Pyrroles and Related Compounds. Part XXIX.[1] Vinylporphyrin β-Keto-esters

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The first total synthesis of 2,4-divinylrhodoporphyrin-XV dimethyl ester (2c) (*via* the *b*-oxobilane route) is reported. General methods for the synthesis of porphyrin β-keto-esters (1) from various rhodoporphyrins by way of the corresponding mixed anhydrides or imidazolides are presented. These are shown to be more efficient than the previous approach *via* porphyrin acid chlorides and sodiomalonic esters. The synthesis and properties of the β-keto-esters from 2-vinyl- and 2,4-divinyl-rhodoporphyrin-XV dimethyl esters are reported; such compounds may be of significance in chlorophyll biosynthesis.

In Part XXVIII [1] we described the synthesis of the β-keto-ester (1a) from rhodoporphyrin-XV dimethyl ester (2a). However, this keto-ester (1a) cannot be of any significance in chlorophyll biosynthesis since it lacks the 2-vinyl substituent ultimately present in the chlorophylls (3). The stage at which the 4-vinyl substituent of the precursor, protoporphyrin-IX (4), is reduced to ethyl is not yet clearly established [2] and hence both the 2-vinyl- and 2,4-divinyl-keto-esters (1b and c) are possible precursors of the plant chlorophylls (3). We have already reported the total synthesis [3] of 2-vinylrhodoporphyrin-XV dimethyl ester (2b) as well as the more efficient preparation of this compound by degradation of phaeophytin-*a*.[4] This paper describes the first total synthesis of 2,4-divinylrhodoporphyrin-XV dimethyl ester (2c) and improved methods for the conversion of the porphyrins (2) into the corresponding β-keto-esters (1).

We began with the synthesis of the divinylporphyrin (2c), and chose the *b*-oxobilane route, with vinyl group generation from 2-chloroethyl substituents because the appropriate pyrrolic intermediates were largely available from work described in earlier parts of this series.

The ethoxycarbonylmethylpyrrole (5a) was treated with 3·3 equiv. of sulphuryl chloride in carbon tetrachloride, and gave the fully characterised trichloromethylpyrrole (5b); hydrolysis with sodium acetate solution then provided the pyrrolecarboxylic acid (5c) in 57% yield from (5a). If the hydrolysis step was not carried out at high dilution, appreciable amounts of the sparingly soluble pyrrocoll (6) were obtained. The carboxylic acid was converted into the t-butyl ester (5d) with isobutene and a trace of mineral acid (82%) or else *via* the crystalline acid chloride (5e) by treatment with t-butyl alcohol and *NN*-dimethyl-

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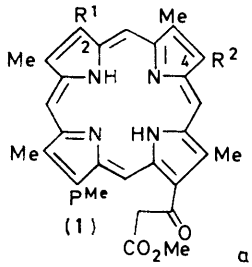
[1] Part XXVIII, M. T. Cox, T. T. Howarth, A. H. Jackson, and G. W. Kenner, preceding paper.

[2] *E.g.*, B. F. Burnham, in 'Metabolic Ptahways,' vol. III, 3rd edn., ed. D. M. Greenberg, Academic Press, New York, 1969, p. 450.

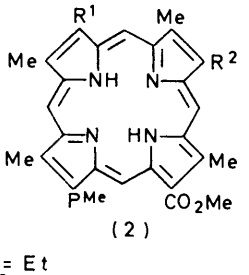
[3] T. T. Howarth, A. H. Jackson, and G. W. Kenner, *J.C.S. Perkin I*, 1974, 502.

[4] G. W. Kenner, S. W. McCombie, and K. M. Smith, *J.C.S. Perkin I*, 1973, 2517.

aniline (50—65%). Elaboration of the benzyl ester function in (5d) was accomplished by hydrogenation over palladised charcoal, to give the carboxylic acid (7a), which was iodinated, and the resultant iodopyrrole (7b) was transformed into the required 2-unsubstituted analogue (7c) by catalytic hydrogenation over Adams catalyst. Coupling with the 2-acetoxymethylpyrrole (5f) [obtained from (5a) with lead tetraacetate] under MacDonald's conditions [5] gave a 62% yield of the pyrromethane (8), which was fully characterised in the usual ways. When the pyrromethane was reduced 'externally' with diborane in tetrahydrofuran on a 2 g scale, the main product (46%) was the required bis-(2-hydroxyethyl)pyrromethane (9a). A minor product (27%) * was identified as the pyrrole



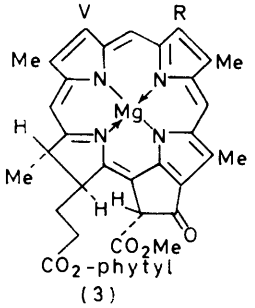
(1)



(2)

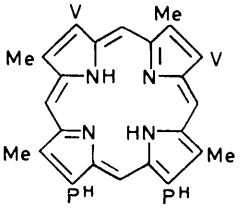
a; R^1 = R^2 = Et
b; R^1 = V, R^2 = Et
c; R^1 = R^2 = V

P^R = $CH_2 \cdot CH_2 \cdot CO_2R$
V = CH:CH_2



(3)

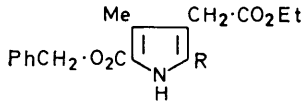
a; R = Me
b; R = CHO



(4)

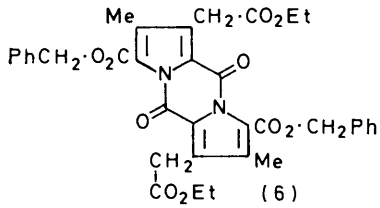
(10a) by both mass spectrometry and conversion into the known pyrrole (10b) with acetic anhydride in pyridine. However, when the reaction was scaled up four-fold, the product distribution was reversed to 18% of (9a) and 70% of (10a). The bis-(2-hydroxyethyl)-pyrromethane was acetylated under the normal conditions to give (9b), which could not be induced to crystallise, but was nonetheless fully characterised by n.m.r. and elemental analysis and shown to be pure by t.l.c. Since insufficient material was available by this route, an alternative approach to (9b) was sought.

The pyrrole (5d) could be reduced with diborane to the hydroxyethylpyrrole (11a) in 91% yield on the 4 g scale. Again, erratic results were obtained when the reaction was scaled up. On the 35 g scale, the product

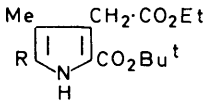


(5)

a; R = Me d; R = CO_2Bu^t
b; R = CCl_3 e; R = COCl
c; R = CO_2H f; R = CH_2OAc

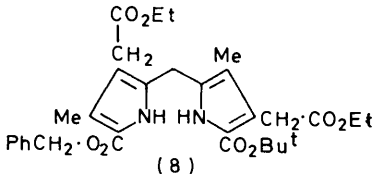


(6)



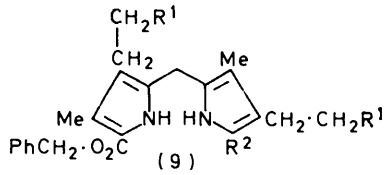
(7)

a; R = HO_2C
b; R = I
c; R = H



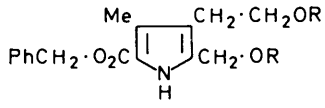
(8)

obtained after chromatography (13·7 g) was an inseparable mixture of the required pyrrole (11a) and the 'over-reduced' pyrrole (12a). Acetylation produced an inseparable mixture of (11b) and (12b), and after hydrogenolysis, the pyrrole acid (11c) was separated from (12b) by base extraction. The pyrrole (12b) so obtained was then trichlorinated and hydrolysed to give the same acid (11c) in 52% yield. Finally, the



(9)

a; R^1 = OH, R^2 = CO_2Bu^t
b; R^1 = OAc, R^2 = CO_2Bu^t
c; R^1 = OAc, R^2 = H



(10)

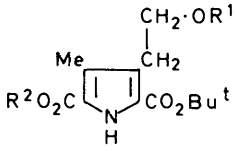
a; R = H
b; R = Ac

pyrrole was converted into the 2-unsubstituted analogue (13b) *via* (13a) in the usual way. Coupling with the acetoxymethylpyrrole (10b) in acetic acid containing sodium acetate [5] gave a 70% yield of the required

* This by-product probably arises by Lewis-acid-catalysed cleavage of the pyrromethane, perhaps assisted by neighbouring group participation by the carbonyl function of the acetate side-chain to form an intermediate lactone which then undergoes reduction with diborane to give (10a).

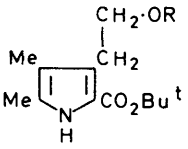
[5] E. J. Tarlton, S. F. MacDonald, and E. Baltazzi, *J. Amer. Chem. Soc.*, 1960, **82**, 4389.

pyrromethane (9b), identical with the sample prepared previously.



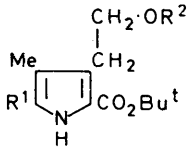
(11)

a; R^1 = H, R^2 = $PhCH_2$
b; R^1 = Ac, R^2 = $PhCH_2$
c; R^1 = Ac, R^2 = H



(12)

a; R = H
b; R = Ac



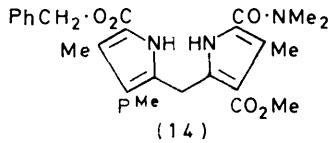
(13)

a; R^1 = I, R^2 = Ac
b; R^1 = H, R^2 = Ac
c; R^1 = R^2 = H

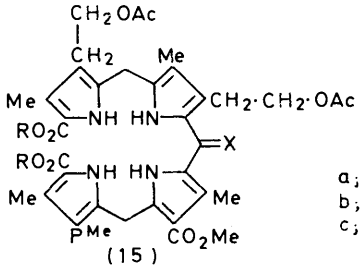
Alternatively, the pyrrole (7c) could be reduced with diborane to give a high yield of the (2-hydroxyethyl)-pyrrole (13c), which was then acetylated to give (13b), from which the required pyrromethane could be prepared as described.

Treatment of (9b) with trifluoroacetic acid, followed by a basic work-up, gave the 5-unsubstituted pyrromethane (9c), which was coupled with the phosphoryl chloride complex of the pyrromethane amide (14) to give the imine salt (15a); after chromatographic purification and hydrolysis, the *b*-oxobilane (15b) was obtained in 39% yield. The 1′,8′-dicarboxylic acid (15c) was isolated after catalytic hydrogenation, and cyclisation with trimethyl orthoformate and trichloroacetic acid in methylene chloride, followed by treatment of the crude product with acetic anhydride in pyridine gave the required triacetoxyporphyrin (16a) in 15% yield from pyrromethanes. The triacetoxyporphyrin was the sole porphyrinic product from the cyclisation, and hydrogenation proceeded *via* a blue-green phlorin, as noted in the rhodoporphyrin-XV case.[3] Reoxidation of the colourless porphyrinogen solution with air in tetrahydrofuran–pyridine during 3 days gave a mixture of two porphyrins which were separated chromatographically. The required porphyrin (16b) was obtained in 76% yield, and the minor product (4%) was shown (t.l.c.) to be a mono-acetoxyethyl-mono-hydroxyethyl derivative. Both compounds gave the bis-(2-hydroxyethyl)porphyrin (16c) when treated with sulphuric acid in methanol. Treatment of (16c) with thionyl chloride in dimethylformamide and chloroform in the presence of anhydrous potassium carbonate gave an 83% yield of the bis-(2-chloroethyl)porphyrin (16d). Treatment of the corresponding zinc chelate with a 1M-solution of potassium t-butoxide in t-butyl alcohol accomplished vinylation, and selective re-esterification[1] of the diacid gave a 47% yield of the required 2,4-divinylrhodoporphyrin-XV 7-methyl ester (17c). A further 10% of 2,4-divinylrhodoporphyrin-XV dimethyl ester (2c) was obtained by treatment of the recrystallisation mother-liquors with diazomethane, followed by chromatography.

The analogous 7-methyl ester (17b) of 2-vinylrhodoporphyrin-XV was likewise prepared by selective esterification of the corresponding diacid, and both compounds (17b) and (17c) were transformed into the β-keto-esters, (1b and c), respectively, following the procedure described in Part XXVIII[1] [*i.e.* treatment of the appropriate acid chloride (18) with methyl t-butyl sodiomalonate, giving (19), followed by treatment with trifluoroacetic acid]. Though an acceptable overall yield (47%) of the 2-vinyl-β-keto-ester (1b) was obtained in this way, the yield (9·6%) in the divinyl series was disappointing. Moreover, the reaction sequence required the use of a large excess of sodiomalonate, and this was incompatible with our desire

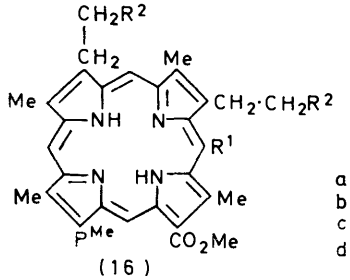


(14)



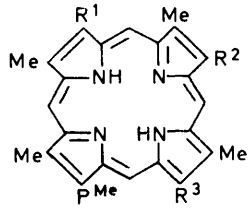
(15)

a; X = $\overset{+}{N}Me_2$, R = $PhCH_2$
b; X = O, R = $PhCH_2$
c; X = O, R = H



(16)

a; R^1 = R^2 = OAc
b; R^1 = H, R^2 = OAc
c; R^1 = H, R^2 = OH
d; R^1 = H, R^2 = Cl



(17) R^3 = CO_2H
(18) R^3 = COCl
(19) R^3 = $CO{\cdot}CH(CO_2Me)(CO_2Bu^t)$
(20) R^3 = $CO_2{\cdot}COBu^t$
(21) R^3 = $CO_2{\cdot}CO_2Et$
(22) R^3 = $CO{\cdot}N{\cdot}CH{:}CH{\cdot}N{:}CH$

a; R^1 = R^2 = Et
b; R^1 = V, R^2 = Et
c; R^1 = R^2 = V

to incorporate a ^{14}C label into the molecule by using labelled malonate. We therefore investigated other, more efficient methods for β-keto-ester construction.

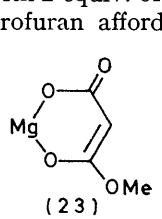
Our first concern was to prepare an alternative to

the porphyrin acid chloride (18) which was usually used as the dication directly from the oxalyl chloride reaction; in this way, 2 equiv. of sodiomalonate were consumed merely by quenching the dication. Attempts to obtain the acid chloride as its crystalline free base were unsuccessful. We were thus only able to reduce the quantity of sodiomalonate to 4 equiv. [without significantly reducing the yield of the keto-diester (19)], but in order to reduce the requirement still further, an alternative activated derivative was sought.

Reaction of (17a) with an excess of trimethylacetyl chloride in the presence of pyridine or *NN*-di-isopropylethylamine afforded a good yield of the crystalline mixed anhydride (20a), and this reacted satisfactorily with 1 equiv. of methyl t-butyl sodiomalonate in the presence of an additional 1 equiv. of sodium hydride. After treatment with trifluoroacetic acid, the β-keto-ester (1a) was obtained in 43% yield. A similar sequence afforded the 2-vinyl-β-keto-ester *via* the readily characterised mixed anhydride (20b). Alternatively, reaction of (17a) in pyridine with ethyl chloroformate gave the mixed anhydride (21a), which also reacted well with sodiomalonate, but this sequence was not investigated further on account of the poor solubility of the anhydride (21a) as compared with the pivalic anhydride (20a).

Carboximidazolides [6] are of considerable utility as acylating agents, and the porphyrin derivative (22a) was readily obtained from the acid (17a) and *NN'*-carbonyldi-imidazole in refluxing tetrahydrofuran. However, on reaction with several equivalents of t-butyl methyl sodiomalonate, deprotonation of the macrocycle to the green dianion occurred, and the desired nucleophilic displacement was not apparent. This difficulty was overcome by conversion of (22a) into the zinc chelate (zinc acetate in methanol) prior to reaction with the sodiomalonate; the overall yield of β-keto-ester (1a) was, however, lower than that obtained *via* the mixed anhydrides (20a) and (21a).

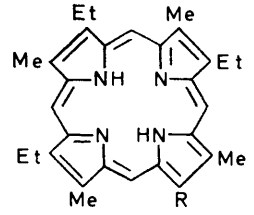
The highest yields of β-keto-ester were obtained by the method of Bram and Vilkas; [7] treatment of methyl hydrogen malonate with 2 equiv. of isopropylmagnesium bromide in tetrahydrofuran afforded the chelate (23),



(23)

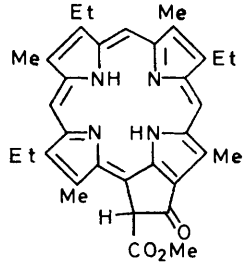
and reaction with the imidazolide (22a) gave the keto-ester (1a) in 80% yield. Similarly, in the 2-vinyl series, the acid (17b) was converted *via* the imidazolide (22b) into the keto-ester (1b) in 70% overall yield. The superiority of this route was particularly marked in the 2,4-divinyl series, which had afforded less than 10% of the keto-ester (1c) by the acid chloride–sodiomalonate route; conversion of the acid (17c) into the imidazolide (22c) and reaction with (23) gave the required β-keto-ester (1c) in an overall yield of 49% from (17c) [or 71% from (22c)].

In connection with model experiments on the conversion of phaeoporphyrins into phaeophorbides, we required quantities of a model phaeoporphyrin. We selected compound (25) for this purpose on account of the availability of the requisite porphyrin carboxylic acid (24a),[8] which was transformed into the imidazolide (24b) and then into the β-keto-ester (24c) (74%). The cyclisation of this and other β-keto-esters into phaeoporphyrins is described in the following paper.[9]



(24)

a; R = CO_2H
b; R = CO·N·CH:CH·N:CH
c; R = $CO·CH_2·CO_2Me$



(25)

EXPERIMENTAL

M.p.s were measured on a microscope hot-stage apparatus. Neutral alumina (Woelm) was used for chromatographic separations, and reactions were followed by t.l.c. and spectrophotometry as described in earlier parts of this series. Visible absorption spectra were measured with a Unicam SP 800 spectrophotometer, ^1H n.m.r. spectra (solutions in deuteriochloroform with tetramethylsilane as internal standard) with a Varian A-60 or HA-100 spectrometer, and mass spectra with an A.E.I. MS9 instrument (at 50 μA and 70 eV, with direct inlet and source temperature between 200 and 220°).

Pyrroles

Benzyl 4-Ethoxycarbonylmethyl-3-methyl-5-trichloromethylpyrrole-2-carboxylate (5b).—Benzyl 4-ethoxycarbonylmethyl-3,5-dimethylpyrrole-2-carboxylate [10] (6·2 g) in dry carbon tetrachloride (100 ml) was stirred at room temperature during the dropwise addition of sulphuryl chloride (5·4 ml, 3·3 equiv.) in carbon tetrachloride (20 ml). After 2 h at room temperature the mixture was warmed to 45—50° and more sulphuryl chloride (2·0 ml) was added. Stirring was continued for a further 4 h at 50° before the solution was decanted from a trace of dark, oily material, and evaporated to dryness. The residual pale brown oil solidified on trituration with ether–petroleum (b.p. 60—80°). Recrystallisation from ether–n-hexane afforded the *trichloromethylpyrrole* (6·2 g, 74%) as pale pink prisms, m.p. 78—80° (Found: C, 51·6; H, 4·3; N, 3·5. $C_{18}H_{18}Cl_3NO_4$ requires C, 51·6; H, 4·3; N, 3·35%), τ 0·70 (NH),

[6] H. A. Staab and W. Rohr, ' Newer Methods of Preparative Organic Chemistry,' vol. V, ed. W. Foerst, Verlag Chemie–Academic Press, Weinheim and New York, 1969, p. 61.
[7] G. Bram and M. Vilkas, *Bull. Soc. chim. France*, 1964, 945.
[8] R. V. H. Jones, G. W. Kenner, and K. M. Smith, *J.C.S. Perkin I*, 1974, 53.
[9] G. W. Kenner, S. W. McCombie, and K. M. Smith, following paper.
[10] A. H. Jackson, G. W. Kenner, and J. Wass, *J.C.S. Perkin I*, 1974, 480.

2·70 and 4·72 ($PhCH_2$), 6·25 (s), 5·90 (q), and 8·81 (t) (CH_2·CO_2·CH_2·CH_3), and 7·76 (Me).

2-Benzyloxycarbonyl-4-ethoxycarbonylmethyl-3-methylpyrrole-5-carboxylic Acid (5c).—Benzyl 4-ethoxycarbonylmethyl-3,5-dimethylpyrrole-2-carboxylate (20·0 g) in carbon tetrachloride (350 ml) at 45—55° was stirred during the dropwise addition of sulphuryl chloride (17·5 ml). After a total of 4·5 h, the solution was evaporated *in vacuo*, and the residue was heated under reflux with a solution of sodium acetate (65 g) in water (400 ml) and dioxan (400 ml) during 2 h. After cooling, the solution was added to water; the mixture was acidified with concentrated hydrochloric acid (20 ml) and then extracted with ether (2 × 500 ml). The extracts were washed with water (1 l) and then extracted with sodium carbonate solution (5% w/v; 2 × 200 ml). The carbonate extracts were treated during 1 h with a gentle stream of air, and were then saturated with sulphur dioxide gas. The product was filtered off, washed with water, and recrystallised from aqueous methanol, giving the *pyrrolecarboxylic acid* (12·5 g, 57%) as cream needles, m.p. 131—132° (Found: C, 62·5; H, 5·3; N, 4·0. $C_{18}H_{19}NO_6$ requires C, 62·6; H, 5·55; N, 4·1%), τ −0·27 (CO_2H), 0·19br (NH), 2·61 and 4·63 ($PhCH_2$), 5·83 (q) and 8·76 (t) (OEt), 6·17 (CH_2) and 7·72 (Me).

The ethereal layer from the preparation was dried ($MgSO_4$) and evaporated; trituration of the residue with ether gave a pale yellow crystalline compound, and recrystallisation from methylene chloride–n-hexane gave the *pyrrocoll* (6) (2·8 g, 13·5%) as long fibrous needles, m.p. 195—196° (Found: C, 65·9; H, 5·3; N, 4·5. $C_{36}H_{34}N_2O_{10}$ requires C, 66·0; H, 5·2; N, 4·3%), τ 2·70 and 4·68 ($2PhCH_2$), 6·12 (s), 5·90 (q), and 8·82 (t) ($2CH_2$·CO_2·CH_2·CH_3), and 8·01 (2Me).

It was subsequently found that the yield of carboxylic acid (5c) could be increased to 75% (at the expense of the pyrrocoll) by carrying out the hydrolysis at double dilution.

2-Benzyloxycarbonyl-4-ethoxycarbonylmethyl-3-methylpyrrole-5-carbonyl Chloride (5e).—The carboxylic acid (5c) (16·3 g) was warmed with thionyl chloride (3 ml) at 40—45° during 90 min. Dry benzene (20 ml) was added and the solvents were evaporated off *in vacuo*. Addition and evaporation of dry benzene (50 ml) and light petroleum (b.p. 60—80°) (50 ml) caused the *acid chloride* (16·5 g, 96%) to crystallise. Recrystallisation from methylene chloride–light petroleum (b.p. 60—80°) gave pale yellow prisms, m.p. 90—92° (Found: C, 59·4; H, 4·8; N, 3·85. $C_{18}H_{18}ClNO_5$ requires C, 59·4; H, 5·0; N, 3·85%), τ 0·26br (NH), 2·61 and 4·66 ($PhCH_2$), 6·23 (s), 5·88 (q), and 8·77 (t) (CH_2·CO_2·CH_2·CH_3), and 6·74 (Me).

Benzyl 4-Ethoxycarbonylmethyl-3-methyl-5-t-butoxycarbonylpyrrole-2-carboxylate (5d).—(*a*) The foregoing carbonyl chloride (15·0 g) in dry t-butyl alcohol (22 ml) and freshly distilled *NN*-dimethylaniline (12 ml) was heated at 90° during 4 h and then cooled overnight. Ether (75 ml) was added with stirring, and the ethereal solution was washed with 6N-sulphuric acid [total of 200 ml, which was re-extracted with ether (30 ml)], 10% sodium carbonate solution (50 ml), and finally water (150 ml). Drying ($MgSO_4$) and evaporation left a semi-crystalline residue which was chromatographed on alumina (grade III), with light petroleum (b.p. 60—80°) containing increasing proportions of benzene as eluant. Evaporation of the appropriate eluates (t.l.c.) gave the *pyrrole t-butyl ester* (10·7 g, 68%). A sublimed sample had m.p. 64—65° (Found: C, 65·9; H, 6·5; N, 3·7. $C_{22}H_{27}NO_6$ requires C, 65·8; H, 6·8; N, 3·5%), τ 0·51br (NH), 2·61 and 4·63 ($PhCH_2$), 6·20 (s), 5·83 (q), and 8·76 (t) (CH_2·CO_2·CH_2·CH_3), 7·73 (Me), and 8·44 (Bu^t).

(*b*) 2-Benzyloxycarbonyl-4-ethoxycarbonylmethyl-3-methylpyrrole-5-carboxylic acid (10·0 g) was suspended in chloroform (200 ml) and cooled in an ice-bath. Isobutene (100 ml) and concentrated sulphuric acid (1·5 ml) were added and the mixture was stirred at room temperature overnight in a flask equipped with a pressure relief valve. The stopper was removed and stirring was continued for 40 min before aqueous 7% sodium hydrogen carbonate (100 ml) was added, stirring then being continued for 1 h. The organic layer was dried ($MgSO_4$) and evaporated *in vacuo* to give a brown oil which gave crystals (9·6 g, 82%) from light petroleum (b.p. 60—80°) identical with the material from (*a*).

Benzyl 4-(2-Hydroxyethyl)-3-methyl-5-t-butoxycarbonylpyrrole-2-carboxylate (11a),—The foregoing pyrrole (4·0 g) in tetrahydrofuran (100 ml) was treated during 1 h with diborane generated externally from the dropwise addition of boron trifluoride–ether complex (30 ml) to sodium borohydride (5·7 g) in bis-(2-methoxyethyl) ether (50 ml).* The products of two identical reactions of this scale were combined at this stage, and next day methanol was added cautiously until effervesence ceased. Evaporation *in vacuo* gave an oil which slowly crystallised (6·5 g, 91%). A sublimed sample had m.p. 85—87° (Found: C, 66·8; H, 6·8; N, 3·9. $C_{20}H_{25}NO_5$ requires C, 66·8; H, 7·0; N, 3·9%), τ 0·40br (NH), 2·62 and 4·69 ($PhCH_2$), 6·98 (t) and 6·23 (t) (CH_2·CH_2O), 7·49br (OH), and 8·46 (Bu^t). When the experiment was carried out with 35 g of starting pyrrole, the product (13·7 g) obtained was a mixture of the required hydroxyethylpyrrole and t-butyl 3-(2-hydroxyethyl)-4,5-dimethylpyrrole-2-carboxylate, as indicated by n.m.r. spectroscopy. The two pyrroles proved inseparable at this stage, but could be separated after acetylation and hydrogenation (see later).

Benzyl 4-(2-Acetoxyethyl)-3-methyl-5-t-butoxycarbonylpyrrole-2-carboxylate (11b).—The foregoing (2-hydroxyethyl)-pyrrole (6·5 g) in pyridine (32 ml) and acetic anhydride (6·1 ml) was kept at room temperature for 90 min, before dropwise addition to stirred water (1 l). The solution was extracted with ether, and the extract was dried ($MgSO_4$) and evaporated *in vacuo* to give an oil which slowly crystallised (5·6 g, 77%). A sublimed portion had m.p. 54—56° (Found: C, 66·0; H, 6·6; N, 3·65. $C_{22}H_{27}NO_6$ requires C, 65·8; H, 6·8; N, 3·5%), τ 0·53br (NH), 2·62 and 4·66 ($PhCH_2$), 6·93 (t), 5·80 (t), and 8·00 (s) (CH_2·CH_2·OCOMe), 7·69 (Me), and 8·43 (Bu^t).

3-(2-Acetoxyethyl)-4-methyl-2-t-butoxycarbonylpyrrole-5-carboxylic Acid (11c).—The foregoing pyrrole benzyl ester (5·6 g) in tetrahydrofuran (120 ml) containing triethylamine (0·5 ml) and 10% palladised charcoal (560 mg) was hydrogenated at room temperature until uptake ceased. Filtration through Celite and evaporation to dryness gave a yellow oil which crystallised from ether–light petroleum (b.p. 60—80°) as *needles* (3·9 g, 90%), m.p. 151—152° (Found: C, 57·7; H, 6·75; N, 4·3. $C_{15}H_{21}NO_6$ requires C, 57·9; H, 6·8; N, 4·5%), τ −0·72 (CO_2H), 0·46br (NH), 6·91 (t), 5·78 (t), and 7·97 (s) (CH_2·CH_2·OCOMe), 7·64 (Me), and 8·40 (Bu^t).

The mixture from the large-scale diborane reduction described above was acetylated and then hydrogenated

* A gentle stream of nitrogen was used as a carrier gas.

as just described. Removal of the catalyst and evaporation gave an oil which was dissolved in ether (250 ml) and extracted with aqueous sodium carbonate. Neutralisation of these extracts with sulphur dioxide gas gave the pyrrole acid, identical with the foregoing sample. The ether layer was dried ($MgSO_4$) and evaporated to give a solid which was shown by n.m.r. to be t-butyl 3-(2-acetoxyethyl)-4,5-dimethylpyrrole-2-carboxylate: τ 1·13br (NH), 6·99 (t), 5·83 (t), and 7·98 (s) ($CH_2{\cdot}CH_2{\cdot}OCOMe$), 7·82 and 8·05 (2Me), and 8·45 (Bu^t). It was possible to convert this latter pyrrole into the required carboxylic acid (11c) in 52% yield by trichlorination and hydrolysis in the usual manner.

3-Ethoxycarbonylmethyl-4-methyl-2-t-butoxycarbonylpyrrole-5-carboxylic Acid (7a).—Benzyl 4-ethoxycarbonylmethyl-3-methyl-5-t-butoxycarbonylpyrrole-2-carboxylate (18·0 g) in tetrahydrofuran (360 ml) containing triethylamine (1·0 ml) and 10% palladised charcoal (1·80 g) was hydrogenated until uptake ceased. Filtration through Celite and evaporation yielded an *oil* which crystallised from ether–petroleum (b.p. 40—60°); yield 14·6 g (100%), m.p. 129—131° (Found: C, 57·9; H, 6·6; N, 4·65. $C_{15}H_{21}NO_6$ requires, C, 57·9; H, 6·8; N, 4·5%), τ 0·30 (CO_2H), 1·08br (NH), 6·20 (s), 5·85 (q), and 8·76 (t) ($CH_2{\cdot}CO_2{\cdot}CH_2{\cdot}CH_3$), 7·71 (Me), and 8·43 ($Bu^t$).

t-Butyl 3-Ethoxycarbonylmethyl-5-iodo-4-methylpyrrole-2-carboxylate (7b).—The foregoing pyrrole (12·1 g) in methanol (175 ml) at 60° was treated with iodine (10·1 g) and potassium iodide (16·3 g) in methanol (120 ml) and water (23 ml). The addition was complete in 6 h and the solution was cooled before being diluted with water to give the *iodopyrrole* as a pale yellow solid (13·4 g; 88%). Two recrystallisations from light petroleum (b.p. 60—80°) gave needles, m.p. 90—91° (Found: C, 42·7; H, 5·2; N, 3·5. $C_{14}H_{20}INO_4$ requires C, 42·8; H, 5·1; N, 3·6%), τ 0·84br (NH), 6·17 (t), 5·82 (t), and 8·74 (s) ($CH_2{\cdot}CO_2{\cdot}CH_2{\cdot}CH_3$), 8·01 (Me), and 8·42 ($Bu^t$).

t-Butyl 3-(2-Acetoxyethyl)-5-iodo-4-methylpyrrole-2-carboxylate (13a).—This compound was similarly prepared from 3-(2-acetoxyethyl)-4-methyl-2-t-butoxycarbonylpyrrole-5-carboxylic acid (2·8 g), and after chromatography on alumina (grade III) was obtained as flat *needles*, m.p. 106—107° [from light petroleum (b.p. 60—80°)] (Found: C, 42·9; H, 5·1; N, 3·5. $C_{14}H_{20}INO_4$ requires C, 42·8; H, 5·1; N, 3·6%), τ 1·03br (NH), 6·93 (t), 5·82 (t), and 7·98 (s) ($CH_2{\cdot}CH_2{\cdot}OCOMe$), 8·00 (Me), and 8·45 ($Bu^t$).

On one occasion, the product from the reaction was not as above but was the *deacetylated product*, m.p. 98—100° (from aqueous acetone) (Found: C, 41·3; H, 5·0; N, 3·9. $C_{12}H_{18}INO_3$ requires C, 41·0; H, 5·2; N, 4·0%), τ 0·90br (NH), 6·97 (t) and 6·22 (t) ($CH_2{\cdot}CH_2O$), 7·86 (OH), 8·00 (Me), and 8·44 (Bu^t).

Benzyl 5-Acetoxymethyl-4-ethoxycarbonylmethyl-3-methylpyrrole-2-carboxylate (5f).—Lead tetra-acetate (3·10 g) was added to benzyl 4-ethoxycarbonylmethyl-3,5-dimethylpyrrole-2-carboxylate (2·0 g) in glacial acetic acid (80 ml) during 5 min. After 2·5 h the solution was poured into water (500 ml) and the precipitate was collected. The *acetoxymethylpyrrole* (2·15 g, 96%), m.p. 125—126°, was obtained as needles [from light petroleum (b.p. 60—80°)] (Found: C, 64·3; H, 6·45; N, 3·7. $C_{20}H_{23}NO_6$ requires C, 64·3; H, 6·2; N, 3·75%), τ 0·36br (NH), 2·64 and 4·69 ($PhCH_2$), 4·92 (CH_2O), 6·52 (s), 5·88 (q), and 8·78 (t) ($CH_2{\cdot}CO_2{\cdot}CH_2{\cdot}CH_3$), 7·71 (Me), and 8·00 (COMe).

Benzyl 4-(2-Acetoxyethyl)-5-acetoxymethyl-3-methylpyrrole-2-carboxylate (10b).—The *acetoxymethylpyrrole* (28·9 g; 98%) was obtained similarly from benzyl 4-(2-acetoxyethyl)-3,5-dimethylpyrrole-2-carboxylate [11] (25·0 g) by treatment with lead tetra-acetate (38·7 g). A sublimed portion had m.p. 125—126° (Found: C, 64·2; H, 6·1; N, 3·5. $C_{20}H_{23}NO_6$ requires C, 64·3; H, 6·2; N, 3·75%), τ 0·69br (NH), 2·62 and 4·69 ($PhCH_2$), 4·95 (CH_2O), 7·21 (t), 5·90 (t), 7·95 (s), and 7·97 (s) ($CH_2{\cdot}CH_2{\cdot}OCO{\cdot}CH_3$ and COMe), and 7·69 (Me).

Methyl 2-Acetoxymethyl-5-dimethylcarbamoyl-4-methylpyrrole-3-carboxylate.—Methyl 5-dimethylcarbamoyl-2,4-dimethylpyrrole-3-carboxylate [3] (30 g) was stirred in acetic acid (2·5 l) containing acetic anhydride (60 ml). Lead tetra-acetate (65·4 g, 1·1 equiv.) was added in portions during 90 min and the mixture was set aside for 3 days before being diluted with water (5·5 l). The solution was extracted with chloroform (*ca.* 800 ml) and the organic layer was washed with 10% sodium carbonate solution (500 ml) and water (500 ml), dried ($MgSO_4$), and evaporated. Two recrystallisations from methylene chloride–light petroleum (b.p. 60—80°) gave needles (17·4 g, 50%) of the *acetoxymethylpyrrole*, m.p. 137—139·5° (Found: C, 55·3; H, 6·4; N, 9·9. $C_{13}H_{18}N_2O_5$ requires C, 55·4; H, 6·4; N, 10·0%), τ −0·70br (NH), 4·41 (CH_2O), 6·15 (OCH_3), 6·89 (NMe_2), 7·69 (Me), and 7·96 (COMe).

t-Butyl 3-(2-Hydroxyethyl)-4-methylpyrrole-2-carboxylate (13c).—t-Butyl 3-ethoxycarbonylmethyl-5-iodo-4-methylpyrrole-2-carboxylate (11·3 g) was dissolved in methanol (150 ml) containing hydrated sodium acetate (12 g) and Adams catalyst (110 mg). The mixture was hydrogenated until uptake ceased (4 h) and was then poured into water (1 l) and extracted with methylene chloride (3 × 75 ml). The extracts were washed with water (100 ml), dried ($MgSO_4$), and evaporated to leave a pale yellow oil (the 2-unsubstitited pyrrole) which was taken up in tetrahydrofuran (60 ml) and reduced with a stream of diborane generated by dropwise addition of boron trifluoride–ether complex (45 ml) to a stirred mixture of sodium borohydride (10 g) in bis-(2-methoxyethyl) ether (45 ml). (The diborane was swept out of the flask with a stream of dry nitrogen, and impurities were removed by passage through a −78° trap before passage through the pyrrole solution.) The solution was then treated carefully with dry methanol (50 ml) and evaporated, and the residue was taken up in ether (250 ml). This solution was washed with aqueous 5% sodium hydroxide (3 × 75 ml) and saturated brine (100 ml), dried (Na_2SO_4), and evaporated to dryness to give an oil which crystallised on trituration with ether–hexane, giving the *hydroxethylpyrrole* (6·2 g, 84%) as pale yellow prisms, m.p. 82—85°. A portion was chromatographed on alumina (grade V), with methylene chloride as eluant. Recrystallisation from methylene chloride–n-hexane gave white prisms, m.p. 86—87° (Found: C, 63·7; H, 8·5; N, 6·05. $C_{12}H_{19}NO_3$ requires C, 64·0; H, 8·5; N, 6·2%), τ 1·00br (NH), 3·24 (d, α-H), 7·08 (t) and 6·30 (t) ($CH_2{\cdot}CH_2OH$), 7·81 (OH), 8·03 (Me), and 8·50 (Bu^t).

Pyrromethanes

Benzyl 3,4′-Bis(ethoxycarbonylmethyl)-3′,4-dimethyl-5′-t-butoxycarbonylpyrromethane-5-carboxylate (8).—t-Butyl 3-ethoxycarbonylmethyl-4-methylpyrrole-2-carboxylate [obtained by hydrogenation of the corresponding iodopyrrole

[11] R. P. Carr, A. H. Jackson, G. W. Kenner, and G. S. Sach, *J. Chem. Soc.* (*C*), 1971, 487.

(9·0 g) in methanol (180 ml) containing anhydrous sodium acetate (2·7 g) and Adams platinum oxide (70 mg)], benzyl 5-acetoxymethyl-4-ethoxycarbonylmethyl-3-methylpyrrole-2-carboxylate (8·55 g), and anhydrous sodium acetate (3·6 g) in acetic acid (135 ml) were heated at 130° (oil-bath) for 15 min. The pale yellow solution was poured into water and the mixture was extracted with chloroform. The extracts were washed with aqueous 10% sodium carbonate and then water, dried ($MgSO_4$), and evaporated to an oil which soon crystallised (8·20 g, 62%), m.p. 114—120°. Recrystallisation from methylene chloride–light petroleum (b.p. 60—80°) gave *rosettes*, m.p. 123—124° (Found: C, 66·3; H, 6·9; N, 4·9. $C_{32}H_{40}N_2O_8$ requires C, 66·2; H, 6·9; N, 4·8%), τ 0·68br and 1·08br (2NH), 2·64 and 4·73 ($PhCH_2$), 5·84 (q) and 8·77 (t) (2OEt), 6·13 (bridge CH_2), 6·20 (4′-CH_2), 6·60 (3-CH_2), 7·71 and 8·02 (2Me), and 8·49 (Bu^t).

Benzyl 3,4′-Bis-(2-hydroxyethyl)-3′,4-dimethyl-5′-t-butoxycarbonylpyrromethane-5-carboxylate (9a).—Diborane was generated externally from sodium borohydride (4·56 g) and boron trifluoride–ether complex (30 ml) in bis-(2-methoxyethyl) ether (120 ml) and was carried in a stream of dry nitrogen into a solution of the foregoing pyrromethane (2·32 g) in tetrahydrofuran (100 ml). Next day methanol was added cautiously until effervescence ceased and the solution was evaporated *in vacuo* to give a brownish green oil. This product was combined with the products of two similar reductions carried out on 3·02 g of starting pyrromethane. The resultant yellow-brown oil (8·7 g) was chromatographed on alumina (grade III) and the *pyrromethane* (identified by t.l.c.), eluted with ethyl acetate–benzene (15 : 85) gave needles (1·32 g, 18%), m.p. 136—137° (from benzene) (Found: C, 67·8; H, 7·3; N, 5·6. $C_{28}H_{36}N_2O_6$ requires C, 67·7; H, 7·3; N, 5·6%), τ 0·39br and 1·08br (2NH), 2·67 and 4·73 ($PhCH_2$), 6·18 (CH_2), 7·35 (t) and 7·06 (t) ($2CH_2{\cdot}CH_2OH$), 7·72 and 8·00 (2Me), and 8·50 (Bu^t) (other resonances were not well resolved). *Benzyl 4-(2-hydroxyethyl)-5-hydroxymethyl-3-methylpyrrole-2-carboxylate* (10a) (2·95 g, 70%) was the major product, identified from its mass spectrum (M^+ 289) and by acetylation to the known diacetyl derivative (10b).

Benzyl 3,4′-Bis-(2-acetoxyethyl)-3′,4-dimethyl-5′-t-butoxycarbonylpyrromethane-5-carboxylate (9b).—Benzyl 4-(2-acetoxyethyl)-5-acetoxymethyl-3-methylpyrrole-2-carboxylate (15·3 g, 1·3 equiv.), anhydrous sodium acetate (5·5 g), and t-butyl 3-(2-acetoxyethyl)-4-methylpyrrole-2-carboxylate [obtained by hydrogenation of the corresponding 5-iodopyrrole (13·4 g) over Adams platinum oxide] were dissolved in warm glacial acetic acid (170 ml) and then heated at 130° during 25 min. After cooling, the solution was poured into 6 : 1 water–chloroform (1200 ml) and the organic phase was washed with aqueous 10% sodium carbonate (200 ml) and water (200 ml), dried ($MgSO_4$), and evaporated *in vacuo*. The residual oil was chromatographed on alumina (grade III) [gradient elution with light petroleum through benzene to ethyl acetate–benzene (1 : 9)]. The fractions containing the desired product (t.l.c.) were evaporated to a yellow-brown oil (13·8 g; 70% based on 5-iodopyrrole) which could not be induced to crystallise. The i.r. spectrum indicated at least 90% purity and a sample was purified by thick-layer chromatography on silica gel [acetone–light petroleum (b.p. 60—80°) (2 : 3 v/v)] (Found: C, 66·3; H, 7·2; N, 4·5. $C_{32}H_{40}N_2O_8$ requires C, 66·2; H, 6·9; N, 4·8%), τ 0·94br and 1·12br (2NH), 2·68 and 4·73 ($PhCH_2$), 5·83 (t) and 5·94 (t) ($2CH_2{\cdot}CH_2O$), 6·13 (t, CH_2), 6·98 (t) and 7·29 (t) ($2CH_2{\cdot}CH_2O$), 7·70 (4-Me), and 8·00 (3′-Me and 2COMe). Some 5-acetoxymethylpyrrole (1·02 g) was also recovered.

This pyrromethane was also prepared in quantitative yield by treatment of benzyl 3,4′-bis-(2-hydroxyethyl)-3′,4-dimethyl-5′-t-butoxycarbonylpyrromethane-5-carboxylate with acetic anhydride in pyridine.

b-*Oxobilane*

Dibenzyl 2,4-Bis-(2-acetoxyethyl)-6-methoxycarbonyl-7-(2-methoxycarbonylethyl)-1,3,5,8-tetramethyl-b-oxobilane-1′,8′-dicarboxylate (15b).—Benzyl 5′-dimethylcarbamoyl-3′-methoxycarbonyl-3-(2-methoxycarbonylethyl)-4,4′-dimethylpyrromethane-5-carboxylate[3] (12·3 g, 1·1 equiv.) was dissolved in freshly distilled phosphoryl chloride (80 ml) and the solution warmed at 50° during 90 min. The solvent was removed *in vacuo*, the last traces being removed by addition and evaporation of dry 1,2-dibromoethane.

Benzyl 3,4′-bis-(2-acetoxyethyl)-3′,4-dimethyl-5′-t-butoxycarbonylpyrromethane-5-carboxylate (12·4 g) was dissolved in dry methylene chloride (50 ml) and trifluoroacetic acid (150 ml) and the solution was set aside with a slow stream of nitrogen gas passing through it for agitation. After 80 min, the solvents were evaporated off and the residual oil was dissolved in methylene chloride (*ca.* 200 ml). The solution was washed with aqueous 10% sodium carbonate (100 ml) and water (100 ml), dried ($MgSO_4$), and evaporated and the resultant 5′-unsubstituted pyrromethane was taken up in methylene chloride (20 ml) and added to the phosphoryl chloride complex in methylene chloride (10 ml). A slow stream of nitrogen was passed through the solution at 47° during 26 h. The solution was then diluted to 150 ml with methylene chloride, washed with water (3 × 150 ml), dried ($MgSO_4$), and evaporated to give a dark brown oil which was purified by chromatography on alumina (grade III). Elution with benzene through to ethyl acetate–benzene (7 : 3) removed by-products, and then elution with methanol yielded the imine salt ($\lambda_{max.}$ 406 nm). Methylene chloride (300 ml) and aqueous 10% sodium carbonate (300 ml) were added and the mixture was heated under reflux and stirred vigorously during 3 h. After cooling, the organic layer was washed with water (2 × 200 ml), dried ($MgSO_4$), and evaporated to give a brown oil (9·5 g) ($\lambda_{max.}$ 354 nm). T.l.c. showed only one component and the ^1H n.m.r. spectrum indicated that it was essentially the required compound. For the purposes of further experiments, the yield was estimated to be 8 g (39%); τ 0·05br and 0·42br (4NH), 2·65 and 4·74 ($2PhCH_2$), 5·80 and 6·08 (*a*- and *c*-CH_2), 6·27 (6-OMe), 6·49 (7-OMe), and 7·70, 7·74, 7·81, 7·97, 8·03, and 8·08 (1-, 3-, 5-, and 8-Me and 2COMe).

Porphyrins

β-Acetoxy-2,4-bis-(2-acetoxyethyl)-6-methoxycarbonyl-7-(2-methoxycarbonylethyl)-1,3,5,8-tetramethylporphin (16a).—(a) *Hydrogenolysis of* b-*oxobilane*. The foregoing *b*-oxobilane (15b) (8 g) in tetrahydrofuran (130 ml) containing triethylamine (9 drops) and 10% palladised charcoal (1·3 g) was hydrogenated at room temperature and atmospheric pressure until uptake had ceased (3·5 h). Filtration on Celite and evaporation gave the dicarboxylic acid (15c) as a brown foam.

(b) *Macrocycle formation and oxidation to porphyrin*. The foregoing dicarboxylic acid (15c) was dissolved in methylene chloride (1665 ml) containing trimethylortho-

formate (17·4 ml). A 1M-solution of trichloroacetic acid in methylene chloride (470 ml) was added and the solution was stirred at room temperature in the dark during 2·5 h ($\lambda_{max.}$ 510 nm). Pyridine (50 ml) was added and the solution was set aside in the light during 66 h ($\lambda_{max.}$ 405 and 700 nm). Evaporation gave a green residue which was dissolved in pyridine (140 ml) and acetic anhydride (41 ml) (green ⟶ red-brown). After 45 min at room temperature the solution was evaporated and the residue was dissolved in methylene chloride (250 ml). This solution was washed with water (250 ml), dried ($MgSO_4$), and evaporated to dryness. The residue was kept at 60° and 0·3 mmHg during 3 h, then chromatographed on alumina, with methylene chloride as eluant. The product was dried at 70° and 0·5 mmHg for 3 h. Crystallisation from methyl chloride–methanol gave fluffy brown needles of the *porphyrin* (2·32 g, 38%), m.p. 189—192° (Found: C, 65·1; H, 5·7; N, 7·6. $C_{40}H_{44}N_4O_{10}$ requires C, 64·85; H, 6·0; N, 7·6%), τ (0·1M) −0·52, 0·41, and 0·98 (3 *meso*-H), 5·54 (6-OMe), 6·21 (5-Me), 6·35 (7-OMe), 6·44 (β-COMe), 6·93, 6·95, and 7·03 (1-, 3-, and 8-Me), 7·87 and 7·98 (2- and 4-COMe), and 14·03br (2NH), $\lambda_{max.}$ ($CHCl_3$) 410 (ε 194,000), 509 (11,400), 546 (8700), 579 (6800), and 622 nm (1200), $\lambda_{max.}$ ($CHCl_3$–HCl) 432 (ε 252,000), 570 (12,400), and 617 nm (9300).

2,4-*Bis*-(2-*acetoxyethyl*)-6-*methoxycarbonyl*-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethylporphin* (16b).—The foregoing porphyrin (2·32 g) in tetrahydrofuran (700 ml) containing triethylamine (1·5 ml) and 10% palladised charcoal (2·32 g) was hydrogenated at atmospheric pressure and room temperature until uptake had ceased and the solution was colourless (4 h). The catalyst was filtered off through Celite, which was washed through with pyridine (50 ml). More pyridine (200 ml) was added and air was passed through the filtrate during 3 days. The solution was evaporated and the residue was chromatographed on alumina (grade III). Elution with chloroform gave the *porphyrin* (1·63 g, 76%), m.p. 194—197° (from chloroform–methanol) (Found: C, 66·7; H, 6·2; N, 8·1. $C_{38}H_{42}N_4O_8$ requires C, 66·8; H, 6·2; N, 8·2%), τ (0·09M) −0·68, 0·38, 0·46, and 0·52 (4 *meso*-H), 5·34 ($2CH_2{\cdot}CH_2{\cdot}O$), 5·55 (6-O*Me*), 5·94 ($2CH_2{\cdot}CH_2O$ and $CH_2{\cdot}CH_2{\cdot}CO$), 6·27 (5-Me), 6·33 (7-OMe), 6·63, 6·67, and 6·71 (1-, 3-, and 8-Me), and 7·94 and 8·04 (2COMe), $\lambda_{max.}$ ($CHCl_3$) 407 (ε 196,000), 508 (11,100), 547 (13,800), 577 (7600), and 631 nm (1500), $\lambda_{max.}$ ($CHCl_3$–HCl) 426 (ε 228,000), 565 (13,500), and 613 nm (9700). A second fraction, (70 mg, 4%) eluted with methanol–chloroform (1 : 99) contained a mono-(2-acetoxyethyl)-mono-(2-hydroxyethyl)porphyrin, demonstrated by its hydrolysis to the corresponding bis-(2-hydroxyethyl)porphyrin (below).

2,4-*Bis*-(2-*hydroxyethyl*)-6-*methoxycarbonyl*-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethylporphin* (16c).—The foregoing bis-(2-acetoxyethyl)porphyrin (1·63 g) was treated with 5% v/v concentrated sulphuric acid in methanol (1400 ml) at room temperature in the dark during 66 h. The violet solution was poured into water (1300 ml) containing sodium acetate trihydrate (95 g) and chloroform (400 ml). After shaking, aqueous 7% sodium hydrogen carbonate (1300 ml) was added cautiously, followed by pyridine (250 ml) (required to redissolve the precipitated porphyrin). The organic layer was washed with water (500 ml), dried ($MgSO_4$), and evaporated. The purple residue was crystallised from tetrahydrofuran–light petroleum (b.p. 60—80°) giving the *porphyrin* (1·21 g, 84%) as irregularly shaped crystals, m.p. 158—160°. The same product (53 mg) was obtained by treatment of the minor porphyrin fraction from the foregoing preparation with 5% sulphuric acid in methanol as above (Found: C, 68·0; H, 6·7; N, 9·2. $C_{34}H_{38}N_4O_6$ requires C, 68·2; H, 6·4; N, 9·4%), τ ($CF_3{\cdot}CO_2H$) −1·85, −1·18, −1·03, and −0·96 (4 *meso*-H), 4·77 ($2CH_2{\cdot}CH_2O$), 5·38 (m, $2CH_2{\cdot}CH_2{\cdot}OH$, $CH_2{\cdot}CH_2{\cdot}CO$, and 6-O*Me*), 5·88 (5-Me), 6·2; (1-, 3-, and 8-Me and 7-OMe), and 6·60 ($CH_2{\cdot}CH_2{\cdot}CO$), $\lambda_{max.}$ (pyridine) 409 (ε 192,000), 509 (11,800), 548 (14,700), 577 (8500), and 632 nm (2000), $\lambda_{max.}$ ($CHCl_3$–HCl) 423 (ε 212,000), 563 (13,500), and 612 nm (8800).

2,4-*Bis*-(2-*chloroethyl*)-6-*methoxycarbonyl*-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethylporphin* (16d).—The foregoing porphyrin (1·22 g) was dissolved with stirring in chloroform (600 ml) and dimethylformamide (100 ml), and anhydrous potassium carbonate (20 g) was added, followed by thionyl chloride (20 ml). The mixture was stirred for 4 h, with warming from time to time on a steam-bath, then poured into water (600 ml). The mixture was shaken until effervescence ceased, then the organic layer was washed with water (500 ml) and evaporated *in vacuo*, the last traces of dimethylformamide being removed at 50° and 0·5 mmHg, leaving a crystalline residue, which was purified by dissolving in pyridine and filtering through alumina. The *bis*-(2-*chloroethyl*)*porphyrin* (1·08 g, 83%) was obtained as shiny purple hexagonal plates from chloroform–light petroleum (b.p. 60—80°), m.p. 262—264° (Found: C, 64·4; H, 5·7; N, 8·7. $C_{34}H_{36}Cl_2N_4O_4$ requires C, 64·4; H, 5·7; N, 8·7%), τ ($CF_3{\cdot}CO_2H$) −1·83, −1·22, −1·07, and −0·97 (4 *meso*-H), 5·35 (6-OMe), 5·89 (7-OMe), and 6·21 (1-, 3-, 5-, and 8-Me) (other resonances were difficult to assign unambiguously), $\lambda_{max.}$ ($CHCl_3$) 408 (ε 178,000), 509 (11,400), 548 (13,900), 577 (7800), and 633 nm (1800), $\lambda_{max.}$ ($CHCl_3$–HCl) 428 (ε 223,000), 566 (13,500) and 615 nm (9600).

7-(2-*Methoxycarbonylethyl*)-1,3,5,8-*tetramethyl*-2,4-*divinylporphin*-6-*carboxylic Acid* (' 2,4-*Divinylrhodoporphyrin*-XV 7-*Methyl Ester* ') (17c).—The foregoing 2,4-bis-(2-chloroethyl)porphyrin (500 mg) was dissolved in chloroform (150 ml) and treated with a saturated solution of zinc acetate in methanol (50 ml) for 5 min at 60°. The mixture was poured into water (200 ml) and chloroform (200 ml) and the organic layer was washed with water (300 ml), dried ($MgSO_4$), and evaporated. The solid zinc chelate was treated with M-potassium t-butoxide in t-butyl alcohol (325 ml) in the dark, under nitrogen for 7 days. The solution was then poured into 2N-sulphuric acid (375 ml) and chloroform (400 ml). After shaking, pyridine (100 ml) was added and the organic layer was washed with water (250 ml), dried ($MgSO_4$), and evaporated *in vacuo*. The residue was then treated with 4% v/v concentrated sulphuric acid in methanol (400 ml) in the dark during 22 h. The mixture was poured into chloroform (400 ml) and 8% ammonia (*d* 0·88) in water (400 ml), and the organic layer was washed with water (250 ml), dried ($MgSO_4$), and evaporated. The residue was crystallised from tetrahydrofuran–benzene to give irregularly shaped purple crystals (201 mg, 47%), m.p. >300°, which were recrystallised from pyridine–methanol (Found: C, 72·2; H, 5·9; N, 10·2. $C_{33}H_{32}N_4O_4$ requires C, 72·2; H, 5·9; N, 10·2%), τ ($CF_3{\cdot}CO_2H$) −1·72, −1·08, −0·97, and −0·86 (4 *meso*-H), 1·80 (m) and 3·58 (m) ($2CH{\cdot}CH_2$), 5·44 (t) and 6·65 (t) ($CH_2{\cdot}CH_2{\cdot}CO$), 5·93 (5-Me), and 6·23—6·28 (OMe and 1-, 3-, and 8-Me), $\lambda_{max.}$ (pyridine) 415 (ε 139,000), 515

(10,300), 554 (10,500), 585 (7000), and 639 nm (2400), $\lambda_{max.}$ ($CHCl_3$–HCl) 430 (ε 138,000), 572 (10,200), and 621 nm (7100), $\lambda_{max.}$ (0·1M-NaOMe–MeOH) 405 (ε 121,000), 507 (10,700), 541 (8500), 579 (5600), and 631 nm (3200). The mother liquors from the crystallisation were treated with an excess of diazomethane in ether and, after chromatography on alumina (grade III), and crystallisation from chloroform–light petroleum (b.p. 60—80°), 2,4-*divinylrhodoporphyrin*-XV *dimethyl ester* (2c) (43 mg, 10%) was obtained as purple needles, m.p. 258—260° (sample placed on block at 250° and heated rapidly; when placed on the block at 230° and heated slowly, the sample did not melt) (Found: C, 72·8; H, 6·3; N, 10·0. $C_{34}H_{34}N_4O_4$ requires C, 72·6; H, 6·1; N, 10·0%), τ −0·16, 0·11 (2H), and 0·70 (4 *meso*-H), 2·06, 2·32 (m, $2CH{:}CH_2$), 3·99 (m, $2CH{:}CH_2$) 5·63 (6-OMe), 6·08 ($CH_2{\cdot}CH_2{\cdot}CO$), and 6·36, 6·61, 6·65, 6·77, and 6·91 (7-OMe and 1-, 3-, 5-, and 8-Me), $\lambda_{max.}$ ($CHCl_3$) 413 (ε 177,000), 515 (11,000), 556 (13,700), 583 (8100), and 637 nm (1800), $\lambda_{max.}$ ($CHCl_3$–HCl) 430 (ε 191,000), 571 (12,700), and 620 nm (8600).

4-*Ethyl*-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethyl*-2-*vinylporphin*-6-*carboxylic Acid* (' 2-*Vinylrhodoporphyrin*-XV 7-*Methyl Ester*') (17b).—(a) *From the corresponding* 2-(2-*chloroethyl*)*porphyrin*. 2-(2-Chloroethyl)-4-ethyl-6-methoxycarbonyl-7-(2-methoxycarbonylethyl)-1,3,5,8-tetramethylporphin [3] (250 mg) in chloroform (60 ml) was treated with a saturated solution of zinc acetate in methanol (25 ml) for 5 min at 60°. The mixture was poured into saturated aqueous sodium acetate trihydrate solution (200 ml) and chloroform (200 ml), water was added and the mixture was filtered through a glass sinter to break the resultant emulsion. The organic layer was washed with water (100 ml), dried ($MgSO_4$), and evaporated. The zinc chelate was then dissolved in tetrahydrofuran (60 ml) containing water (0·2 ml), and M-potassium t-butoxide in t-butyl alcohol (160 ml) was added. The solution was stirred under nitrogen in the dark during 19 h, then poured into 2N-sulphuric acid (180 ml) and chloroform (200 ml). After shaking, pyridine (30 ml) was added and the separated organic phase was washed with water (150 ml), dried ($MgSO_4$), and evaporated. The resultant solid was treated with 4% v/v sulphuric acid in methanol (200 ml) for 16 h in the dark, and then poured into chloroform (200 ml) and 5% ammonia (*d* 0·88) in water (200 ml). The organic layer was washed with water (100 ml), dried ($MgSO_4$), and evaporated to give a solid residue, which was dissolved in a minimal quantity of hot tetrahydrofuran; the solution was filtered hot. The product was crystallised by gradual addition of benzene to the boiling solution, giving purple needles of the *porphyrincarboxylic acid* (165 mg, 72%), m.p. >300° (Found: C, 72·0; H, 5·95; N, 9·9. $C_{33}H_{34}N_4O_4$ requires C, 72·0; H, 6·2; N, 10·2%), τ ($CF_3{\cdot}CO_2H$) −1·98, −1·30, −1·17, and −1·11 (4 *meso*-H), 1·74 (m) and 3·53 (m) ($CH{:}CH_2$), 5·87 (5-Me), 6·22 (6H), 6·25, and 6·29 (OMe and 1-, 3-, and 8-Me), 6·59 (t, $CH_2{\cdot}CH_2{\cdot}CO$), and 8·18 (t, $CH_2{\cdot}CH_3$), $\lambda_{max.}$ (pyridine) 409 (ε 189,000), 511 (10,000), 552 (17,200), 579 (9200), and 634 nm (1100), $\lambda_{max.}$ ($CHCl_3$–HCl) 427 (ε 206,000), 569 (12,000), and 620 nm (12,900). $\lambda_{max.}$ (0·1M-NaOMe–MeOH) 399 (ε 146,000), 503 (10,500), 550 (12,000), 572 (6700), and 624 nm (1900). The mother liquors from the crystallisation were evaporated, and the residue was treated with an excess of diazomethane in ether. The product was chromatographed on alumina (grade III); elution with chloroform and crystallisation from chloroform–light petroleum (b.p. 60—80°) gave 2-vinylrhodoporphyrin-XV dimethyl ester (5 mg; 2%), identical with an authentic sample.

(b) *From* 2-*vinylrhodoporphyrin*-XV *dimethyl ester* (2b). The ester (2b) (850 mg) in warm pyridine (175 ml) was refluxed during 4 h with a solution of potassium hydroxide (20 g) in water (25 ml) and methanol (150 ml). The solution was cooled, diluted with iced water (1 l), acidified with concentrated sulphuric acid (15 ml) in water (100 ml), and then stirred during 10 min. The precipitated porphyrin diacid was filtered off on Celite, and washed with warm water followed by absolute methanol. A mixture of dry methanol (650 ml) and concentrated sulphuric acid (20 ml) was passed slowly through the bed of Celite, thereby dissolving the porphyrin, and the resultant solution was kept at room temperature during 6 h before addition to water (1·5 l). The porphyrin was extracted with methylene chloride (3 × 400 ml) and the extracts were washed with water (1 l), dried ($MgSO_4$), and evaporated. The residue was crystallised from tetrahydrofuran–benzene to give the porphyrincarboxylic acid (760 mg, 88%) as tiny needles, m.p. >300°, identical with the foregoing sample.

2,4-*Diethyl*-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethyl*-6-*trimethylacetoxycarbonylporphin* (20a).—Rhodoporphyrin-XV 7-methyl ester [1] (100 mg) was stirred at room temperature for 30 min with methylene chloride (4·5 ml), pyridine (1·5 ml), and pivaloyl chloride (0·28 ml). The solution was then evaporated to dryness and the residue was chromatographed on alumina (grade V). Elution with methylene chloride gave a single porphyrin; crystallisation from methylene chloride–n-hexane gave the *mixed anhydride* (91 mg, 83%) as small purple prisms, m.p. 218—220° (Found: C, 71·5; H, 6·8; N, 9·1. $C_{38}H_{44}N_4O_5$ requires C, 71·7; H, 7·0; N, 8·8%), τ (0·1M) −0·54, 0·55, 0·68, and 0·73 (4 *meso*-H), 6·3 (m); 6·88 (t), and 6·34 (s) ($CH_2{\cdot}CH_2{\cdot}CO_2Me$), 6·3 (m) and 8·36 (t) (2Et), 6·42, 6·73 (6H), and 6·78 (1-, 3-, 5-, and 8-Me), and 8·36 (Bu^t), $\lambda_{max.}$ (CH_2Cl_2) 409·5 (ε 174,000), 513 (8100), 554 (15,100), 578 (9300), and 634 nm (1500), $\lambda_{max.}$ (CH_2Cl_2–$CF_3{\cdot}CO_2H$) 412 (ε 281,000), 558 (12,600), and 608 nm (9800), *m/e* 636 (3%), 621 (4), 551 (9), and 507 (100).

4-*Ethyl*-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethyl*-6-*trimethylacetoxycarbonyl*-2-*vinylporphin* (20b).—2-Vinylrhodoporphyrin-XV 7-methyl ester (55 mg) was stirred during 30 min at room temperature with a mixture of methylene chloride (5 ml), pivaloyl chloride (60 mg), and *NN*-di-isopropylethylamine (130 mg). The solution was evaporated and the residue was chromatographed on alumina (grade V). Elution with methylene chloride and crystallisation from methylene chloride–n-hexane gave purple needles (52 mg, 82%) of the *mixed anhydride*, m.p. 232—234° (Found: C, 72·0; H, 6·7; N, 8·7. $C_{38}H_{42}N_4O_5$ requires C, 71·9; H, 6·7; N, 8·8%), τ (0·08M) −0·42, 0·69, 0·80, and 0·96 (4 *meso*-H), 2·18 (m) and 4·00 (m) ($CH{:}CH_2$), 5·85 (t), 6·89 (t), and 6·36 (s) ($CH_2{\cdot}CH_2{\cdot}CO_2Me$), 6·3 (m) and 8·42 (t) (Et), 6·29, 6·76, 6·78, and 6·82 (4Me), and 8·32 (Bu^t), $\lambda_{max.}$ (CH_2Cl_2) 410 (ε 181,000), 516·5 (7500), 560 (19,000), 582·5 (12,500), and 636 nm (1600), $\lambda_{max.}$ (CH_2Cl_2–$CF_3{\cdot}CO_2H$) 415·5 (ε 269,000), 564 (11,800), and 616 nm (12,500), *m/e* 634 (100%), 550 (20), and 533 (24).

6-*Ethoxycarbonyloxycarbonyl*-2,4-*diethyl*-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethylporphin* (21a).—Rhodoporphyrin-XV 7-methyl ester (110 mg) was stirred during 1 h with a mixture of methylene chloride (20 ml), pyridine (2 ml), and ethyl chloroformate (0·1 ml). The solution was diluted with methylene chloride (100 ml) and washed

with water (3 × 50 ml), dried ($MgSO_4$), and evaporated to dryness. Recrystallisation of the residue from methylene chloride–n-hexane gave the *mixed carbonic anhydride* (125 mg, 91%) as purple microcrystals, m.p. 228—229° (Found: C, 69·1; H, 6·6; N, 9·0. $C_{36}H_{40}N_4O_6$ requires C, 69·2; H, 6·45; N, 9·0%), τ ($CF_3{\cdot}CO_2H$) −1·74, −1·13, −0·92, and −0·85 (4 *meso*-H), 5·24 (q) and 8·34 (t) (OEt), 5·40 (t), 6·53 (t), and 6·23 (s) ($CH_2{\cdot}CH_2{\cdot}CO_2Me$), 5·8 (m) and 8·19 (t) (2Et), and 5·89 and 6·27 (9H) (4Me), $\lambda_{max.}$ (CH_2Cl_2) 410 (ε 175,000), 515 (8200), 556 (16,400), 579 (9700), and 634 nm (1600), $\lambda_{max.}$ (CH_2Cl_2–$CF_3{\cdot}CO_2H$) 413 (ε 315,000), 559 (12,300), and 579·5 nm (9700).

2,4-*Diethyl*-6-(*imidazol*-1-*ylcarbonyl*)-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethylporphin* (22a).—Rhodoporphyrin-XV 7-methyl ester (110 mg) was heated under reflux during 30 min in methylene chloride (20 ml) containing *NN'*-carbonyldi-imidazole (100 mg, 3 equiv.). The solution was then chromatographed on alumina (grade V). Elution with methylene chloride and crystallisation from methylene chloride–n-hexane gave the imidazolide (102 mg, 89%) as small purple plates, m.p. 235—236° (Found: C, 71·5; H, 6·5; N, 14·0. $C_{36}H_{38}N_6O_3$ requires C, 71·7; H, 6·4; N, 13·95%), τ (0·08M) 0·33, 0·41, 0·46, and 0·62 (4 *meso*-H) 1·73, 2·14, and 2·74 (3 imidazole H), 6·06 (t), 7·03 (t), and 6·40 (s) ($CH_2{\cdot}CH_2{\cdot}CO_2Me$), 6·48, 6·64, 6·77, and 6·80 (4Me), and 6·28 (q), 8·29 (t), and 8·31 (t) (2Et) $\lambda_{max.}$ (CH_2Cl_2) 407 (ε 179,000), 510 (9100), 548 (14,200), 573 (8900), and 628 nm (800), $\lambda_{max.}$ (CH_2Cl_2–$CF_3{\cdot}CO_2H$) 413 (ε 244,000), 560 (11,500), and 612 nm (9600), *m/e* 602 (100%) and 535 (56).

4-*Ethyl*-6-(*imidazol*-1-*ylcarbonyl*)-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethyl*-2-*vinylporphin* (22b).—Prepared similarly on a 100 mg scale from 2-vinylrhodoporphyrin-XV 7-methyl ester, the *imidazolide* (92 mg, 84%) crystallised from methylene chloride–n-hexane with m.p. 244—245·5° (Found: C, 71·9; H, 6·2; N, 13·7. $C_{36}H_{36}N_6O_3$ requires C, 72·0; H, 6·05; N, 14·0%), τ (0·06M) 0·23, 0·31, 0·34, and 0·54 (4 *meso*-H), 1·68, 2·12, and 2·71 (3 imidazole H), 2·05 (m) and 3·90 (m) ($CH{:}CH_2$), 5·94 (t), 6·99 (t), and 6·37 (s) ($CH_2{\cdot}CH_2{\cdot}CO_2Me$), 6·19 (q) and 8·28 (t) (Et), and 6·44, 6·62, 6·66, and 6·71 (4Me), *m/e* 600 (88%) and 533 (100).

6-(*Imidazol*-1-*ylcarbonyl*)-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethyl*-2,4-*divinylporphin* (22c).—Prepared in a similar manner to the foregoing analogues, from 2,4-divinylrhodoporphyrin-XV 7-methyl ester (90 mg), the *imidazolide* (67 mg, 68%) was obtained as small needles, m.p. 254—258° (decomp.) (placed in apparatus at 240° and heated rapidly) (from methylene chloride–n-hexane) (Found: 71·75; H, 6·0; N, 13·75. $C_{36}H_{34}N_6O_3$ requires C, 72·2; H, 5·7; N, 14·0%) (the compound exploded repeatedly upon combustion), τ (0·05M) 0·40, 0·47, and 0·69 (2H) (4 *meso*-H), 2·2 (m) and 3·9 (m) ($2CH{:}CH_2$), 1·70, 2·20, and 2·68 (3 imidazole H), 5·90 (t), 6·98 (t), and 6·36 (s) ($CH_2{\cdot}CH_2{\cdot}CO_2Me$), and 6·51 and 6·69 (9H) (4Me), $\lambda_{max.}$ (CH_2Cl_2) 412 (ε 166,000), 516 (9900), 556 (14,500), 581 (9300), and 634 nm (1000), $\lambda_{max.}$ (CH_2Cl_2–$CF_3{\cdot}CO_2H$) 419·5 (ε 233,000), 567 (11,600), and 619 nm (9600), *m/e* 598 (100%), 531 (96), 299 (2), 265·5 (2).

4-*Ethyl*-6-*methoxycarbonylacetyl*-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethyl*-2-*vinylporphin* (1b).—(a) Via *the acid chloride* (18b). 2-Vinylrhodoporphyrin-XV 7-methyl ester (165 mg) was treated with oxalyl chloride (10 ml) during 1 h with occasional warming. The solvent was then evaporated off to leave the acid chloride as a green residue. To methyl t-butyl malonate (5·7 g) in tetrahydrofuran (240 ml) was added sodium hydride (0·77 g) in small quantities; after stirring at room temperature during 1 h (white suspension), the foregoing acid chloride in chloroform (30 ml) was added slowly, and the mixture was stirred at room temperature during 40 min. The solvents were evaporated off and the residue was partitioned between chloroform (200 ml) and 2N-sulphuric acid (120 ml). The organic layer was washed with water (200 ml), dried ($MgSO_4$), and evaporated, and the residue was chromatographed on alumina (grade V) [elution first with benzene, and after the forerun with methanol–chloroform (1 : 9)]. The eluates were evaporated, and the residue was treated with trifluoroacetic acid (10 ml) under a slow stream of nitrogen for 40 min. The trifluoroacetic acid was evaporated off and the residue was dissolved in chloroform (40 ml); the solution was washed with aqueous 7% sodium hydrogen carbonate (50 ml) and water (50 ml), dried ($MgSO_4$), and evaporated. The residue was recrystallised from methylene chloride–light petroleum (b.p. 60—80°) to give the β-*keto-ester* (86 mg, 47%) as purple microcrystals, m.p. 250—254° (sample on block at 210° and heated rapidly; when the sample was placed on the block at 225° and heated slowly, the compound did not melt below 270°) (Found: C, 71·1; H, 6·5; N, 9·4. $C_{36}H_{38}N_4O_5$ requires C, 71·3; H, 6·3; N, 9·2%); the n.m.r. spectrum (0·09M-solution) was complex owing to keto–enol tautomerism, but the following assignments were made: enol OH τ −3·30, 4 *meso*-H (keto) −0·33, 0·54, 0·61, and 0·70, 4 *meso*-H (enol) −0·20, 0·38, 0·44, and 0·61, τ 2·07 (m, $CH{:}CH_2$), 3·92 [m, $CH{:}CH_2$, $CH{:}C(OH)$], 5·43 and 6·39 ($CO{\cdot}CH_2{\cdot}CO_2Me$), 6·08 (keto) and 5·97 (enol) (5-Me), and 8·37 (m, $CH_2{\cdot}CH_3$), $\lambda_{max.}$ (CH_2Cl_2) 409 (ε 176,000), 512·5 (7200), 553 (15,400), 574 (9900), and 635 nm (1300), $\lambda_{max.}$ (CH_2Cl_2–$CF_3{\cdot}CO_2H$) 412 (ε 267,000), 559 (12,200), and 608 nm (8600), $\lambda_{max.}$ (0·1M-NaOMe–MeOH) 401 (ε 154,000), 504·5 (10,500), 542 (12,400), 572 (6900), and 625 nm (2200), *m/e* 548 (100%).

(b) Via *the imidazolide* (22b). A mixture of 2-vinylrhodoporphyrin-XV 7-methyl ester (125 mg) and *NN'*-carbonyldi-imidazole (125 mg) was refluxed during 30 min in dry tetrahydrofuran (25 ml). The solution was evaporated and the residue was chromatographed on alumina (grade V), (elution with methylene chloride). The porphyrin eluates were evaporated and the residue was taken up in methylene chloride (10 ml). Meanwhile, a solution of isopropylmagnesium bromide was prepared from magmesium turnings (0·10 g), isopropyl bromide (0·30 g), and anhydrous tetrahydrofuran (10 ml). After all the metal had dissolved, the solution was cooled to 0° and redistilled methyl hydrogen malonate (0·24 g) was added in tetrahydrofuran (2 ml). The solution was warmed to 60—70° and stirred for 10 min before introduction of the imidazolide solution. It was then heated under reflux at 60—70° for 2·5 h and acetic acid (1 ml) was added. Heating was continued for a further 10 min before the solution was diluted with chloroform (100 ml), washed with 0·1N-hydrochloric acid (100 ml) and water (2 × 100 ml), dried ($MgSO_4$), and evaporated to dryness. The residue was chromatographed on alumina (grade V). Elution with methylene chloride containing 5% acetone and crystallisation from methylene chloride–methanol gave the keto-ester (97 mg, 70%), identical with the sample prepared in (a).

(c) Via *the pivalic mixed anhydride* (20b). The 2-vinyl

pivalic mixed anhydride (20b) (63 mg) in methylene chloride (4 ml) was added to a stirred mixture of methyl t-butyl malonate (17·5 mg) and sodium hydride dispersion (9·2 mg) in dry tetrahydrofuran (2·5 ml). The product was worked up with trifluoroacetic acid, as described in (a), and the keto-ester obtained (28·5 mg, 42%), m.p. 250—253°, was identical with the material prepared in the foregoing reactions above; τ (CF_3·CO_2H) (keto–enol 1 : 1) −1·43, −1·36, −1·06, −1·03, −1·00, −0·96, −0·94, and −0·88 (meso-H), 1·8 (m) and 3·5 (m) ($CH{:}CH_2$), 3·88 (C:CH enol), 5·03 ($CO{\cdot}CH_2$), 5·44 (t), 6·73 (t), and 6·23 (s) ($CH_2{\cdot}CH_2{\cdot}CO_2Me$), 5·79 (q) and 8·23 (t) (Et), and 5·83, 5·98, 6·00, 6·10, 6·23, 6·27, 6·32 and 6·35 (4Me and OMe).

6-(*Methoxycarbonylacetyl*)-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethyl*-2,4-*divinylporphin* (1c).—(a) Via *the acid chloride* (18c). 2,4-Divinylrhodoporphyrin-XV 7-methyl ester (70 mg) was treated with oxalyl chloride (6 ml) as described in (a) above. It was then similarly treated with methyl t-butyl sodiomalonate (from 2·40 g of malonate) and the product was worked up. Treatment with trifluoroacetic acid and then crystallisation from methylene chloride–methanol gave the β-keto-ester (7·4 mg, 9·6%) as purple microcrystals, m.p. 179—185° (placed on block at 135° and heated rapidly; the material softened at 170°) (Found: C, 71·2; H, 6·2; N, 9·3. $C_{36}H_{36}N_4O_5$ requires C, 71·5; H, 6·0; N, 9·3%), $\lambda_{max.}$ (CH_2Cl_2) 414 (ε 169,000), 515 (9100), 555 (13,100), 583 (8400), and 637 nm (1300), $\lambda_{max.}$ (CH_2Cl_2–$CF_3{\cdot}CO_2H$) 416 (ε 234,000), 561 (14,500), and 609 nm (7000), $\lambda_{max.}$ (0·1M-NaOMe–MeOH) 405 (ε 162,000), 507 (12,400), 543 (10,800), 576·5 (6100), and 630 nm (3600).

(b) Via *the imidazolide* (22c). A solution (5 ml) of the magnesiomalonate prepared as described in (b) above was treated with the 2,4-divinylimidazolide (22c) (48 mg), heated at 50—60° under nitrogen during 2·5 h, then cooled. The solution was diluted with methylene chloride (50 ml) and washed with 0·1N-sulphuric acid (50 ml) and water (2 × 50 ml), dried ($MgSO_4$), and evaporated. The residue was chromatographed on alumina (grade V). Elution with methylene chloride–acetone (20 : 1) and crystallisation from methylene chloride–methanol gave the β-keto-ester (34·5 mg, 71%), identical with the product from (a).

2,4-*Diethyl*-6-*methoxycarbonylacetyl*-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethylporphin* (1a).—(a) Via *the pivalic anhydride* (20a). A solution of malonate anion was prepared by addition of sodium hydride dispersion (14·5 mg) to a stirred solution of methyl t-butyl malonate (52 mg) in dry tetrahydrofuran (7 ml). The 2,4-diethyl pivalic anhydride (64 mg) in methylene chloride (4 ml) was then introduced and the mixture was stirred at room temperature during 5 min before being added to water (50 ml) containing concentrated sulphuric acid (0·5 ml). The porphyrins were extracted with chloroform (25 ml) and the extract was washed with water (2 × 50 ml), dried (Na_2SO_4), and evaporated. The residue was chromatographed on alumina (grade V); elution with methylene chloride resulted in rapid removal of unchanged (20a). Further elution with 5% methanol in methylene chloride yielded the keto-diester; these fractions were evaporated and the residue was dissolved in trifluoroacetic acid (10 ml). After 30 min, the solvent was evaporated off and the residue was taken up in methylene chloride (25 ml); the solution was washed with water (50 ml) and aqueous 1% sodium carbonate, dried ($MgSO_4$), and evaporated. Crystallisation from methylene chloride–methanol gave the keto-ester (1a) (25 mg, 41%) as purple needles, identical with a sample prepared by the acid chloride route.[1]

(b) Via *the imidazolide* (22a). Treatment of the rhodoporphyrin-XV imidazolide (22a) (120 mg) with the magnesium complex of methyl hydrogen malonate as described in (b) for the 2-vinyl and 2,4-divinyl cases gave the β-keto-ester (97 mg, 80%), m.p. 292—294° (from methylene chloride–n-hexane), identical with a sample prepared by the acid chloride approach.[1]

(c) *From the mixed carbonic anhydride* (21a). This preparation was carried out exactly as in (a), with a solution of the mixed carbonic anhydride (63 mg) in chloroform (5 ml). The final yield of β-keto-ester was 24 mg (40%).

(d) *From the carboxylic acid* (17a) via *the imidazolide zinc complex*. The porphyrin acid (17a) (55 mg) was refluxed for 1 h in methylene chloride (5 ml) with *NN'*-carbonyldiimidazole (25 mg) before a solution of zinc(II) acetate (100 mg) in methanol (5 ml) was added. The mixture was warmed gently during 5 min and methylene chloride (25 ml) was then added. The purple-green solution was washed with water (3 × 50 ml), dried ($MgSO_4$), and evaporated, and the residue was kept at 0·1 mmHg during 30 min. Methylene chloride (4 ml) was added and the solution was then added to a solution of malonate anion prepared in the usual way from sodium hydride dispersion (25 mg) and methyl t-butyl malonate (87 mg) in tetrahydrofuran (10 ml). The mixture was stirred at room temperature during 40 min and then added to chloroform (50 ml) and N-hydrochloric acid (20 ml). The organic phase was washed with water (2 × 50 ml), dried ($MgSO_4$), and evaporated and the residue was stirred for 40 min at room temperature with trifluoroacetic acid (5 ml) and then partitioned between water (100 ml) and chloroform (50 ml). The organic layer was washed with water (2 × 50 ml), dried ($MgSO_4$), and evaporated and the residue was chromatographed on alumina (grade V) (elution with methylene chloride containing 5% acetone). Evaporation of the eluates gave the β-keto-ester (21 mg, 34%), which was crystallised from methylene chloride–methanol.

(e) *From the pivalic anhydride* (20a) *and* 1 *equiv. of methyl t-butyl malonate*. This preparation was conducted exactly as in (a), by addition of the mixed pivalic anhydride (20a) (64 mg, 0·1 mmol) in methylene chloride (4 ml) to a stirred solution/suspension of methyl t-butyl malonate (17·5 mg, 0·1 mmol) and sodium hydride dispersion (9·2 mg, 0·2 mmol) in dry tetrahydrofuran (2·5 ml). After 5 min, the mixture was worked up as in (a) and gave the β-keto-ester (25·5 mg, 43%), identical with samples prepared earlier.

2,4,8-*Triethyl*-6-(*imidazol*-1-*ylcarbonyl*)-1,3,5,7-*tetramethylporphin* (24b).—The corresponding porphyrincarboxylic acid [8] (24a) (300 mg of a crude mixture containing acid, ester, and non-porphyrinic material) was refluxed with carbonyldi-imidazole (500 mg) in dry tetrahydrofuran (40 ml) and dry methylene chloride (30 ml) during 5 h. The solution was evaporated *in vacuo*, and the residue was chromatographed on alumina (grade III) in purified chloroform. Material from the faster-running band, on recrystallisation from methylene chloride–methanol, gave the methyl ester [8] (88 mg). The more polar band was eluted to give the *imidazolide* (140 mg) as red needles, m.p. 250—252° (Found: C, 74·3; H, 6·7; N, 15·4. $C_{34}H_{36}N_6O$ requires C, 75·0; H, 6·7; N, 15·4%), τ (0·03M) −0·60, 0·02, and 0·06 (2H) (4 *meso*-H), 1·57, 2·09, and 2·66 (3 imidazole H), 6·00 (q), 6·06 (q), and 8·19 (t) (3Et), and 6·38, 6·42, 6·52, and 6·54 (4Me), $\lambda_{max.}$ (CH_2Cl_2) 406 (ε 158,000), 509·5 (8900),

548 (14,400), 571 (9700), and 625 nm (600), $\lambda_{max.}$ (CH_2Cl_2–$CF_3{\cdot}CO_2H$) 411 (ε 243,000), 558 (11,100), and 608 nm (9200), *m/e* 544 (100%) and 457 (92).

2,4,8-*Triethyl*-6-(*methoxycarbonylacetyl*)-1,3,5,7-*tetramethylporphin* (24c).—A solution of isopropylmagnesium bromide in tetrahydrofuran was prepared by refluxing under dry nitrogen a mixture of magnesium turnings (0·24 g), isopropyl bromide (1·4 ml), and dry tetrahydrofuran (10 ml) until dissolution of the metal was complete. The solution was cooled, and methyl hydrogen malonate (0·55 ml) in tetrahydrofuran (2 ml) was added dropwise with stirring. The solution was stirred for a further 10 min and a solution of the foregoing imidazolide (85 mg) in dry tetrahydrofuran (20 ml) was then introduced. The mixture was refluxed (oil-bath at 75°) for 45 min; t.l.c. then indicated complete consumption of the imidazolide. After dilution with chloroform (100 ml) and acetic acid (1 ml), the mixture was refluxed for 10 min, cooled, washed with water (2 × 100 ml), and evaporated. Chromatography on alumina (grade V) (elution with methylene chloride containing 2% acetone) and crystallisation from chloroform–methanol gave the β-keto-ester (63 mg; 74%) as fine red needles. On the hot-stage, the compound was unchanged up to *ca.* 250°, and then darkened without melting (Found: C, 74·35; H, 6·8; N, 10·3. $C_{34}H_{38}N_4O_3$ requires C, 74·15; H, 7·0; N, 10·2%), τ (0·04M) (*ca.* 30% enol form) −0·48, −0·01, and 0·09 (2H) [*meso*-H (enol)], −0·68, 0·18 (2H), and 0·20 (*meso*-H (keto)], 3·85 (:CH, enol), 5·41 (CH_2, keto), 6·01, 6·29, 6·33, 6·46, and 6·54 (Me and OMe, enol), 6·12, 6·43(2), 6·50, and 6·58 (Me and OMe, keto), and 6·0, 8·20, and 8·22 (Et), $\lambda_{max.}$ (CH_2Cl_2) 407 (ε 165,000), 509 (11,000), 547 (13,500), 572 (9000), and 629 nm (1000), $\lambda_{max.}$ (CH_2Cl_2–$CF_3{\cdot}CO_2H$) 409 (ε 319,000), 554 (14,300), and 601 nm (8100), $\lambda_{max.}$ (CH_2Cl_2–0·1M-KOH–MeOH) 397 (ε 156,000), 499 (11,300), 535 (9600), 567 (5900), and 620 nm (2700). No parent ion was observed in the mass spectrum.

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