, 0.1 mmol) after 0, 10 and 20 min. After a further 10 min saturated aq. ammonium chloride (2 cm^3) was added, followed by water (5 cm^3), and the mixture was extracted with chloroform (2 × 5 cm^3). The combined organic layers were dried and evaporated. PLC [1 mm plate, developed with dichloromethane–methyl acetate (9:1)] gave the unstable butenylpyrrole **8** as a gum (24 mg, 63%), λ_{max}/nm 234 and 292; ν_{max}/cm^{-1} 3470, 1735, 1680 and 1560; δ_H(A) 1.12 (3 H, t, *J* 7, CH_2Me), 1.57 (9 H, s, Bu^t), 2.05–2.78 (4 H, m, $CH_2CH_2CO_2$ and CH_2Me), 3.00 (2 H, m, $CH_2CH_2CO_2$), 3.44 (2 H, s, CH_2CO_2), 3.63 (6 H, s, 2 × OMe), 5.55 (1 H, m, CH=C*H*CH_2), 6.11 (1 H, d, *J* 13, C*H*=$CHCH_2$) and 8.70 (1 H, br s, NH).

2,2,3,3-*Tetramethylmonothiosuccinimide* **10**.—2,2,3,3-Tetramethylsuccinimide[23] (930 mg, 6 mmol) and phosphorus pentasulfide (1.6 g, 7.2 mmol) were heated at reflux, under argon, in THF (30 cm^3) for 2 h. The solvent was then replaced by toluene by alternate addition of toluene and partial evaporation. The resultant solution (~20 cm^3) was filtered through a silica column (18 g) and eluted with 10% methyl acetate in dichloromethane and then with 5% methanol in dichloromethane, and the eluates were evaporated. Column chromatography (silica H; 29 g) of the residue gave three fractions: (i) with dichloromethane–hexane (1:1) to yield the dithiosuccinimide (0.11 g, 9.8%); (ii) with dichloromethane–hexane (3:1) to yield the required monothiosuccinimide (0.54 g, 52.6%); (iii) with dichloromethane–methanol (9:1) to yield starting material (0.34 g, 36.6% recovery). The *monothiosuccinimide* **10** crystallised as pale yellow needles, m.p. 104–115 °C (sublimes) (Found: C, 56.2; H, 7.4; N, 8.1; S, 18.6. $C_8H_{13}NOS$ requires C, 56.1; H, 7.6; N, 8.2; S, 18.7%); λ_{max}/nm 268; ν_{max}/cm^{-1} 3380 and 1750; δ_H(A) 1.21 and 1.28 (each 6 H, s, 2 × Me) and 9.30 (1 H, br s, NH); *m*/*z* 171 (100%, M^+) and 156 (36, M − Me).

Diethyl [5-tert-*Butoxycarbonyl*-4-(2-*methoxycarbonylethyl*)-3-(*methoxycarbonylmethyl*)*pyrrol*-2-*yl*]*methylphosphonate* **11**.—A solution of the crude chloromethylpyrrole **5** [from the methylpyrrole **24** (102 mg, 0.3 mmol)] in toluene (0.5 cm^3) was heated with triethyl phosphite (55 mg, 0.33 mmol) at 80 °C for 6 h, then evaporated (50 °C). PLC (2 × 1 mm plates; developed with 5% methanol in chloroform) gave the *phosphonate* **11** as a gum (115 mg, 81%) (Found: M^+, 475.1950. $C_{21}H_{34}NO_9P$ requires *M*, 475.1971); λ_{max}/nm 276; ν_{max}/cm^{-1} 3440br, 1735 and 1690; δ_H(D) 1.18 (6 H, t, *J* 7, 2 × $POCH_2Me$), 1.46 (9 H, s, Bu^t), 2.47 (2 H, m, $CH_2CH_2CO_2$), 2.92 (2 H, m, $CH_2CH_2CO_2$), 3.13 (2 H, d, *J* 21, CH_2P), 3.43 (2 H, s, CH_2CO_2), 3.57 and 3.58 (each 3 H, s, OMe), 3.97 (4 H, quintet, *J* 7, 2 × $POCH_2Me$) and 9.66 (1 H, br s, NH); *m*/*z* 475 (9%, M^+), 443 (8, M − MeOH), 419 (10, M − C_4H_8) and 387 (100).

tert-*Butyl* 3-(2-*Methoxycarbonylethyl*)-4-*methoxycarbonylmethyl*-5-(*phenylthiomethyl*)*pyrrole*-2-*carboxylate* **12**.—The methylpyrrole **24** (339 mg, 1 mmol) was stirred with potassium carbonate (1.38 g, 10 mmol) at 0 °C in dichloromethane (10 cm^3) during dropwise addition of sulfuryl dichloride (148 mg, 1.1 mmol). After being stirred for 10 min at 0 °C and 10 min at ~20 °C, the mixture was stirred with thiophenol (132 mg, 1.2 mmol) for a further 2 h at 20 °C, then filtered through Celite and evaporated. PLC (4 × 1 mm plates, developed with 10% methyl acetate in dichloromethane) gave the *phenylthiomethylpyrrole* **12** (355 mg, 79%), which was crystallised from ether–hexane as prisms, m.p. 75–76 °C (Found: C, 61.7; H, 6.4; N, 3.3; S, 7.5. $C_{23}H_{29}NO_6S$ requires C, 61.7; H, 6.5; N, 3.1; S, 7.2%); λ_{max}/nm 280; ν_{max}/cm^{-1} 3420, 1720 and 1675; δ_H(A) 1.53 (9 H, s, Bu^t), 2.50 (2 H, m, $CH_2CH_2CO_2$), 2.96 (2 H, m, $CH_2CH_2CO_2$), 3.34 (2 H, s, CH_2CO_2), 3.62 (6 H, s, 2 × OMe), 4.04 (2 H, s, CH_2S), 7.18 (5 H, s, SPh) and 9.23 (1 H, br s, NH); *m*/*z* 447 (2%, M^+), 338 (31, M − SPh) and 282 (100).

tert-*Butyl* 3-(2-*Methoxycarbonylethyl*)-4-*methoxycarbonylmethyl*-5-(*phenylsulfinylmethyl*)*pyrrole*-2-*carboxylate* **14**.—A solution of the phenylthiomethylpyrrole **12** (44.7 mg, 0.1 mmol) in methanol (1 cm^3) was stirred at 40 °C with water (0.1 cm^3) and sodium metaperiodate (22.5 mg, 0.105 mmol) for 20 h. The mixture was diluted with water (5 cm^3) and extracted with dichloromethane (3 × 5 cm^3). PLC of the product (1 mm plate, developed with 10% methyl acetate in dichloromethane) gave the *phenylsulfinylmethylpyrrole* **14** as a gum (44 mg, 95%), which was crystallised from dichloromethane–hexane, m.p. 101–107 °C (Found: C, 59.8; H, 6.1; N, 3.0; S, 7.1. $C_{23}H_{29}NO_7S$ requires C, 59.6; H, 6.3; N, 3.0; S, 6.9%); λ_{max}/nm 280; ν_{max}/cm^{-1} 3420, 1720, 1680 and 1040; δ_H(A) 1.55 (9 H, s, Bu^t), 2.53 (2 H, m, $CH_2CH_2CO_2$), 2.99 (2 H, m, $CH_2CH_2CO_2$), 3.11 (2 H, d, *J* 3, CH_2CO_2), 3.65 and 3.69 (each 3 H, s, OMe), 4.11 (2 H, s, CH_2SO), 7.52 (5 H, s, SOPh) and 9.54 (1 H, br s, NH); *m*/*z* 376 (2%, M^+), 338 (30, M − SOPh) and 282 (100).

tert-*Butyl* 3-(2-*Methoxycarbonylethyl*)-4-*methoxycarbonylmethyl*-5-(*phenylsulfonylmethyl*)*pyrrole*-2-*carboxylate* **15**.—The phenylthiomethylpyrrole **12** (223 mg, 0.5 mmol) in methanol (10 cm^3) was treated with water (1 cm^3) and sodium metaperiodate (107 mg, 0.5 mmol). The stirred mixture was heated under reflux under argon and after 20 min a second equal portion of sodium metaperiodate was added and a third after 9 h. A final portion of metaperiodate (53 mg, 0.25 mmol) was added after a further 12 h. After a total of 45 h, the cooled mixture was mixed with water (25 cm^3) and dichloromethane (10 cm^3) and the separated aqueous layer was extracted with more dichloromethane (3 × 10 cm^3). The combined organic layers were washed with brine (10 cm^3), dried and evaporated. The residue was passed through a silica column (silica H; 2 g) with 5% methyl acetate in dichloromethane as eluent, to give the *phenylsulfonylmethylpyrrole* **15** (222 mg, 93%), which crystallised, m.p. 148–149 °C (Found: C, 57.4; H, 5.8; N, 3.0; S, 6.8. $C_{23}H_{29}NO_8S$ requires C, 57.6; H, 6.1; N, 2.9; S, 6.7%); λ_{max}/nm 272; ν_{max}/cm^{-1} 3420, 1725 and 1680; δ_H(A) 1.56 (9 H, s, Bu^t), 2.48 (2 H, m, $CH_2CH_2CO_2$), 2.94 (2 H, m, $CH_2CH_2CO_2$), 3.04 (2 H, s, CH_2CO_2), 3.53 and 3.59 (each 3 H, s, OMe), 4.32 (2 H, s, CH_2SO_2), 7.50 (5 H, m, SO_2Ph) and 9.15 (1 H, br s, NH); *m*/*z* 338 (31%, M − SO_2Ph) and 282 (100).

tert-*Butyl* 5-*Carboxymethyl*-3-(2-*methoxycarbonylethyl*)-4-(*methoxycarbonylmethyl*)*pyrrole*-2-*carboxylate* **19** *and* tert-*Butyl* 5-*Formyloxymethyl*-3-(2-*methoxycarbonylethyl*)-4-(*methoxycarbonylmethyl*)*pyrrole*-2-*carboxylate* **20**.—A solution of the nitroethylpyrrole **17** (99.5 mg, 0.25 mmol) in THF (0.5 cm^3)–methanol (1 cm^3) was stirred with sodium methoxide (27 mg, 0.5 mmol) for 10 min and then added, under argon, to a

stirred solution of ammonium acetate (346 mg, 3.5 mmol) and 15% aq. titanium(III) chloride (1.5 cm^3, 1.5 mmol) in water (1.5 cm^3)–THF (1.5 cm^3). After 2.5 h, the mixture was extracted with ether (2 × 10 cm^3, then 5 cm^3) and the combined organic layers were washed successively with 5% aq. sodium hydrogen carbonate (10 cm^3) and brine (10 cm^3), dried and evaporated. PLC (2 × 1 mm plates, developed with 5% methanol in dichloromethane) gave the unstable formylmethylpyrrole **18** as a gum (45.4 mg, 49%); λ_{max}/nm 276; ν_{max}/cm^{-1} 3450br, 1740 and 1690; δ_H(A) 1.56 (9 H, s, Bu^t), 2.51 (2 H, m, $CH_2CH_2CO_2$), 2.95 (2 H, m, $CH_2CH_2CO_2$), 3.38 (2 H, s, CH_2CO_2), 3.58 (6 H, 2 × OMe), 3.66 (2 H, br s, CH_2CHO) and 9.52 (2 H, br s, NH and CHO).

A solution of the foregoing formylmethylpyrrole **18** (30.5 mg, 0.083 mmol) in dichloromethane (1.5 cm^3) was stirred, at −5 °C under argon, with MCPBA (85%; 18.6 mg, 0.091 mmol) for 90 min and then evaporated. PLC (1 mm plate, developed with 5% methanol in dichloromethane) yielded the *carboxymethylpyrrole* **19** (2.9 mg, 9.1%) and the *formyloxymethylpyrrole* **20** (6.5 mg, 20.4%). For the carboxymethylpyrrole **19**: (Found: M^+, 383.1594. $C_{18}H_{25}NO_8$ requires *M*, 383.1580); λ_{max}/nm 278; ν_{max}/cm^{-1} 3440, 3400–2500br and 1730br; δ_H(D) 1.54 (9 H, s, Bu^t), 2.52 (2 H, m, $CH_2CH_2CO_2$), 2.98 (2 H, m, $CH_2CH_2CO_2$), 3.46 (2 H, s, 4-CH_2CO_2), 3.64 and 3.66 (each 3 H, s, OMe), 3.67 (2 H, s, 5-CH_2CO_2) and 9.80 (1 H, br s, NH); *m*/*z* 383 (2%, M^+), 369 (2), 327 (30, M − C_4H_8) and 295 (67).

For the formyloxymethylpyrrole **20**: (Found: M^+, 383.1551. $C_{18}H_{25}NO_8$ requires *M*, 383.1580); λ_{max}/nm 270; ν_{max}/cm^{-1} 3440, 1730 and 1690; δ_H(A) 1.57 (9 H, s, Bu^t), 2.53 (2 H, m, $CH_2CH_2CO_2$), 3.00 (2 H, m, $CH_2CH_2CO_2$), 3.51 (2 H, s, CH_2CO_2), 3.61 and 3.63 (each 3 H, s, OMe), 5.19 (2 H, s, CH_2O), 7.98 (1 H, s, OCHO) and 9.16 (1 H, br, s, NH); *m*/*z* 383 (20%, M^+), 338 (12, M − OCHO) and 281 (100).

tert-*Butyl* 5-*Carbamoylmethyl*-3-(2-*methoxycarbonylethyl*)-4-(*methoxycarbonylmethyl*)*pyrrole*-2-*carboxylate* **22**.—A solution of the cyanomethylpyrrole **21** (54.4 mg, 0.15 mmol) in dichloromethane (1 cm^3) was stirred with 30% aq. hydrogen peroxide (0.1 cm^3, 0.8 mmol), 10% aq. sodium hydroxide (0.08 cm^3) and 40% aq. tetrabutylammonium hydroxide (17.5 mg, 0.027 mmol). A second portion of aq. hydrogen peroxide (0.05 cm^3, 0.4 mmol) was added after 1 h. After a further 30 min, the mixture was shaken with water (5 cm^3) and dichloromethane (3 cm^3) and the organic layer was dried and evaporated. PLC (1 mm plate developed with 5% methanol in dichloromethane) gave the *amide* **22** (23.4 mg, 40.8%), which crystallised on drying at 1 mmHg, m.p. 138–139 °C (Found: C, 56.5; H, 6.8; N, 7.4. $C_{18}H_{26}N_2O_7$ requires C, 56.5; H, 6.9; N, 7.3%); λ_{max}/nm 275; ν_{max}/cm^{-1} 3490, 3440, 3350, 1730, 1690 and 1600; δ_H(A) 1.55 (9 H, s, Bu^t), 2.48 (2 H, m, $CH_2CH_2CO_2$), 2.96 (2 H, m, $CH_2CH_2CO_2$), 3.44 and 3.50 (each 2 H, s, CH_2CO_2 and CH_2CON), 3.59 and 3.63 (each 3 H, s, OMe) and 6.07, 6.50 and 10.08 (each 1 H, br s, NH); *m*/*z* 382 (11%, M^+), 326 (40, M − C_4H_8) and 294 (100).

tert-*Butyl* 3-(2-*Methoxycarbonylethyl*)-4-*methoxycarbonylmethyl*-5-*oxamoylpyrrole*-2-*carboxylate* **23**.—(*a*) A solution of the cyanomethylpyrrole **21** (54.6 mg, 0.15 mmol) in dichloromethane (2 cm^3) was stirred at 20 °C with manganese dioxide (261 mg, 3 mmol). After 43 h, the mixture was filtered and the filtrate was evaporated. PLC (1 mm plate, developed with 5% methanol in dichloromethane) gave the keto amide **23** (9.6 mg, 16%).

(*b*) A solution of dinitrogen tetraoxide in tetrachloromethane[11] (0.075 mol dm^{-3}; 2.2 cm^3, 0.16 mmol) was stirred at −20 °C with anhydrous sodium acetate (24.6 mg, 0.3 mmol) and the amide **22** (38.2 mg, 0.1 mmol) was added. The mixture was warmed to 3 °C during 1 h, then treated with further dinitrogen tetraoxide solution (0.6 cm^3, 0.045 mmol), kept at 5 °C overnight, diluted with water (5 cm^3), and extracted with dichloromethane (5 cm^3). The organic layer was washed with 5% aq. sodium hydrogen carbonate (5 cm^3), dried and evaporated. PLC (1 mm plate, developed with 5% methanol in dichloromethane) yielded the *keto amide* **23** (8 mg, 20%), m.p. 187–189 °C (from dichloromethane–hexane) (Found: C, 54.2; H, 6.1; N, 7.2. $C_{18}H_{24}N_2O_8$ requires C, 54.5; H, 6.1; N, 7.1%); λ_{max}/nm 240 and 328; ν_{max}/cm^{-1} 3520sh, 3380, 1740, 1710, 1650 and 1570; δ_H(B) 1.57 (9 H, s, Bu^t), 2.54 (2 H, m, $CH_2CH_2CO_2$), 3.02 (2 H, m, $CH_2CH_2CO_2$), 3.63 and 3.68 (each 3 H, s, OMe), 3.90 (2 H, s, CH_2CO_2) and 5.70 and 7.30 (1 H, br s, NH); *m*/*z* 396 (M^+), 340 (10, M − C_4H_8), 308 (31) and 268 (100).

5-tert-*Butyl Hydrogen* 4-(2-*Methoxycarbonylethyl*)-3-(*methoxycarbonylmethyl*)*pyrrole*-2,5-*dicarboxylate* **26**.—(*a*) A solution of the methylpyrrole **24** (3.39 g, 10 mmol) in dichloromethane (100 cm^3) was stirred vigorously at 0 °C with potassium carbonate (27.6 g, 0.2 mol) during dropwise addition of sulfuryl dichloride (4.32 g, 32 mmol) in dichloromethane (3 cm^3). After 15 min at 0 °C and 2 h at 20 °C, the mixture was filtered (Celite) and evaporated. The residue was heated at reflux for 15 min in acetone (100 cm^3)–water (50 cm^3), the acetone was evaporated off, and the remaining aqueous solution was extracted with dichloromethane (50 cm^3, then 3 × 20 cm^3). The extracts were evaporated, dissolved in ether (75 cm^3) and extracted with 10% aq. sodium carbonate (4 × 25 cm^3). The combined aqueous layers were washed with ether (50 cm^3), acidified with conc. hydrochloric acid and extracted with dichloromethane (50 cm^3, then 3 × 25 cm^3). The combined organic layers were washed with brine (30 cm^3), dried and evaporated to afford the carboxylic acid **26** (1.12 g, 30.3%), which was crystallised from dichloromethane–ether–hexane.

(*b*) A solution of the crude formylpyrrole **25** [prepared as in ref. 7 from the methylpyrrole **24** (10.18 g, 30 mmol) using method (*b*)] in acetone (300 cm^3) was stirred during dropwise addition (30 min) of a solution of potassium permanganate (9.48 g, 60 mmol) in water (260 cm^3)–acetone (190 cm^3). After a further 1 h, part of the acetone (150 cm^3) was evaporated off and to the remainder were added dichloromethane (200 cm^3) and sodium metabisulfite ($Na_2S_2O_5$) (13.65 g). Conc. hydrochloric acid (20 cm^3) was slowly added and the mixture was stirred until both layers became colourless. The aqueous layer was separated and extracted with more dichloromethane (100 cm^3, then 2 × 50 cm^3). The combined organic layers were washed with brine (100 cm^3), filtered, dried and evaporated. Crystallisation of the resultant solid from dichloromethane–ether–hexane gave the *carboxylic acid* **26** (6.98 g, 63%), m.p. 162–163.5 °C (Found: C, 55.0; H, 6.0; N, 3.7. $C_{17}H_{23}NO_8$ requires C, 55.3; H, 6.3; N, 3.8%); λ_{max}/nm 277 and 284sh; ν_{max}/cm^{-1} 3440, 3300–2500br, 1735, 1700 and 1680; δ_H(A) 1.64 (9 H, s, Bu^t), 2.60 (2 H, m, $CH_2CH_2CO_2$), 3.03 (2 H, m, $CH_2CH_2CO_2$), 3.70 and 3.73 (each 3 H, s, OMe), 3.93 (2 H, br s, CH_2CO_2), 9.79 (1 H, br s, NH) and 10.56 (1 H, br s, CO_2H); *m*/*z* 369 (9%, M^+), 313 (27, M − C_4H_8), 281 (88) and 253 (100).

tert-*Butyl* 5-*Iodo*-3-(2-*methoxycarbonylethyl*)-4-(*methoxycarbonylmethyl*)*pyrrole*-2-*carboxylate* **27**.—To a solution of the carboxylic acid **26** (6.65 g, 18 mmol) in ethanol-free chloroform (72 cm^3)–water (54 cm^3) at 50 °C was added sodium hydrogen carbonate (4.54 g, 54 mmol). The mixture was heated to reflux and stirred rapidly during addition (5 min) of a solution of iodine (5.3 g, 20.9 mmol) and potassium iodide (5.4 g, 32.6 mmol) in water (27 cm^3). Vigorous stirring at reflux was continued for 25 min and then sufficient 5% aq. sodium metabisulfite was added to destroy excess of iodine. The separated organic layer was passed through a column of alumina (3 × 3 cm), and eluted first with dichloromethane

extracts (3 × 18 cm^3) of the aqueous layer and then with ether (90 cm^3). The residue from evaporation of the eluates was crystallised from dichloromethane–ether–hexane to give the *iodopyrrole* **27** (7.85 g, 96%), m.p. 90.5–92.5 °C (Found: C, 42.6; H, 5.0; N, 3.1. $C_{16}H_{22}INO_6$ requires C, 42.6; H, 4.9; N, 3.1%); λ_{max}/nm 276; ν_{max}/cm^{-1} 3440, 1735 and 1690; δ_H(A) 1.58 (9 H, s, Bu^t), 2.55 (2 H, m, $CH_2CH_2CO_2$), 3.02 (2 H, m, $CH_2CH_2CO_2$), 3.44 (2 H, s, CH_2CO_2), 3.62 and 3.65 (each 3 H, s, OMe) and 9.24 (1 H, br s, NH); *m/z* 451 (41%, M^+), 395 (30, M − C_4H_8) and 363 (100).

tert-*Butyl* 3-(2-*Methoxycarbonylethyl*)-4-(*methoxycarbonylmethyl*)*pyrrole*-2-*carboxylate* **28**.—A solution of the iodopyrrole **27** (7.85 g, 17.4 mmol) in methanol (87 cm^3) was stirred under hydrogen with sodium acetate (5.71 g, 69.6 mmol) and 10% palladium-on-charcoal (785 mg). After 20 h, hydrogen uptake had ceased and the mixture was filtered and evaporated. The residue was partitioned between 5% aq. sodium hydrogen carbonate (70 cm^3) and dichloromethane (100 cm^3). The organic layer was passed through an alumina column (3 × 3 cm) and eluted first with dichloromethane extracts (35 cm^3, then 2 × 20 cm^3) of the aqueous layer and then with ether (100 cm^3). The residue from evaporation of the eluates was crystallised from dichloromethane–ether–hexane to give the *α-free pyrrole* **28** (5.38 g, 95%), m.p. 51–52 °C (Found: C, 59.2; H, 7.2; N, 4.4. $C_{16}H_{23}NO_6$ requires C, 59.1; H, 7.1; N, 4.3%); λ_{max}/nm 268; ν_{max}/cm^{-1} 3460, 1730 and 1680; δ_H(A) 1.57 (9 H, s, Bu^t), 2.54 (2 H, m, $CH_2CH_2CO_2$), 3.00 (2 H, m, $CH_2CH_2CO_2$), 3.45 (2 H, s, CH_2CO_2), 3.59 and 3.62 (each 3 H, s, OMe), 6.69 (1 H, d, *J* 2, α-H) and 9.57 (1 H, br s, NH); *m/z* 325 (11%, M^+), 269 (27, M − C_4H_8) and 237 (100).

tert-*Butyl* 5-*Benzyloxycarbonylmethyl*-3-(2-*methoxycarbonylethyl*)-4-(*methoxycarbonylmethyl*)*pyrrole*-2-*carboxylate* **29**.—The α-free pyrrole **28** (163 mg, 0.5 mmol) was stirred at 90 °C under argon with copper powder (82 mg) during addition (2 h) of benzyl diazoacetate[6] (0.3 cm^3). After being stirred for a further 10 min, the mixture was chromatographed on a column (silica H, 6 g), with 0–5% methyl acetate in dichloromethane as eluent and then by PLC (3 × 1 mm plates, developed with 8% methyl acetate in dichloromethane) to yield starting material **28** (83 mg, 51% recovery) and the *benzyloxycarbonylmethylpyrrole* **29** (59.8 mg, 25%) as a gum (Found: M^+, 473.2052. $C_{25}H_{31}NO_8$ requires *M*, 473.2050); λ_{max}/nm 275; ν_{max}/cm^{-1} 3440, 1730, 1680 and 1500; δ_H(A) 1.55 (9 H, s, Bu^t), 2.54 (2 H, m, $CH_2CH_2CO_2$), 3.00 (2 H, m, $CH_2CH_2CO_2$), 3.41 (2 H, s, 4-CH_2CO_2), 3.57 and 3.60 (each 3 H, s, OMe), 3.65 (2 H, s, 5-CH_2CO_2), 5.06 (2 H, s, OCH_2Ph), 7.26 (5 H, s, Ph) and 9.52 (1 H, br s, NH); *m/z* 473 (1%, M^+), 373 (5, M − CO_2 − C_4H_8), 358 (5) and 326 (100).

{*Benzyloxycarbonyl*-[5-tert-*butoxycarbonyl*-4-(2-*methoxycarbonylethyl*)-3-(*methoxycarbonylmethyl*)*pyrrol*-2-*yl*]*methyl*} *triphenylphosphonium Chloride* **31**.—A solution of the benzyloxycarbonylmethylpyrrole **29** (43 mg, 0.091 mmol) in dichloromethane (1 cm^3) was stirred with potassium carbonate (124 mg, 0.9 mmol) during dropwise addition of sulfuryl dichloride (13.5 mg, 0.1 mmol) and then for a further 10 min. The mixture was filtered and evaporated to give the crude benzyloxycarbonyl(chloro)methylpyrrole **30** as a gum; δ_H(A) 1.57 (9 H, s, Bu^t), 2.57 (2 H, m, $CH_2CH_2CO_2$), 2.98 (2 H, m, $CH_2CH_2CO_2$), 3.47 (2 H, s, CH_2CO_2), 3.56 and 3.59 (each 3 H, s, OMe), 5.16 (2 H, br s, CH_2Ph), 5.48 (1 H, br s, CH), 7.28 (5 H, br s, Ph) and 9.45 (1 H, br s, NH).

This compound was dissolved in ether (5 cm^3) and treated with a solution of triphenylphosphine (26.2 mg, 0.1 mmol) in ether (1 cm^3) and shortly thereafter the solution was evaporated. A solution of the residue in a small quantity of dichloromethane was diluted with ether to crystallize the *phosphonium chloride* **31** (40 mg, 57%), m.p. 129–136 °C (decomp.) (Found: C, 67.0; H, 5.7; N, 2.0; Cl, 4.8; P, 4.4 $C_{43}H_{45}ClNO_8P$ requires C, 67.1; H, 5.9; N, 1.8; Cl, 4.6; P, 4.0%); λ_{max}/nm 288; ν_{max}/cm^{-1} 3120br, 1730, 1690, 1580 and 1440; δ_H(A) 1.48 (9 H, s, Bu^t), 2.67 (4 H, m, $CH_2CH_2CO_2$), 2.96 (2 H, br s, CH_2CO_2), 3.29 and 3.53 (each 3 H, s, OMe), 5.06 (2 H, d, CH_2Ph), 6.91–7.81 (20 H, m, 4 × Ph), 8.83 (1 H, br s, CH) and 9.20 (1 H, br s, NH).

[*Benzyloxycarbonyl*-(5-tert-*butoxycarbonyl*-3-*ethyl*-4-*methylpyrrol*-2-*yl*)*methyl*]*triphenylphosphonium Bromide* **33**.—A solution of *tert*-butyl 5-benzyloxycarbonylmethyl-4-ethyl-3-methylpyrrole-2-carboxylate **32**[14] (50 mg, 0.14 mmol) in tetrachloromethane (1.5 cm^3) was heated at reflux with *N*-bromosuccinimide (26.2 mg, 0.147 mmol) for 10 min whilst being irradiated by a tungsten lamp and was then filtered and evaporated to give the crude benzyloxycarbonyl(bromo)methylpyrrole as a gum; δ_H(A, CCl_4) 1.13 (3 H, t, *J* 7, CH_2Me), 1.59 (9 H, s, Bu^t), 2.20 (3 H, s, Me), 2.43 (2 H, q, *J* 7, CH_2Me), 5.16 (2 H, br s, CH_2Ph), 5.37 (1 H, s, CH), 7.23 (5 H, s, Ph) and 9.35 (1 H, br s, NH).

This product was dissolved in ether (7 cm^3) and mixed with a solution of triphenylphosphine (39.3 mg, 0.15 mmol) in ether (1.4 cm^3). After 18 h, the precipitate was collected, and washed with ether to give the *phosphonium salt*[33] (60 mg, 61%), m.p. 150 °C (decomp.) (Found: C, 67.1; H, 6.1; N, 2.0. $C_{39}H_{41}BrNO_4P$ requires C, 67.0; H, 5.9; N, 2.0%); λ_{max}/nm 272 and 285sh; ν_{max}/cm^{-1} 3170br, 1720, 1690, 1600, 1580 and 1440; δ_H(C) 0.49 (3 H, t, *J* 7, CH_2Me), 1.51 (9 H, s, Bu^t), 1.70 (2 H, br q, *J* 7, CH_2Me), 2.2 (3 H, s, Me), 5.19 (2 H, br s, CH_2Ph), 7.32 (5 H, br s, Ph), 7.45–7.96 (15 H, m, PPh_3), 8.76 (1 H, d, *J* 19, CHP) and 10.67 (1 H, br s, NH).

*tert-Butyl*5-*Benzyloxycarbonyl*-7-*ethyl*-2,2,3,3,8-*pentamethyl*-1-*oxo*-1,2,3,10-*tetrahydrodipyrrin*-9-*carboxylate* **34**.—A suspension of the phosphonium salt **33** (14 mg, 0.02 mmol) in toluene (1 cm^3) containing tetramethylthiosuccinimide **10** (3.4 mg, 0.02 mmol) was stirred under argon during dropwise addition of a solution of potassium *tert*-butoxide in *tert*-butyl alcohol (1 mol dm^{-3}; 0.03 cm^3, 0.03 mmol). After being stirred for a further 5 min, the resulting clear solution was heated at reflux, under argon, for 96 h. More potassium *tert*-butoxide solution (0.02 cm^3, 0.02 mmol) was added and heating at reflux was continued for a further 48 h. The cooled mixture was quenched with saturated aq. ammonium chloride (0.5 cm^3), diluted with water (5 cm^3) and extracted with dichloromethane (5 cm^3, then 3 cm^3). The combined extracts were dried, filtered and evaporated. PLC (1 mm plate, developed with 5% methyl acetate in dichloromethane) gave recovered starting material **10** (1.8 mg, 53% recovered) and the *lactam* **34** as a gum (1.9 mg, 19%) (Found: M^+, 494.2778. $C_{29}H_{38}N_2O_5$ requires *M*, 494.2780); λ_{max}(MeOH)/nm 274; not shifted by addition of $Zn(OAc)_2$; ν_{max}/cm^{-1} 3440, 3300br, 1730, 1670 and 1600; δ_H(F) 0.78 and 0.88 (each 3 H, s, Me), 0.92 (3 H, t, *J* 7, CH_2Me), 1.04 (6 H, s, 2 × Me), 1.57 (9 H, s, Bu^t), 2.28 (3 H, s, Ar*Me*), 2.30 (2 H, q, *J* 7, CH_2Me), 5.09 and 5.13 (each 1 H, d, *J* 13, CH_2Ph), 7.25 (5 H, m, Ph) and 8.37 and 10.52 (each 1 H, br s, NH); *m/z* 494 (63%, M^+) and 438 (100, M − C_4H_8).

tert-*Butyl* (E)- *and* (Z)-5-*Cyano*-8-(2-*methoxycarbonylethyl*)-7-*methoxycarbonylmethyl*-1-*oxo*-1,2,3,10-*tetrahydrodipyrrin*-9-*carboxylate* **36** *and* **38**.—The phosphonium salt **35** (132 mg, 0.2 mmol) was suspended in a mixture of ether (30 cm^3) and methyl acetate (10 cm^3) and shaken with saturated aq. sodium carbonate (20 cm^3) until no solid remained. The aqueous layer

was separated, and extracted with more ether (15 cm^3) and methyl acetate (5 cm^3). The combined organic layers were dried and evaporated. Benzene (4 × 5 cm^3) was added and then evaporated again to leave the ylide.

The ylide from the phosphonium salt **35** (33 mg, 0.05 mmol) was heated at reflux, under argon, in toluene (3 cm^3) containing monothiosuccinimide **9** (5.8 mg, 0.05 mmol) and a solution of potassium *tert*-butoxide in *tert*-butyl alcohol (0.78 mol dm^{-3}; 0.01 cm^3, 0.0078 mmol). After 2 h, the cooled solution was mixed with saturated aq. ammonium chloride (1 cm^3) and water (5 cm^3), and extracted with chloroform (5 cm^3). The organic layer was dried and evaporated. PLC of the residue (1 mm plate, developed with 5% methanol in chloroform) gave the (*E*)- and (*Z*)-isomers, **36** and **38**, respectively, of the *bicyclic lactam* as gums (12.3 mg, 55% and 3 mg, 13.5%, respectively). The less polar (E)-*isomer* **36** was crystallised from ether–hexane, m.p. 174–178 °C (Found: C, 59.3; H, 5.9; N, 9.4%; M^+, 445.1827. $C_{22}H_{27}N_3O_7$ requires C, 59.3; H, 6.1; N, 9.45%; *M*, 445.1849); λ_{max}(MeOH)/nm 245 and 276; shifted by addition of $Zn(OAc)_2$ to 245, 289, 295, 305 and 362; ν_{max}/cm^{-1} 3430, 3200br, 2200w, 1760, 1730br and 1635; δ_H(D) 1.56 (9 H, s, Bu^t), 2.50 (2 H, m, $CH_2CH_2CO_2$), 2.65 (2 H, m, CH_2CH_2CONH), 2.93 (2 H, m, $CH_2CH_2CO_2$), 3.20 (2 H, m, CH_2CH_2CONH), 3.45 (2 H, s, CH_2CO_2), 3.67 and 3.77 (each 3 H, s, OMe) and 8.94 and 9.30 (each 1 H, br s, NH); *m/z* 445 (15%, M^+), 389 (72, M − C_4H_8), 357 (55) and 277 (100).

The (Z)-*isomer* **38** was an oil (Found: M^+, 445.1836). λ_{max}(MeOH)/nm 248 and 274; not shifted by addition of $Zn(OAc)_2$; ν_{max}/cm^{-1} 3430, 3220br, 2200w, 1760, 1730br and 1635; δ_H(D) 1.57 (9 H, s, Bu^t), 2.60 (4 H, m, $CH_2CH_2CO_2$ and CH_2CH_2CONH), 2.91 (4 H, m, $CH_2CH_2CO_2$ and CH_2CH_2-CONH), 3.52 (2 H, s, CH_2CO_2), 3.68 and 3.70 (each 3 H, s, OMe) and 8.46 and 9.07 (each 1 H, br s, NH); *m/z* 445 (19%, M^+), 389 (100, M − C_4H_8) and 357 (64).

tert-*Butyl* (E)- *and* (Z)-5-*Cyano*-8-(2-*methoxycarbonylethyl*)-7-*methoxycarbonylmethyl*-2,2,3,3-*tetramethyl*-1-*oxo*-1,2,3,10-*tetrahydrodipyrrin*-9-*carboxylate* **37** *and* **39**.—A suspension of the phosphonium salt **35** (132 mg, 0.2 mmol) in toluene (10 cm^3) containing tetramethylthiosuccinimide **10** (34.2 mg, 0.2 mmol) was stirred under argon during dropwise addition of a solution of potassium *tert*-butoxide in *tert*-butyl alcohol (0.78 mol dm^{-3}; 0.38 cm^3, 0.3 mmol). After being stirred for a further 5 min, the solution was heated at reflux, under argon, for 6 h, cooled, mixed with saturated aq. ammonium chloride (1 cm^3) and water (20 cm^3) and extracted with dichloromethane (20 cm^3, then 10 cm^3). The combined organic layers were dried and evaporated. PLC (2 × 1 mm plates, developed with 10% methyl acetate in dichloromethane) gave the (*E*)-isomer **37** of the *bicyclic lactam* as needles (88.6 mg, 88%), m.p. 155–156 °C and the more polar (*Z*)-isomer **39** as a gum (1.7 mg, 1.7%). For the (E)-*isomer* **37**: (Found: C, 62.1; H, 7.0; N, 8.2%; M^+, 501.2443. $C_{26}H_{35}N_3O_7$ requires C, 62.3; H, 7.0; N, 8.4%; *M*, 501.2474); λ_{max}(MeOH)/nm 252 and 274sh; shifted by addition of $Zn(OAc)_2$ to 251, 294 and 364; ν_{max}/cm^{-1} 3420, 3300br, 2200, 1730, 1680 and 1620; δ_H(A) 1.15 and 1.47 (each 6 H, s, 2 × Me), 1.59 (9 H, s, Bu^t), 2.52 (2 H, m, $CH_2CH_2CO_2$), 2.94 (2 H, m, $CH_2CH_2CO_2$), 3.39 (2 H, s, CH_2CO_2), 3.63 and 3.67 (each 3 H, s, OMe) and 8.15 and 8.99 (each 1 H, br s, NH); *m/z* 501 (22%, M^+), 445 (100, M − C_4H_8) and 413 (53).

For the (Z)-*isomer* **39** (Found: M^+, 501.2455); λ_{max}(MeOH)/nm 254 and 268; not shifted by $Zn(OAc)_2$; ν_{max}/cm^{-1} 3420, 3380, 2200, 1730, 1680 and 1620; δ_H(B) 0.93 and 1.07 (each 6 H, s, 2 × Me), 1.56 (9 H, s, Bu^t), 2.54 (2 H, m, $CH_2CH_2CO_2$), 2.99 (2 H, m, $CH_2CH_2CO_2$), 3.47 (2 H, s, CH_2CO_2), 3.64 and 3.66 (each 3 H, s, OMe) and 8.88 and 9.80 (each 1 H, br s, NH); *m/z* 501 (23%, M^+), 445 (77, M − C_4H_8), 413 (41) and 277 (100).

tert-*Butyl* 5-*Azidomethyl*-3-(2-*methoxycarbonylethyl*)-4-(*methoxycarbonylmethyl*)*pyrrole*-2-*carboxylate* **41**.—A solution of the chloromethylpyrrole **5** was prepared as before from the methylpyrrole **24** (3.0 g, 8.83 mmol) and was evaporated to give a pale yellow gum, which crystallised on evacuation at 1 mmHg.

To a solution of the chloromethylpyrrole (2 g, 5.3 mmol) in acetone (25 cm^3), was added a solution of sodium azide (0.5 g, 7.7 mmol) in water (4 cm^3) dropwise during 5 min. The resulting mixture was stirred at room temperature for a further 15 min and was then partitioned between water (50 cm^3) and ether (50 cm^3). The aqueous layer was extracted with further ether (2 × 20 cm^3). The combined ether solutions were washed with water, dried and evaporated to yield the *azidomethylpyrrole* **41** (1.87 g, 91% from the chloromethylpyrrole) as crystals, m.p. 92–93 °C (from ether–hexane) (Found: C, 53.8; H, 6.45; N, 13.9%; $M^+ - N_2$, 352.1650. $C_{17}H_{24}N_4O_6$ requires C, 53.7; H, 6.35; N, 14.7%; $C_{17}H_{24}N_2O_6$ requires *m/z*, 352.1634); ν_{max}/cm^{-1} 2100 and 1660; δ_H 1.60 (9 H, s, Bu^t), 2.60 (2 H, m, $CH_2CH_2CO_2$), 2.93 (2 H, m, $CH_2CH_2CO_2$), 3.45 (2 H, s, CH_2CO_2), 3.60 (6 H, s, 2 × OMe), 4.28 (2 H, s, CH_2N_3) and 9.17 (1 H, br s, NH).

tert-*Butyl* 5-*Formamidomethyl*-3-(2-*methoxycarbonylethyl*)-4-(*methoxycarbonylmethyl*)*pyrrole*-2-*carboxylate* **42**.—To a solution of the azidomethylpyrrole **41** (800 mg, 2.1 mmol) in ether (30 cm^3) were added acetic formic anhydride (3 cm^3) and palladium black (150 mg). The mixture was stirred under hydrogen for 8 h and then filtered through Celite. The filtrate was diluted with ether (30 cm^3), washed with 5% aq. sodium hydrogen carbonate (3 × 15 cm^3), dried and evaporated. Flash chromatography [silica gel; CH_2Cl_2, then ether–CH_2Cl_2(1:2)] gave the *formamidomethylpyrrole* **42** (514 mg, 64%), m.p. 126–131 °C (from dichloromethane–hexane) (Found: M^+, 382.1725. $C_{18}H_{26}N_2O_7$ requires *M*, 382.1740); ν_{max}/cm^{-1} 1730 and 1690; δ_H 1.55 (9 H, s, Bu^t), 2.50 (2 H, m, $CH_2CH_2CO_2$), 2.90 (2 H, m, $CH_2CH_2CO_2$), 3.45 (2 H, br s, CH_2CO_2), 3.60 and 3.68 (each 3 H, s, OMe), 4.25 (2 H, d, *J* 6, CH_2N), 8.05 (1 H, br s, CHO) and 9.40 (1 H, br, NH).

tert-*Butyl* 5-*Isocyanomethyl*-3-(2-*methoxycarbonylethyl*)-4-(*methoxycarbonylmethyl*)*pyrrole*-2-*carboxylate* **43**.—To a solution of the formamidomethylpyrrole **42** (50 mg, 0.13 mmol) in pyridine (0.5 cm^3) was added toluene-*p*-sulfonyl chloride (34 mg, 0.2 mmol). The mixture was stirred at room temperature for 3 h and then poured on to ice–water (5 cm^3) and extracted with ether (3 × 15 cm^3). The extract was dried and evaporated. PLC (ethyl acetate) gave the unstable isocyanide **43** as a gum (28 mg, 82% based on consumed starting material); ν_{max}/cm^{-1} 2150, 1730 and 1690; δ_H 1.60 (9 H, s, Bu^t), 2.55 (2 H, m, $CH_2CH_2CO_2$), 3.00 (2 H, $CH_2CH_2CO_2$), 3.50 (2 H, s, CH_2CO_2), 3.67 and 3.70 (each 3 H, s, OMe), 4.67 (2 H, s, CH_2NC) and 9.35 (1 H, br s, NH); *m/z* (f.d.) 364.

Diethyl Azido-[5-tert-*butoxycarbonyl*-4-(2-*methoxycarbonylethyl*)-3-(*methoxycarbonylmethyl*)*pyrrol*-2-*yl*]*methylphosphonate* **48**.—A solution of the phosphonate **11** (1.43 g, 3 mmol) in dichloromethane (50 cm^3) containing potassium carbonate (4.1 g, 38 mmol) was stirred at 0 °C during the dropwise addition of a solution of a sulfuryl dichloride (406 mg, 3 mmol) in dichloromethane (2 cm^3) (2 min). The mixture was stirred at 0 °C for 10 min, then at room temperature for 10 min, and was then filtered through Celite. The filtrate was evaporated to leave the chloride **47** as a gum which solidified on evacuation to 1 mmHg.

The foregoing chloride was dissolved in acetone (50 cm^3) and a solution of sodium azide (500 mg, 7.7 mmol) in water (4 cm^3) was added. The resulting solution was stirred at room temperature for 30 min, concentrated to ~10 cm^3, and partitioned between water and ether. The organic layer was

dried and evaporated to yield the azide **48** as an oil (1.44 g, 92%) which solidified on storage, m.p. 80–87 °C (decomp.) (Found: $M^+ - N_2$, 488.1897. $C_{21}H_{33}N_2O_9P$ requires *m/z*, 488.1923); ν_{max}/cm^{-1} 2100, 1740 and 1700; δ_H 1.20 and 1.32 (each 3 H, t, *J* 6, OCH_2Me), 1.53 (9 H, s, Bu^t), 2.58 (2 H, m, $CH_2CH_2CO_2$), 3.00 (2 H, m, $CH_2CH_2CO_2$), 3.55 (2 H, s, CH_2CO_2), 3.62 and 3.68 (each 3 H, s, OMe), 4.20 (4 H, m, 2 × OCH_2Me), 4.92 (1 H, d, *J* 18, CHN_3) and 9.50 (1 H, br s, NH).

Diethyl [5-tert-*Butoxycarbonyl*-4-(2-*methoxycarbonylethyl*)-3-(*methoxycarbonylmethyl*)*pyrrol*-2-*yl*](*formamido*)*methylphosphonate* **49**.—A solution of the azidomethylphosphonate **48** (200 mg, 0.387 mmol) in anhydrous ethanol (30 cm^3) containing palladium black (100 mg) and conc. hydrochloric acid (0.15 cm^3) was stirred under hydrogen for 3 h, then filtered through Celite and evaporated. The residue was stirred in ether (25 cm^3) with acetic formic anhydride (1 cm^3) during the addition of triethylamine (0.2 cm^3), and after a further 15 min the mixture was poured onto ice–water (10 cm^3). The organic layer was separated, washed successively with 5% aq. sodium hydrogen carbonate (3 × 15 cm^3) and water, dried and evaporated. Flash column chromatography (silica gel; 4% MeOH in EtOAc) gave the formamide **49** (130 mg, 65%) as an oil (Found: $M^+ - C_4H_8$, 462.1372. $C_{18}H_{27}N_2O_{10}P$ requires *m/z*, 462.1403); δ_H 1.15 and 1.32 (each 3 H, t, *J* 5, OCH_2Me), 1.55 (9 H, s, Bu^t), 2.60 (2 H, m, $CH_2CH_2CO_2$), 3.05 (2 H, m, $CH_2CH_2CO_2$), 3.55 (2 H, br s, CH_2CO_2), 3.68 and 3.72 (each 3 H, s, OMe), 4.15 (4 H, m, 2 × OCH_2Me), 6.00 (1 H, dd, *J* 6 and 18, CHP), 8.30 (1 H, s, CHO) and 8.38 and 10.40 (each 1 H, s, NH); *m/z* (f.d.) 518.

Diethyl [5-tert-*Butoxycarbonyl*-4-(2-*methoxycarbonylethyl*)-3-(*methoxycarbonylmethyl*)*pyrrol*-2-*yl*](*isocyano*)*methylphosphonate* **50**.—A solution of the formamidomethylphosphonate **49** (34 mg, 0.065 mmol) in dichloromethane (10 cm^3) was stirred at −40 °C during the addition of a solution of phosphorus trichloride oxide (10 mg, 0.065 mmol) in dichloromethane (0.5 cm^3) followed by a solution of triethylamine (13 mg, 0.128 mmol) in dichloromethane (0.5 cm^3). The mixture was allowed to warm to room temperature during 1 h and was then stirred for a further 3 h. Further quantities of phosphorus trichloride oxide (10 mg) and triethylamine (20 mg) were added and the mixture was stirred for 30 min, then was poured onto ice-cold 10% aq. sodium hydrogen carbonate (15 cm^3) and extracted with dichloromethane (2 × 10 cm^3). The organic solution was dried and evaporated to yield a gum (28 mg, 85%). NMR spectroscopy of this product after filtration through a short column of silica gel showed the pure isocyanide **50** (Found: $M^+ - NC - C_4H_9$, 417.1173. $C_{17}H_{24}NO_9P$ requires *m/z*, 417.1189); ν_{max}/cm^{-1} 2140, 1740 and 1600; δ_H 1.20 and 1.35 (each 3 H, t, *J* 6, OCH_2Me), 1.58 (9 H, s, Bu^t), 2.60 (2 H, m, $CH_2CH_2CO_2$), 2.95 (2 H, m, $CH_2CH_2CO_2$), 3.52 (2 H, s, CH_2CO_2), 3.67 and 3.70 (each 3 H, s, OMe), 4.23 (4 H, m, 2 × OCH_2Me), 5.30 (1 H, d, *J* 18, CHNC) and 9.55 (1 H, br s, NH); *m/z* (f.d.) 500.

tert-*Butyl* (E)- *and* (Z)-5-(1-*Isocyanobut*-1-*enyl*)-3-(2-*methoxycarbonylethyl*)-4-(*methoxycarbonylmethyl*)*pyrrole*-2-*carboxylate* **51**.—To a stirred solution of the isocyanomethylphosphonate **50** (40 mg, 0.08 mmol) in THF (5 cm^3) at 0 °C was added sodium hydride (50% dispersion in oil; 4 mg, 0.083 mmol). The mixture was allowed to warm to room temperature, was stirred for a further 15 min, then was cooled again to 0 °C and a solution of freshly distilled propionaldehyde (7 mg, 0.097 mmol) in THF (1 cm^3) was added. After 15 min at 0 °C and 30 min at room temperature the mixture was evaporated. PLC (ether) gave the *alkene derivative* **51** as an oil (8 mg, 25%) (Found: M^+, 404.1945. $C_{21}H_{28}N_2O_6$ requires *M*, 404.1947); ν_{max}/cm^{-1} 1740, 1700 and 1690; δ_H 1.15 (3 H, m, Me), 1.55 (9 H, s, Bu^t), 2.13 (2 H, m, CH_2Me), 2.55 (2 H, m, $CH_2CH_2CO_2$), 3.00 (2 H, m, $CH_2CH_2CO_2$), 3.60 (2 H, s, CH_2CO_2), 3.75 (6 H, s, 2 × OMe), 6.75 (1 H, t, *J* 8, C=CH) and 8.90 (1 H, br s, NH).

tert-Butyl (Z)-8-(2-*Methoxycarbonylethyl*)-7-*methoxycarbonylmethyl*-3,3-*dimethyl*-1-*methylthio*-2,3-*dihydrodipyrrin*-9-*carboxylate*.—The thiolactam **54**[20] (75 mg, 0.162 mmol), DBU (1 drop) and trimethyloxonium tetrafluoroborate (100 mg, 0.81 mmol) were stirred in dichloromethane (2 cm^3) under argon for 30 min. The mixture was poured into ice-cold 20% aq. potassium carbonate (20 cm^3) and extracted with dichloromethane (20 cm^3, then 2 × 15 cm^3). The combined extracts were dried and evaporated to give the *title thioimidate* as needles (60 mg, 78%), m.p. 122–124 °C (from ether–hexane) (Found: C, 60.0; H, 7.3; N, 5.9. $C_{24}H_{34}N_2O_6S$ requires C, 60.2; H, 7.2; N, 5.9%); λ_{max}/nm 254 and 360; ν_{max}/cm^{-1} 3400br, 1730 and 1665; δ_H(F) 1.24 (6 H, m, 2 × Me), 1.54 (9 H, s, Bu^t), 2.54 (2 H, m, $CH_2CH_2CO_2$), 2.67 (3 H, s, SMe), 2.69 (2 H, s, CH_2CS), 2.96 (2 H, m, $CH_2CH_2CO_2$), 3.53 (2 H, s, CH_2CO_2), 3.64 and 3.65 (each 3 H, s, OMe), 5.61 (1 H, s, CH=CN) and 9.1 (1 H, br s, NH); δ_C 14 (SMe), 20 ($CH_2CH_2CO_2$), 28 (CMe_3), 28.5 (CMe_2), 29.5 (CH_2CO_2), 34 ($CH_2CH_2CO_2$), 43 (CMe_2), 50.5 and 51 (2 × OMe), 79 (CMe_3), 98 (CH=CN), 114, 119, 128 and 131 (4 × pyrrole-C), 159.5 (CH=CN), 162 (CO_2Bu^t), 172 and 174 (2 × CO_2Me) and 178 (N=CS); *m/z* 478 (37%, M^+), 424 (100, $M - C_4H_8$), 363 (15), 347 (11) and 345 (15).

tert-*Butyl* (Z)-1-*Benzyloxycarbonylmethylthio*-8-(2-*methoxycarbonylethyl*)-7-*methoxycarbonylmethyl*-3,3-*dimethyl*-2,3-*dihydrodipyrrin*-9-*carboxylate*.—THF (2 cm^3) was stirred with sodium hydride (50% suspension in mineral oil; 9.2 mg) under argon and the mixture was cooled to −10 °C. A solution of the thiolactam **54** (81 mg) in THF (1 cm^3) was then added during 10 min, followed by benzyl bromoacetate (44 mg). The mixture was stirred at −10 °C for 20 min and 0 °C for 30 min, then poured into 20% aq. potassium carbonate (15 cm^3) at 0 °C and extracted with dichloromethane (20 cm^3, then 2 × 15 cm^3). The combined extracts were washed with water (10 cm^3), dried and evaporated. Filtration through a column of silica gel (10 g) in ether gave the *title thioimidate* as an oil (88.7 mg, 83%) (Found: M^+, 612.2485, $C_{32}H_{40}N_2O_8S$ requires *M*, 612.2505); λ_{max}(EtOH)/nm 252 and 360; ν_{max}/cm^{-1} 3350br, 1760 and 1700; δ_H(D) 1.26 (6 H, s, 2 × Me), 1.52 (9 H, s, Bu^t), 2.65 (2 H, m, $CH_2CH_2CO_2$), 2.7 (2 H, s, CH_2CS), 3.02 (2 H, m, $CH_2CH_2CO_2$), 3.54 (2 H, s, CH_2CO_2), 3.78 (6 H, s, 2 × OMe), 4.20 (2 H, s, SCH_2CO_2), 5.30 (2 H, s, CH_2Ph), 5.68 (1 H, s, CHCN), 7.25 (5 H, s, Ph) and 10.54 (1 H, br s, NH); *m/z* 612 (89%, M^+), 556 (100, $M^+ - C_4H_8$) and 482 (16).

tert-*Butyl* (1Z,4Z)- *and* (1E,4Z)-1-*Benzyloxycarbonylmethylene*-8-(2-*methoxycarbonylethyl*)-7-*methoxycarbonylmethyl*-3,3-*dimethyl*-1,2,3,10-*tetrahydrodipyrrin*-9-*carboxylate* **61**.—2-(Trimethylsilyl)ethanol (2.5 g, 21.2 mmol) was dissolved in benzene (60 cm^3). A fraction of the benzene (~10 cm^3) was removed by distillation to ensure dryness. Dicyclohexylcarbodiimide (DCC) (4.37 g, 21.2 mmol) and copper(I) iodide (25 mg) were added and the mixture was heated at reflux for 2 h and was then cooled to room temperature. Benzyl hydrogen malonate (4.522 g, 23.3 mmol) was added and the mixture was heated at reflux for a further 3 h, cooled, filtered through Celite and evaporated. The residue was dissolved in hexane (20 cm^3), filtered through Celite and again evaporated. The residue was dissolved in dichloromethane (25 cm^3), washed successively with 0.2 mol dm^{-3} hydrochloric acid (20 cm^3) and 5% aq. sodium hydrogen carbonate (20 cm^3), dried (Na_2SO_4) and evaporated. Chromatography on silica [50 g; eluent, ether–hexane (1:1)] gave benzyl 2-(trimethylsilyl)ethyl malonate as an oil (6.43 g, 95%); δ_H(A; CD_2Cl_2) 0.1 (9 H, s, $SiMe_3$), 1.05 (2 H, br t, *J* 8,

CH_2CH_2Si), 3.5 [2 H, s, $CH_2(CO_2)_2$], 4.3 (2 H, br t, *J* 8, CH_2CH_2Si), 5.3 (2 H, s, CH_2Ph) and 7.4 (5 H, s, Ph); *m/z* 294 (100%, M^+).

To a solution of benzyl 2-(trimethylsily)ethyl malonate (200 mg, 0.68 mmol) in tetrachloromethane (5 cm^3) was slowly added a solution of bromine (109 mg, 0.68 mmol) in tetrachloromethane (3 cm^3). The solution was stirred for 50 min, then evaporated, and the residue was dissolved in dichloromethane (20 cm^3), washed with 5% aq. sodium hydrogen carbonate (2 × 10 cm^3), dried (Na_2SO_4) and evaporated. PLC [eluent, hexane–methyl acetate (9:1)] gave benzyl 2-(trimethylsilyl)ethyl bromomalonate **55** as an oil (152 mg, 60%); δ_H(E; CD_2Cl_2) 0.1 (9 H, s, $SiMe_3$), 1.0 (2 H, br t, *J* 8, CH_2CH_2Si), 4.35 (2 H, br t, *J* 8, CH_2CH_2Si), 4.90 (1 H, s, CHBr), 5.3 (2 H, s, CH_2Ph) and 7.45 (5 H, s, Ph); *m/z* 374 and 372 (100 and 100%, M^+).

The thiolactam **54**[20] (78 mg, 0.168 mmol) was stirred in dichloromethane (5 cm^3) under argon with benzyl 2-(trimethylsilyl)ethyl bromomalonate **55** (69 mg, 0.185 mmol) and DBU (5 drops) for 65 min. Saturated aq. ammonium chloride (10 cm^3) and dichloromethane (10 cm^3) were added and the organic layer was separated, washed with water (5 cm^3), dried and evaporated. PLC [developer, ether–hexane (2:1)] afforded the thioimidate **57** as an oil (100 mg, 81%); λ_{max}/nm 250 and 360; ν_{max}/cm^{-1} 3300br, 1760 and 1700; δ_H(F) 0.01 (9 H, s, $SiMe_3$), 0.9 (2 H, br t, *J* 8, CH_2CH_2Si), 1.3 (6 H, m, 2 × Me), 1.55 (9 H, s, Bu^t), 2.6 (2 H, m, $CH_2CH_2CO_2$), 2.7 (2 H, s, CH_2CSN), 3.05 (2 H, m, $CH_2CH_2CO_2$), 3.6 (2 H, s, CH_2CO_2), 3.7 and 3.8 (each 3 H, s, OMe), 4.25 (2 H, m, CH_2CH_2Si), 5.25 (2 H, ABq, *J* 16, CH_2Ph), 5.6 (1 H, s, SCH), 5.7 (1 H, s, CH=CN), 7.3 (5 H, s, Ph) and 10.6 (1 H, br s, NH); *m/z* 756 (100%, M^+) and 724 (55, M − S).

The thioimidate **57** (100 mg, 0.132 mmol), triphenylphosphine (173 mg, 0.66 mmol) and DBU (10 drops) were heated at reflux in toluene (7 cm^3) under nitrogen for 1 h. After addition of acetic acid (0.5 cm^3), the solution was evaporated, and PLC on silica [developer, ether–hexane (2:1)] gave the enamine **59** as an oil (79 mg, 82.5%), which was a mixture of two isomers; they were not separated; λ_{max}/nm 276 and 318; ν_{max}/cm^{-1} 3300br, 1750 and 1650; δ_H(D; C_6D_6) (major isomer) −0.003 (9 H, s, $SiMe_3$), 0.91 (6 H, s, CMe_2), 0.8–1.1 (2 H, m, CH_2Si), 1.59 (9 H, s, Bu^t), 2.99 (2 H, s, $CH_2C{=}C$), 2.8–3.1 (4 H, m, $CH_2CH_2CO_2$), 3.35 and 3.40 (each 3 H, s, OMe), 3.54 (2 H, s, CH_2CO_2), 4.2–4.6 (2 H, m, CH_2CH_2Si), 5.26 (2 H, s, CH_2Ph), 5.35 (1 H, s, CH), 7.1–7.5 (5 H, m, Ph) and 8.8 and 11.3 (each 1 H, br s, NH); (minor isomer) − 0.022 (9 H, s, $SiMe_3$), 0.94 (6 H, s, CMe_2), 0.8–1.1 (2 H, m, CH_2Si), 1.58 (9 H, s, Bu^t), 3.05 (2 H, s, $CH_2C{=}C$), 2.8–3.1 (4 H, m, $CH_2CH_2CO_2$), 3.36 and 3.40 (each 3 H, s, OMe), 3.54 (2 H, s, CH_2CO_2), 4.2–4.6 (2 H, m, CH_2CH_2Si), 5.27 (2 H, s, CH_2Ph), 5.36 (1 H, s, CH), 7.1–7.5 (5 H, m, Ph) and 8.8 and 11.1 (each 1 H, br s, NH); *m/z* 724 (100%, M^+).

The trimethylsilylethyl ester **59** (33 mg, 0.045 mmol) was stirred in THF (10 cm^3) under argon at 50 °C for 17 h with tetrabutylammonium fluoride (1 mol dm^{-3} in THF; 0.5 cm^3) and the solution was then evaporated. The residue was dissolved in dichloromethane (10 cm^3) and the solution was washed successively with saturated aq. ammonium chloride (5 cm^3) and water (5 cm^3), dried and evaporated. PLC on silica [developer, acetone–hexane (3:7)] gave the *enamine* **61** as an oil (9.13 mg, 35%) (Found: M^+, 580.2797. $C_{32}H_{40}N_2O_8$ requires *M*, 580.2784); λ_{max}/nm 280 and 308; ν_{max}/cm^{-1} 3400br, 1720, 1710 and 1240; δ_H(E; CD_3COCD_3) 1.32 (6 H, s, CMe_2), 1.59 (9 H, s, Bu^t), 2.67 (2 H, s, $CH_2C{=}N$), 2.675 (2 H, m, $CH_2CH_2CO_2$), 2.97 (2 H, m, $CH_2CH_2CO_2$), 3.52 (2 H, s, CH_2CO_2), 3.62 and 3.66 (each 3 H, s, OMe), 4.84 (1 H, s, $C{=}CHCO_2$), 5.15 (2 H, s, CH_2Ph), 5.35 (1 H, s, CH=CN), 7.37 (5 H, s, Ph) and 9.9 and 10.1 (each 1 H, br s, NH); *m/z* 580 (100%, M^+), 524 (55, M − C_4H_8) and 416 (86, M − C_4H_8 − C_7H_8O).

Benzyl 13,17-*Bis*-(2-*methoxycarbonylethyl*)-12,18-*bis*(*methoxycarbonylmethyl*)-2,2,8,8-*tetramethylisobacteriochlorin*-5-*carboxylate* **65**.—See earlier for general directions for photochemical cyclisations. The enamine **60** (72.2 mg, 0.106 mmol) was stirred in dry TFA (3 cm^3) under argon for 2.5 h and then the TFA was evaporated off under a stream of argon. PLC [developer, ether–hexane (2:1)] afforded the α-free enamine **62** as an oil (30.8 mg, 60%); δ_H(D) 1.05 (6 H, s, CMe_2), 2.1 (2 H, s, $CH_2C{=}C$), 2.65 (2 H, t, *J* 8, $CH_2CH_2CO_2$), 3.0 (2 H, t, *J* 8, $CH_2CH_2CO_2$), 3.35 and 3.45 (each 3 H, s, OMe), 3.55 (2 H, s, CH_2CO_2), 5.0 (1 H, s, $C{=}CHCO_2$), 5.25 (2 H, s, CH_2Ph), 5.4 (1 H, s, CH=CN), 6.2 (1 H, d, *J* 3, α-H), 7.1–7.4 (5 H, m, Ph) and 10.1 (1 H, br s, NH); *m/z* 480 (60%, M^+), 442 (85) and 372 (100, M − $PhCH_2OH$). The same α-free enamine **62** was also obtained from the *tert*-butyl ester **61** under the same conditions.

To the α-free enamine **62** (30.8 mg, 0.064 mmol) under argon was added a solution of formyl imidate[7] **63** (25.4 mg, 0.066 mmol) in methanol (1.5 cm^3)–trimethyl orthoformate (0.4 cm^3), followed by TFA (0.4 cm^3). The solution was stirred for 10 min, then diluted with THF (20 cm^3), and neutralised with Hünig's base until the blue colour just turned purple. The resulting solution was sealed under vacuum and irradiated for 96 h. The residue obtained after evaporation was dissolved in dichloromethane (25 cm^3), and the solution was washed successively with 0.2 mol dm^{-3} hydrochloric acid (20 cm^3) and 5% aq. sodium hydrogen carbonate (20 cm^3), dried and evaporated. PLC [developer, dichloromethane–methyl acetate (9:1)] gave the *isobacteriochlorin* **65** as purple prisms (36.1 mg, 67.7% from **62**, 41.3% overall), m.p. 164.5–166 °C (from chloroform–hexane) (Found: C, 67.0; H, 6.5; N, 6.7. $C_{46}H_{52}N_4O_{10}$ requires C, 67.3; H, 6.4; N, 6.8%); λ_{max}/nm 589 ($\varepsilon_{max}/dm^3\ mol^{-1}\ cm^{-1}$ 34 400), 545 (20 100), 376 (101 600) and 275 (51 200); ν_{max}/cm^{-1} 1730 and 1600; δ_H(F; C_6D_6) 1.57 (12 H, s, 2 × CMe_2), 2.88 (4 H, t, *J* 8, 2 × $CH_2CH_2CO_2$), 3.62 (4 H, t, *J* 8, 2 × $CH_2CH_2CO_2$), 3.65 and 3.68 (each 6 H, s, 2 × OMe), 3.69 (4 H, s, 3 + 7-CH_2), 4.18 (4 H, s, 2 × CH_2CO_2), 5.48 (2 H, s, CH_2Ph), 7.19 (2 H, s, 10 + 20-H), 7.47 (5 H, m, Ph) and 8.30 (1 H, s, 15-H); *m/z* 820 (100%, M^+).

In earlier experiments, before the above procedure had been developed, the yield of isobacteriochlorins was lower and it was accompanied by a lower-R_f, deep blue band. This arose by adventitious hydrolysis of the imidate function of **64** to give the corresponding *seco-lactam*. (Found: MH^+, 839.3810. $C_{46}H_{55}N_4O_{11}$ requires *m/z* 839.3867); δ_H(F) 1.22 (6 H, s, 3-Me_2), 1.29 (6 H, s, 17-Me_2), 2.22 (2 H, s, 2-H_2), 2.57 (4 H, m, 2 × $CH_2CH_2CO_2$), 2.59 (2 H, s, 18-H_2), 2.94 and 2.96 (each 2 H, t, *J* 7, $CH_2CH_2CO_2$), 3.47 (4 H, s, 2 × CH_2CO_2), 3.52, 3.60, 3.61 and 3.62 (each 3 H, s, OMe), 4.75 (2 H, br s, OCH_2Ph), 4.82 (1 H, s, 20-H), 5.46 (1 H, s, 15-H), 5.50 (1 H, s, 5-H), 6.81 (1 H, s, 10-H) and 7.1–7.2 (5 H, m, Ph).

13,17-*Bis*-(2-*methoxycarbonylethyl*)-12,18-*bis*(*methoxycarbonylmethyl*)-2,2,8,8-*tetramethylisobacteriochlorin*-5-*carboxylic Acid* **66**.—The isobacteriochlorin **65** (2.45 mg) was dissolved in 5 mol dm^{-3} hydrogen bromide in acetic acid (2.0 cm^3) at 0 °C and the solution was allowed to warm to room temperature during 1 h and evaporated. PLC [developer, dichloromethane–methanol (9:1)] gave the isobacteriochlorin acid **66** as a purple solid (1.50 mg, 69%) (Found: M^+ − CO_2, 686.3321. $C_{38}H_{46}N_4O_8$ requires *m/z*, 686.3315); $\lambda_{max}(CH_2Cl_2)$/nm 376, 546 and 589; ν_{max}/cm^{-1} 3700–3200br, 1760 and 1600; $\delta_H(CD_2Cl_2)$ 1.67 (12 H, s, 2 × CMe_2), 2.91 (4 H, t, *J* 8, 2 × $CH_2CH_2CO_2$), 3.62 (4 H, t, *J* 8, 2 × $CH_2CH_2CO_2$), 3.68 and 3.76 (each 6 H, s, 2 × OMe), 3.97 (4 H, s, 3- + 7-CH_2), 4.22 (4 H, s, 2 × CH_2CO_2), 7.20 (2 H, s, 10- + 20-H) and 8.31 (1 H, s, 15-H); *m/z* 730 (30%, M^+) and 686 (100, M − CO_2).

13,17-*Bis*-(2-*methoxycarbonylethyl*)-12,18-*bis*(*methoxycar-*

bonylmethyl)-2,2,8,8-*tetramethylisobacteriochlorin* **67**.—The isobacteriochlorin acid **66** (1.35 mg) was dissolved in TFA (0.5 cm^3) and the solution was slowly evaporated to dryness. The residue was then heated to 140 °C under high vacuum (0.1 mmHg) for 20 min. The entire process was then repeated. PLC [developer, dichloromethane–methyl acetate (9:1)] gave the isobacteriochlorin **67** as a purple crystalline solid (0.79 mg, 62%), identical with an authentic sample;[7] δ_C(F; CD_2Cl_2) 21.3 (2 × $CH_2CH_2CO_2$), 30.3 (2 × CMe_2), 31.9 (2 × CH_2CO_2), 37.1 (2 × $CH_2CH_2CO_2$), 43.0 (2 × CMe_2), 50.8 (C-3 + -7), 51.07 and 52.47 (each 2 × OMe), 91.4 (C-5), 92.1 (C-10 + -20), 107.8 (C-15), 122.7, 137.0, 139.0, 160.5, 162.7 and 166.8 (12 × pyrrolic-C) and 171.3 and 172.0 (4 × CO_2).

tert-*Butyl* (E)-5-*Cyano*-8-(2-*methoxycarbonylethyl*)-7-*methoxycarbonylmethyl*-3,3-*dimethyl*-1-*thioxo*-1,2,3,10-*tetrahydrodipyrrin*-2-*carboxylate* **69**.—The *meso*-cyano lactam **68**[1] (127 mg, 0.267 mmol) and Lawesson's reagent[17] (59.7 mg, 0.147 mmol) were dissolved in toluene (30 cm^3), and the solution was heated at reflux under argon and stirred for 50 min. The solution was then evaporated and PLC [ether–hexane, (2:1)] gave the meso-*cyano thiolactam* **69** (121 mg, 92%) as an oil (Found: M^+, 489.1935. $C_{24}H_{31}N_3O_6S$ requires *M*, 489.1935); λ_{max}-(CH_2Cl_2)/nm 323 and 269; [+$Zn(OAc)_2$ in MeOH] 410 and 280; ν_{max}/cm^{-1} 2930, 2215, 1735 and 1630; δ_H(D) 1.58 (9 H, s, Bu^t), 1.62 (6 H, m, 2 × Me), 2.54 (2 H, m, $CH_2CH_2CO_2$), 2.95 (2 H, m, $CH_2CH_2CO_2$), 2.99 (2 H, s, CH_2C=S), 3.43 (2 H, s, CH_2CO_2), 3.67 and 3.75 (each 3 H, s, OMe) and 9.7 and 9.9 (each 1 H, br s, NH); *m/z* 489 (55%, M^+) and 433 (100, M − C_4H_8).

tert-*Butyl* (E)-1-[*Benzyloxycarbonyl*(tert-*butoxycarbonyl*)-*methylthio*]-5-*cyano*-8-(2-*methoxycarbonylethyl*)-7-*methoxycarbonylmethyl*-3,3-*dimethyl*-2,3-*dihydrodipyrrin*-9-*carboxylate* **70**.—A solution of benzyl hydrogen malonate (2.0 g, 10.3 mmol) and *tert*-butyl alcohol (10 cm^3) in THF (25 cm^3) was stirred with DCC (2.40 g) and 4-(dimethylamino)pyridine (200 mg) for 24 h, then filtered and evaporated. The residue was dissolved in ether (50 cm^3) and washed successively with 1 mol dm^{-3} hydrochloric acid (20 cm^3) and 5% aq. sodium hydrogen carbonate (20 cm^3), and the solution was dried and evaporated to give benzyl *tert*-butyl malonate as an oil (2.11 g, 82%) (Found: $M^+ - C_4H_8$, 194.0587. $C_{10}H_{10}O_4$ requires *m/z*, 194.0579); λ_{max}/nm 217; ν_{max}/cm^{-1} 1735 and 1720; δ_H(A) 1.55 (9 H, s, Bu^t), 3.35 [2 H, s, $CH_2(CO_2)_2$], 5.20 (2 H, s, CH_2Ph) and 7.35 (5 H, s, Ph); *m/z* 250 (2%, M^+) and 194 (100, M − C_4H_8).

To a stirred solution of benzyl *tert*-butyl malonate (700 mg, 2.8 mmol) in tetrachloromethane (60 cm^3) was slowly added a solution of bromine (448 mg, 2.8 mmol) in tetrachloromethane (10 cm^3). The mixture was evaporated, the residue was dissolved in ether (30 cm^3) and the solution was washed with 5% aq. sodium hydrogen carbonate (2 × 10 cm^3), dried and evaporated to give benzyl *tert*-butyl bromomalonate **56** as an oil (720 mg, 78%), which was chromatographed [eluent, hexane–methyl acetate (4:1)] immediately prior to use in subsequent steps; λ_{max}/nm 210; ν_{max}/cm^{-1} 1750 and 1740; δ_H(A) 1.45 (9 H, s, Bu^t), 4.65 (1 H, s, CHBr), 5.15 (2 H, s, CH_2Ph) and 7.25 (5 H, s, Ph); *m/z* 330 and 328 (1%, M^+), 315 and 313 (4, M − Me), 273 and 271 (M − C_4H_9), 249 (20, M − Br) and 193 (100, M − Br − C_4H_8).

The *meso*-cyano thiolactam **69** (121 mg, 0.247 mmol), sodium hydride (50% suspension in mineral oil; 11.4 mg, 0.248 mmol) and THF (20 cm^3) were stirred at room temperature under argon for 10 min and then a solution of benzyl *tert*-butyl bromomalonate **56** (82.3 mg, 0.25 mmol) in THF (5 cm^3) was added. The mixture was stirred for a further 10 min, filtered and evaporated. PLC [developer, dichloromethane–methyl acetate (19:1)] gave the *thioimidate* **70** as an oil (128 mg, 70%) (Found: M^+, 737.2974. $C_{38}H_{47}N_3O_{10}S$ requires *M*, 737.2981); λ_{max}/nm 265 and 372; ν_{max}/cm^{-1} 3400br, 2200, 1760, 1700 and 1600; δ_H(D; CD_2Cl_2) 1.33 (9 H, s, Bu^t), 1.51 (6 H, s, CMe_2), 1.525 (9 H, s, Bu^t), 2.55 (2 H, m, $CH_2CH_2CO_2$), 2.91 (2 H, s, CH_2CS), 2.95 (2 H, m, $CH_2CH_2CO_2$), 3.63 and 3.68 (each 3 H, s, OMe), 3.85 (2 H, s, CH_2CO_2), 5.19 (2 H, ABq, *J* 14, CH_2Ph), 5.48 (1 H, s, SCH), 7.3 (5 H, s, Ph) and 11.1 (1 H, br s, NH); *m/z* 737 (2%, M^+), 705 (4, M − S), 605 (55) and 549 (100).

tert-*Butyl* (1E,4E)- *and* (1Z,4E)-1-[*Benzyloxycarbonyl*(*tert-butoxycarbonyl*)*methylene*]-5-*cyano*-8-(2-*methoxycarbonylethyl*)-7-*methoxycarbonylmethyl*-3,3-*dimethyl*-1,2,3,10-*tetrahydrodipyrrin*-9-*carboxylate* **71**.—The *meso*-cyano thioimidate **70** (100 mg, 0.136 mmol), triphenylphosphine (142 mg) and DBU (4 drops) were heated at reflux in toluene (25 cm^3) under argon for 30 min and the mixture was then evaporated. Chromatography on silica [30 g; eluent, dichloromethane–hexane (1:1; 150 cm^3), gradually changing to dichloromethane–methyl acetate (19:1)] gave the meso-*cyano enamine* **71** as an oil (62 mg, 65%) (Found: M^+, 705.3262. $C_{38}H_{47}N_3O_{10}$ requires *M*, 705.3261); λ_{max}/nm 276 and 329; [+$Zn(OAc)_2$] 301 and 429; ν_{max}/cm^{-1} 3400br, 2170, 1760, 1700 and 1600; δ_H(F; CD_2Cl_2) (major isomer) 1.40 and 1.56 (each 9 H, s, Bu^t), 1.56 (6 H, s, CMe_2), 2.56 (2 H, m, $CH_2CH_2CO_2$), 3.0 (2 H, m, $CH_2CH_2CO_2$), 3.11 (2 H, s, CH_2CN), 3.41 (2 H, s, CH_2CO_2), 3.61 and 3.66 (each 3 H, s, OMe), 5.14 (2 H, s, CH_2Ph), 7.33 (5 H, br s, Ph) and 8.97 and 10.4 (each 1 H, br s, NH); (minor isomer) 1.33 (9 H, s, Bu^t), 1.54 (6 H, s, CMe_2), 1.57 (9 H, s, Bu^t), 2.56 (2 H, m, $CH_2CH_2CO_2$), 3.0 (2 H, m, $CH_2CH_2CO_2$), 3.09 (2 H, s, CH_2CN), 3.42 (2 H, s, CH_2CO_2), 3.60 and 3.64 (each 3 H, s, OMe), 5.17 (2 H, s, CH_2Ph), 7.33 (5 H, br s, Ph) and 8.97 and 10.4 (each 1 H, br s, NH); *m/z* 705 (22%, M^+), 592 (36) and 442 (100).

Benzyl 10-*Cyano*-13,17-*bis*-(2-*methoxycarbonylethyl*)-12,18-*bis*(*methoxycarbonylmethyl*)-2,2,8,8-*tetramethylisobacteriochlorin*-5-*carboxylate* **74**.—See earlier for general directions for photochemical cyclisations. The *meso*-cyano enamine **71** (49.0 mg, 0.069 mmol) was cooled to 0 °C under argon and TFA (1.0 cm^3) was added. The solution was stirred for 10 min and then evaporated, first under a stream of argon and then under high vacuum, to give the diacid **72** as an oil; δ_H(D) 1.56 (6 H, s, CMe_2), 2.55 (2 H, m, $CH_2CH_2CO_2$), 3.0 (2 H, m, $CH_2CH_2CO_2$), 3.23 (2 H, s, CH_2CN), 3.65 (2 H, s, CH_2CO_2), 3.68 and 3.71 (each 3 H, s, OMe), 5.33 (2 H, s, CH_2Ph), 7.40 (5 H, m, Ph), 8.7–9.7 (2 H, br s, 2 × CO_2H) and 10.4 and 12.1 (each 1 H, br s, NH).

The diacid and PTSA (53 mg, 0.28 mmol) were stirred and heated at reflux in dichloromethane (6 cm^3) for 20 h and the mixture was then evaporated. PLC [developer, ether–hexane (1:1)] afforded the unstable α-free enamine **73** as an oil (9.2 mg, 26%), which appeared from its ^1H NMR spectrum to be a mixture of isomers at C-5′; δ_H (D) (major isomer) 1.54 (6 H, s, CMe_2), 2.4–2.7 (4 H, m, $CH_2CH_2CO_2$), 3.41 (2 H, s, CH_2C=C), 3.58 and 3.66 (each 3 H, s, OMe), 3.73 (2 H, s, CH_2CO_2), 4.65 (1 H, s, C=CH), 5.4 (2 H, s, CH_2Ph), 6.65 (1 H, d, *J* 4, α-CH), 7.3 (5 H, m, Ph) and 8.0 and 9.6 (each 1 H, br s, NH); *m/z* 505 (100%, M^+).

To the α-free enamine **73** (9.2 mg, 0.018 mmol) under argon was added a solution of formyl imidate[7] **63** (8 mg, 0.02 mmol) in methanol (0.8 cm^3)–trimethyl orthoformate (0.15 cm^3). TFA (0.1 cm^3) was then added and the solution was stirred for 20 min, then diluted with THF (20 cm^3) and neutralised with Hünig's base. More THF (15 cm^3) was added and the solution was degassed, sealed under vacuum, irradiated for 100 h and then evaporated. The residue was dissolved in dichloromethane (25 cm^3), and the solution was washed successively with 0.2 mol dm^{-3} hydrochloric acid (15 cm^3) and

5% aq. sodium hydrogen carbonate (15 cm^3), dried and evaporated. PLC [developer, dichloromethane–methyl acetate (4:1)] afforded the *isobacteriochlorin* **74** as a purple oil (4.51 mg, 34%) (Found: M^+, 845.3613. $C_{47}H_{51}N_5O_{10}$ requires *M*, 845.3635); λ_{max}/nm (protonated) 380, 409, 580 and 628; ν_{max}/cm^{-1} 2230, 1730 and 1600; δ_H(F; CD_2Cl_2) 1.65 and 1.89 (each 6 H, s, CMe_2), 2.88 (4 H, t, *J* 8, 2 × $CH_2CH_2CO_2$), 2.96 (4 H, t, *J* 8, 2 × $CH_2CH_2CO_2$), 3.65 (6 H, s, 2 × OMe), 3.70 and 3.74 (each 2 H, s, 3-CH_2 and 7-CH_2), 3.72 and 3.80 (each 3 H, s, OMe), 4.32 and 4.64 (each 2 H, s, CH_2CO_2), 5.56 (2 H, s, CH_2Ph), 7.43 (1 H, s, 20-H), 7.44–7.48 (5 H, m, Ph) and 8.72 (1 H, s, 15-H); *m/z* 845 (100%, M^+).

Acknowledgements

Grateful acknowledgement is made to the SERC for Studentships (to M. H. B. and P. J. H) and to the SERC and Roche Products Ltd. for financial support. We also thank Professor D. H. R. Barton for a valuable gift of material and Mr. C. Sporikou for large-scale synthesis of the starting pyrrole.

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Paper 2/02005J
Received 16*th April* 1992
Accepted 18*th May* 1992