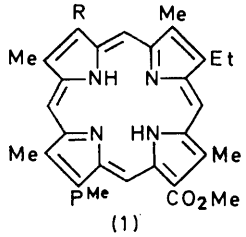
Pyrroles and Related Compounds. Part XXVII.[1] Syntheses of Porphyrins with a Nuclear Carboxy-group

By **T. Trefor Howarth, Anthony H. Jackson,†** and **George W. Kenner,*** The Robert Robinson Laboratories, University of Liverpool, P.O. Box 147, Liverpool L69 3BX

The synthesis of 2,6,7-triethyl-4-methoxycarbonyl-1,3,5,8-tetramethylporphin (2) by the *a*-oxobilane route is reported. The *b*-oxobilane approach is used in the synthesis of rhodoporphyrin-XV dimethyl ester (1a) and in the first total synthesis of 2-vinylrhodoporphyrin-XV dimethyl ester (1b); both of these compounds are important degradation products from chlorophyll-*a*. The vinyl group in the latter porphyrin was generated by elimination of hydrogen chloride from the zinc complex of the corresponding (2-chloroethyl)porphyrin. In order to minimise deactivation of the terminal rings during closure of the macrocycle, it was found to be advantageous to site the electron-withdrawing methoxycarbonyl functions on the internal rings of the open-chain tetrapyrrolic intermediates.

In order to apply some of the more promising β-keto-ester syntheses described in Part XXVI [1] to the porphyrin series, we required porphyrins with a carbonyl group directly attached to the macrocycle. Rhodoporphyrin-XV dimethyl ester (1a) is a well known example, readily accessible by degradation of chlorophyll-*a*, and the chlorophylls are an abundant source of this class of compound.[2] We foresaw the need, however, for other porphyrins not accessible by degradation, and consequently for versatile synthetic methods. Only a few such compounds were synthesised by H. Fischer [3a] because the pyrromethene method is inefficient when an ester group is present in one of the β-positions. A much-improved version of the pyrromethene synthesis has



(1)

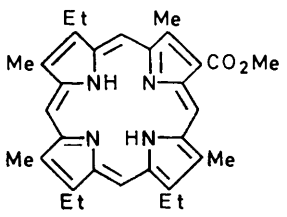
P^{Me} = $CH_2 \cdot CH_2 \cdot CO_2Me$

a; R = Et
b; R = CH:CH_2
c; R = $CH_2 \cdot CH_2 \cdot OAc$
d; R = $CH_2 \cdot CH_2 \cdot OH$
e; R = $CH_2 \cdot CH_2Cl$

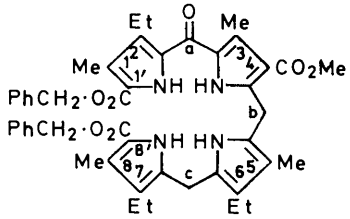
been devised,[4] and it gives satisfactory results in synthesis of rhodoporphyrins.[5] We have used this method to advantage in one instance,[6] but it would not serve for all our purposes.

At the time this investigation began we had recently developed two new general porphyrin syntheses,[7] namely the *a*-,[8] and *b*-oxobilane[9] methods. It was desirable to test the scope of each method in the synthesis of porphyrins containing a nuclear carboxy-group, and we began with a simple, but useful case, and the *a*-oxobilane method.

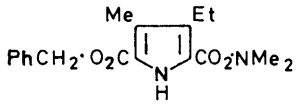
The key step in the *a*-oxobilane route to porphyrins is the cyclisation of a *b*-bilene-1′,8′-dicarboxylic acid hydrochloride by attack of an electrophilic one-carbon unit (trimethyl orthoformate) at the 1′- and 8′-positions. On account of the strongly electron-withdrawing nature of the key methoxycarbonyl substituent, we considered it advisable to site this function on one of the internal rings of the intermediate *a*-oxobilane; thus, we settled on the



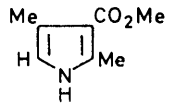
(2)



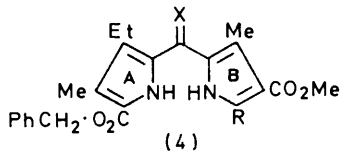
(3)



(5)



(6)



(4)

a; X = O, R = Me
b; X = $\overset{+}{N}Me_2$, R = Me
c; X = O, R = CH_2Cl

model porphyrin (2) as the initial synthetic target, and planned to approach this *via* the *a*-oxobilane (3).

The A–B pyrroketone (4a) was synthesised by methods

† *Present address:* Department of Chemistry, University College, Cardiff.

[1] Part XXVI, T. T. Howarth, A. H. Jackson, J. Judge, G. W. Kenner, and D. J. Newman, preceding paper.

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

[3] (*a*) H. Fischer and H. Orth, 'Die Chemie des Pyrrols,' Akademische Verlag, Leipzig, vol. IIi, 1937, pp. 319, 525; (*b*) for an analogous cleavage with bromine, see *ibid.*, vol. I, 1934, p 364.

[4] R. L. N. Harris, A. W. Johnson, and I. T. Kay, *J. Chem. Soc.* (*C*), 1966, 22.

[5] P. Bamfield, R. L. N. Harris, A. W. Johnson, I. T. Kay, and K. W. Shelton, *J. Chem. Soc.* (*C*), 1966, 1436.

[6] R. V. H. Jones, G. W. Kenner, and K. M. Smith, *J.C.S. Perkin I*, 1974, 531.

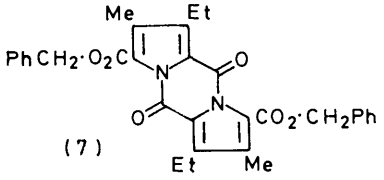
[7] A. H. Jackson, G. W. Kenner, G. McGillivray, and G. S. Sach, *J. Amer. Chem. Soc.*, 1965, **87**, 676.

[8] A. H. Jackson, G. W. Kenner, and G. S. Sach, *J. Chem. Soc.* (*C*), 1967, 2045.

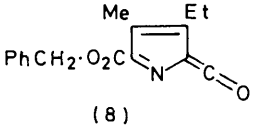
[9] A. H. Jackson, G. W. Kenner, G. McGillivray, and K. M. Smith, *J. Chem. Soc.* (*C*), 1968, 294.

which we have reported earlier.[10] Treatment of the phosphoryl chloride complex of the pyrrole amide (5) with 3-methoxycarbonyl-2,4-dimethylpyrrole (6) gave the imine salt (4b), which afforded the required pyrroketone (4a) in an overall yield of 70% when hydrolysed with aqueous sodium carbonate. Chlorination of the 5'-methyl group in (4a) with t-butyl hypochlorite (normally the reagent of choice for this transformation [8]) gave only low yields (15—20%) of the required 5'-chloromethylpyrroketone (4c); the major product from this reaction was the pyrrocoll (7), which was identified by comparison with an authentic sample.[11] In view of the 80—90% yield normally achieved in similar chlorinations (*e.g.* ref. 8) of pyrroketones bearing four alkyl β-substituents, we surmise that the anomalous product is obtained as a result of the electron-withdrawing effect of the methoxycarbonyl group, which is presumably deactivating the 5'-methyl group towards chlorination, and thereby allowing the reagent to cleave the pyrroketone link by reaction at the 2'-position, with the keten (8) as a possible intermediate.[3b]

Further investigation showed that treatment of the

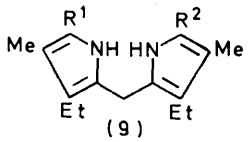


(7)



(8)

pyrroketone (4a) with sulphuryl chloride in tetrahydrofuran–ether gave a 63% yield of the required product (4c), which was obtained crystalline and was fully characterised.

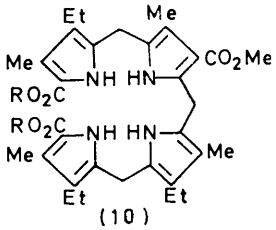


(9)

a; R^1 = R^2 = $CO_2{\cdot}CH_2Ph$
b; R^1 = $CO_2{\cdot}CH_2Ph$, R^2 = CO_2H
c; R^1 = R^2 = CO_2H
d; R^1 = $CO_2{\cdot}CH_2Ph$, R^2 = H

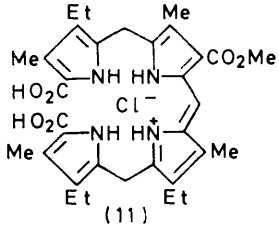
At the time this work was in progress, we had not developed our methods [12] for the differential protection of the 5- and 5'-carboxy-functions of pyrromethanes. Thus, the pyrromethane 5,5'-dibenzyl ester (9a) was hydrogenated over palladised charcoal until 1 mol. equiv. of hydrogen had been taken up. The resultant mixture of dibenzyl ester (9a), monoacid monoester (9b), and diacid (9c) was separated by extraction of their ethereal solution with 2N-sodium hydroxide. The aqueous solution, containing the disodium salt of the diacid (9c) was separated, leaving the diester (9a) and the sodium salt of the monoacid (9b) in the ether. Further extraction with water and acidification of the aqueous layer gave a 32% yield of the required C–D building block (9b).

The pyridinium salt of (4c) was coupled with the lithium salt of the pyrromethane-5'-carboxylic acid (9b) in formamide at 100° and gave the fully characterised



(10)

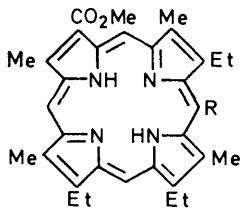
a; R = CH_2Ph
b; R = H



(11)

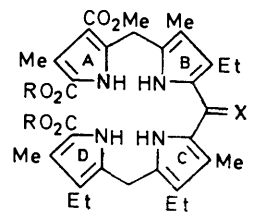
a-oxobilane 1',8'-dibenzyl ester (3) in 48% yield. Cyclisation of this compound to porphyrin followed the usual sequence of transformations; [8] reduction of the oxo-function with diborane * gave the bilane (10a), which was hydrogenated over palladised charcoal to afford the corresponding 1',8'-dicarboxylic acid (10b). Oxidation with t-butyl hypochlorite gave the *b*-bilene hydrochloride (11) (together with unknown quantities of the *a*- and *c*-bilenes, owing to random oxidation),† which was cyclised in methylene chloride containing trimethyl orthoformate and trichloroacetic acid, to give a 29% yield of the required porphyrin (2). The product was shown to be isomerically pure and free of other porphyrinic contaminants by t.l.c. and the usual physical techniques. Investigations into the synthesis of β-keto-esters using this compound are described in Part XXVIII.[13]

Having further extended the generality of the *a*-oxobilane synthesis as described above, we next turned to the more versatile *b*-oxobilane method, and decided to synthesise the porphyrin (12a) from the *b*-oxobilane (13a) bearing the methoxycarbonyl substituent on terminal ring A; in this way, we proposed to test our reservations



(12)

a; R = H b; R = OAc



(13)

a; X = O, R = CH_2Ph
b; X = $\overset{+}{N}Me_2$, R = CH_2Ph
c; X = O, R = H

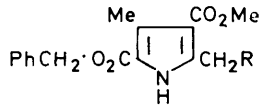
regarding closure of the macrocycle with a *b*-oxobilane deactivated in one of the terminal rings.

* Reduction was unusually slow, possibly owing to diminution of the dipolar character of the carbonyl group by the electron-withdrawing methoxycarbonyl function.

† *a*- and *c*-Bilenes are not cyclised to porphyrin under our normal conditions.

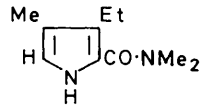
[10] J. A. Ballantine, A. H. Jackson, G. W. Kenner, and G. McGillivray, *Tetrahedron*, 1966, Suppl. 7, 241.
[11] J. A. Ballantine, I.C.I. Fellowship Report, Liverpool, 1961.
[12] P. J. Crook, A. H. Jackson, and G. W. Kenner, *J. Chem. Soc.* (*C*), 1971, 474.
[13] M. T. Cox, T. T. Howarth, A. H. Jackson, and G. W. Kenner, following paper.

The pyrroles (14a) and (15), heated under reflux in acetic acid containing sodium acetate,[14] gave a 64%

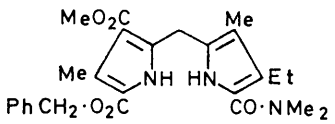


(14)

a; R = Cl
b; R = OAc



(15)

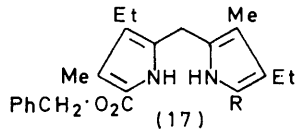


(16)

yield of the pyrromethane amide (16), together with 18% of the acetoxymethylpyrrole (14b), a readily separable by-product. Coupling of the phosphoryl chloride complex of (16) with the pyrromethane (9d) [obtained from the corresponding 5′-carboxylic acid (9b) by thermal decarboxylation] gave the imine salt (13b), which was purified chromatographically before being hydrolysed with aqueous sodium carbonate to the *b*-oxobilane 1′,8′-dibenzyl ester (13a). Debenzylation was accomplished by hydrogenation over palladised charcoal, and afforded the 1′,8′-dicarboxylic acid (13c) as an amorphous solid, in an overall yield of 42% from the pyrromethane amide (16). Cyclisation with trimethyl orthoformate and trichloroacetic acid in methylene chloride proceeded slowly; spectrophotometry indicated maximum formation of porphyrin after *ca.* 5 days. Even then, only a 21% yield of the *meso*-acetoxyporphyrin (12b) was obtained after treatment of the crude reaction mixture with acetic anhydride in pyridine. The product was shown to be pure by the usual spectroscopic methods, but in view of the low overall yield (*ca.* 9%) from pyrromethanes, this route, involving placement of the electron-withdrawing group on one of the terminal rings of the *b*-oxobilane, was abandoned.

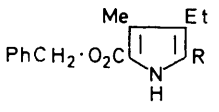
Rhodoporphyrin-XV dimethyl ester (1a), a more ambitious target, was next chosen for synthesis, and on account of the foregoing results, the methoxycarbonyl substituent was sited on an internal ring of the *b*-oxobilane. This particular synthetic target was chosen for two reasons. (i) Rhodoporphyrin-XV is an important degradation product from chlorophyll-*a*. (ii) Synthesis of the corresponding β-keto-ester [by elaboration of the 6-methoxycarbonyl substituent in (1a)] would furnish a compound which might eventually be cyclised to phaeoporphyrin-a_5, another important chlorophyll degradation product.

The more laborious part of the synthesis involved construction of the pyrromethanes (17a) and (18). Thus, treatment of the readily available pyrrolecarboxylic acid (19a) with thionyl chloride gave the acid chloride (19b), which was transformed into the corresponding t-butyl ester (19c) by treatment with t-butyl alcohol and *NN*-dimethylaniline. Catalytic hydrogenation afforded the pyrrolecarboxylic acid (20), the lithium salt of which was coupled with the pyridinium salt (21)



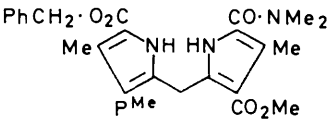
(17)

a; R = H
b; R = CO_2Bu^t
c; R = CHO

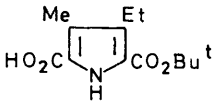


(19)

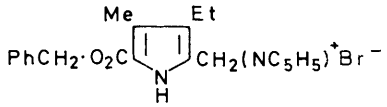
a; R = CO_2H
b; R = COCl
c; R = CO_2Bu^t



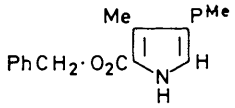
(18)



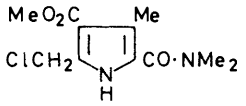
(20)



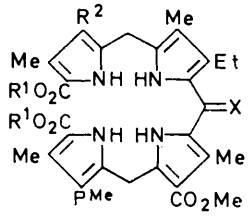
(21)



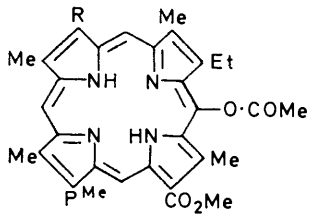
(22)



(23)



(24)



(25)

a; R^1 = CH_2Ph, X = $\overset{+}{N}Me_2$, R^2 = Et
b; R^1 = CH_2Ph, X = O, R^2 = Et
c; R^1 = H, X = O, R^2 = Et
d; R^1 = CH_2Ph, X = $\overset{+}{N}Me_2$, R^2 = $CH_2·CH_2·OAc$
e; R^1 = CH_2Ph, X = O, R^2 = $CH_2·CH_2·OAc$
f; R^1 = H, X = O, R^2 = $CH_2·CH_2·OAc$

a; R = Et
b; R = $CH_2·CH_2·OAc$

in formamide at 100°, to give a 41% yield of the pyrromethane (17b).* The 5′-unsubstituted pyrromethane (17a),† obtained from (17b) by treatment with cold tri-

* We have subsequently found that an improved yield of this pyrromethane can be obtained by coupling the corresponding 2-unsubstituted and 2-acetoxymethyl pyrroles in either methanol or acetic acid containing toluene-*p*-sulphonic acid; *cf.* ref. 15.

† The identity of this oily compound was established by treatment with the phosphoryl chloride complex of dimethylformamide; hydrolysis gave the 5-formyl compound (17c), which was fully characterised.

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

[15] J. A. S. Cavaleiro, A. M. d'A. R. Gonsalves, G. W. Kenner, and K. M. Smith, *J.C.S. Perkin I*, 1973, 2471.

fluoroacetic acid followed by a basic work-up, was then coupled with the phosphoryl chloride complex of the pyrromethane amide (18) [obtained by treatment of the pyrroles (22) and (23) with hot acetic acid containing sodium acetate [14]] * to give the tetrapyrrolic imine salt (24a), which was purified in the normal way [9] and then hydrolysed to the *b*-oxobilane 1′,8′-dibenzyl ester (24b). Hydrogenation over palladised charcoal gave the 1′,8′-dicarboxylic acid (24c), which was cyclised with trimethyl orthoformate–trichloroacetic acid; [9] treatment of the crude product with acetic anhydride in pyridine gave the required *meso*-acetoxyporphyrin (25a) in 50% yield from the *b*-oxobilane 1′,8′-dibenzyl ester (24b). Hydrogenation of (25a) over palladised charcoal, followed by treatment of the resultant colourless porphyrinogen solution with iodine–sodium acetate, gave a 60% yield of rhodoporphyrin-XV dimethyl ester (1a). Alternatively, oxidation of the porphyrinogen with air (in presence of a small amount of pyridine) gave a 79% yield of (1a); we have subsequently shown [16] that oxidation with 2,3-dichloro-5,6-dicyanobenzoquinone is even more efficient. This last method also has the advantage that oxidation to porphyrin is almost instantaneous.

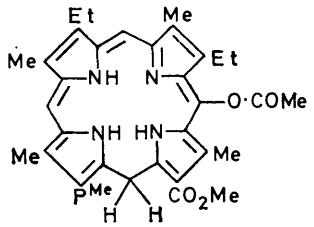
The identity of the final product, (1a), was established by all the normal spectroscopic techniques, as well as by elemental analysis, and confirmed by m.p. and mixed m.p. determination with authentic rhodoporphyrin-XV dimethyl ester, obtained by degradation of phaeophytins (*e.g.* ref. 2).

It is interesting that although hydrogenation of the *meso*-acetoxyporphyrin (25a) ultimately afforded a colourless solution of the porphyrinogen (*cf.* ref. 9), an intermediate blue colour was noted. When the reaction was monitored spectrophotometrically, it was shown that the absorption due to *meso*-acetoxyporphyrin [$\lambda_{max.}$ (tetrahydrofuran) 409, 511, 546, 584, and 638 nm] changed to that of a phlorin [17] (390, 570, and 605 nm); the latter also showed the expected changes [17] upon acidification. Moreover, when the hydrogenation was stopped at this ' blue ' stage and the mixture was oxidised with iodine, only the *meso*-acetoxyporphyrin (25a) was recovered. Thus, it appears that reduction to phlorin had occurred at the α-, γ-, or δ-position, since reduction at the β-position would give a species which would be expected to eliminate acetic acid and the ultimate product would have lacked the acetoxy-substituent. Electronically, it is reasonable to assume that the γ-position is the most electron-deficient (due to proximity of the 6-methoxycarbonyl function), and this is indicated by the n.m.r. spectrum, which shows the signal for that proton at low field. Since reduction would be expected to occur preferentially at the point of lowest electron density, we propose that the phlorin intermediate has the structure (26).

* Only a 5% yield of a similar pyrromethane was obtained by the pyridinium salt–lithium carboxylate method (Experimental section).

[16] S. W. McCombie, Ph.D. Thesis, Liverpool, 1972.
[17] R. B. Woodward, *Ind. chim. Belge*, 1962, **27**, 1293.

In order to complete the present series of experiments, we required the synthesis of a rhodoporphyrin bearing a vinyl substituent. Such a compound is 2-vinylrhodoporphyrin-XV dimethyl ester (1b), the 6-β-keto-ester

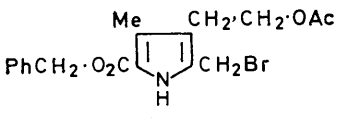


(26)

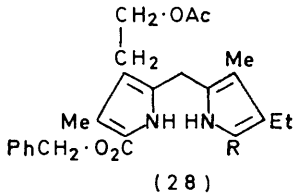
of which (after magnesiation and hydrolysis of the 7-propionic function), might be a precursor in the biosynthesis of the chlorophylls. Our plans for future biosynthetic investigations demanded not only the synthesis of the 2-vinyl-6-keto-ester, but also the 2,4-divinyl-6-keto-ester, and so we concentrated on the construction of the 2-vinyl compound (1b) in our initial experiments. The syntheses of the 2,4-divinyl analogue, and of the keto-ester derivatives of both 2-vinyl and 2,4-divinylrhodoporphyrins, are described in Part XXIX.[18]

Taking into account the success encountered in the *b*-oxobilane approach outlined above, we decided to adopt the same strategy once more, and moreover, to generate the vinyl substituent from the corresponding 2-chloroethyl group, as we had done in our successful syntheses of protoporphyrin-IX,[19] and of pemptoporphyrin and chlorocruoroporphyrin.[20]

Thus, the lithium salt of the pyrrolecarboxylic acid (20) was coupled with the pyridinium salt of the bromomethylpyrrole (27) and the pyrromethane (28a) was isolated as a pale yellow oil in 62% yield. Treatment with cold trifluoroacetic acid furnished the 5′-unsubstituted analogue (28b), which was coupled with the



(27)



(28)
a; R = CO_2Bu^t
b; R = H

phosphoryl chloride complex of the pyrromethane amide (18) to give the imine salt (24d). Chromatographic purification, followed by hydrolysis with sodium carbonate solution, afforded the *b*-oxobilane dibenzyl ester

[18] M. T. Cox, A. H. Jackson, G. W. Kenner, S. W. McCombie, and K. M. Smith, *J.C.S. Perkin I*, 1974, 516.
[19] R. P. Carr, A. H. Jackson, G. W. Kenner, and G. S. Sach, *J. Chem. Soc.* (*C*), 1971, 487.
[20] A. H. Jackson, G. W. Kenner, and J. Wass, *J.C.S. Perkin I*, 1974, 480.

(24e), which was isolated in good yield as a pale yellow oil. After catalytic hydrogenation [to give (24f)] and cyclisation with trimethyl orthoformate, the crude oxophlorin mixture was treated with acetic anhydride in pyridine, to give the *meso*-acetoxyporphyrin (25b) in 51% yield from (24e). Hydrogenation and reoxidation with air gave a 66% yield of the 2-(2-acetoxyethyl)-porphyrin (1c). As in the case of the hydrogenation of the *meso*-acetoxyrhodoporphyrin (25a), the reduction proceeded *via* a phlorin.

When the (2-acetoxyethyl)porphyrin (1c) was treated with 5% w/v sulphuric acid in methanol, the (2-hydroxyethyl)porphyrin (1d) was obtained in 95% yield. The latter was converted into the 2-chloroethyl derivative (1e) in 75% yield by treatment with mesyl chloride in pyridine. The 2-chloroethyl compound, in the form of its zinc chelate, was then treated with potassium t-butoxide in t-butyl alcohol, and after re-esterification and demetallation, 2-vinylrhodoporphyrin-XV dimethyl ester (1b) was obtained in 40% yield, thereby completing the first total synthesis of this important degradation product from chlorophyll-*a*. The structure of the synthetic product was confirmed by n.m.r. and mass spectroscopy, and by elemental analysis and mixed m.p. comparison with an authentic sample.

EXPERIMENTAL

M.p.s were measured on a microscope hot-stage apparatus. Neutral alumina (Woelm; Brockmann Grade III) was used for chromatographic separations, and reactions were followed by t.l.c. and spectroscopy as described in earlier parts of this series. Electronic spectra were measured with a Unicam SP 800 spectrophotometer, ^{1}H n.m.r. spectra with Varian A-60 and HA-100 spectrometers, and mass spectra with an A.E.I. MS9 instrument (at 50 μA and 70 eV, with direct inlet and source temperatures between 200 and 220°).

Pyrroles

Benzyl 3-Methoxycarbonyl-2,4-dimethylpyrrole-5-carboxylate.—Benzyl acetoacetate (260 g) in glacial acetic acid (500 ml) was cooled in an ice-bath and sodium nitrite (95 g) in water (150 ml) was added with stirring at such a rate that the reaction temperature was maintained at *ca.* 5°; the mixture was then left overnight at 0°. The solution was then added in portions, together with an intimate mixture of zinc powder (194 g) and anhydrous sodium acetate (194 g), to a vigorously stirred solution of methyl acetoacetate (173 g) in glacial acetic acid (400 ml) so that the reaction temperature was maintained at *ca.* 70°. During the addition, a solid separated, and this was redissolved by addition of more acetic acid (1 l). The cooled solution was decanted from the residual zinc into water (20 l) and the product was filtered off and dried *in vacuo* at 50°. Recrystallisation from aqueous methanol gave the *pyrrole* as fluffy needles (280 g, 72%), m.p. 141—142° (Found: C, 66·7; H, 5·9; N, 4·95. $C_{16}H_{17}NO_4$ requires C, 66·9; H, 6·0; N, 4·9%), τ ($CDCl_3$) 0·1br (NH), 2·68 and 4·70 ($PhCH_2$), 6·22 (OMe), and 7·42 and 7·54 (2Me), $\nu_{max.}$ (Nujol) 1675 and 1710 cm^{-1}.

Benzyl 2-Chloromethyl-3-methoxycarbonyl-4-methylpyrrole-5-carboxylate (14a).—The foregoing pyrrole (15 g) in glacial acetic acid (100 ml) was warmed on a water-bath at 50°, and sulphuryl chloride (4·23 ml) in glacial acetic acid (15 ml) was added with stirring during 30 min. The solution was then heated at 70° during 30 min and after cooling the *chloromethylpyrrole* crystallised as pink fluffy needles. Recrystallisation from benzene–petroleum (b.p. 40—60°) gave material (11·4 g, 65%) of m.p. 142—143° (Found: C, 59·7; H, 4·9; N, 4·6. $C_{16}H_{16}ClNO_4$ requires C, 59·7; H, 5·0; N, 4·35%), τ ($CDCl_3$) 0·08br (NH), 2·71 and 4·70 ($PhCH_2$), 5·13 (CH_2Cl), 6·21 (OMe), and 7·47 (4-Me), $\nu_{max.}$ (Nujol) 1665 and 1715 cm^{-1}.

Methyl 5-Dimethylcarbamoyl-2,4-dimethylpyrrole-3-carboxylate.—*NN*-Dimethylacetoacetamide (50 g, 0·388 mol) in glacial acetic acid (225 ml) was cooled in an ice-bath, and sodium nitrite (26·8 g, 0·388 mol) in water (40 ml) was added with stirring at such a rate that the reaction temperature was maintained at *ca.* 5°. The mixture was maintained, with stirring, at 0° during a further 2 h before it was added in portions, together with an intimate mixture of zinc powder (60·5 g, 0·854 mol) and anhydrous sodium acetate (60·5 g), to a stirred solution of methyl acetoacetate (53·75 g, 0·427 mol) in glacial acetic acid (90 ml), such that the reaction temperature was maintained at *ca.* 70°. The mixture was stirred for a further 1 h and finally heated under reflux for 3 h. The resultant pale yellow solution was decanted from the residual zinc into water (4 l) and after scratching the *product* separated as prisms (53·2 g, 62%), m.p. 152·5—154°. Recrystallisation from benzene–petroleum (b.p. 60—80°) raised the m.p. to 153·5—154·5° (Found: C, 59·2; H, 7·4; N, 12·5. $C_{11}H_{16}N_2O_3$ requires C, 58·9; H, 7·2; N, 12·5%), τ ($CDCl_3$) −0·6br (NH), 6·16 (OMe), 6·88 (NMe_2), and 7·57 and 7·71 (2Me), $\nu_{max.}$ (Nujol) 1600 and 1690 cm^{-1}, *m/e* 224 (M^+).

Methyl 2-(2-Chloroethyl)-5-dimethylcarbamoyl-4-methylpyrrole-3-carboxylate (23).—The foregoing pyrrole (3 g) in carbon tetrachloride (150 ml) was cooled to *ca.* 2°, and t-butyl hypochlorite (1·45 g, 1 equiv.) in carbon tetrachloride (15 ml) was added with stirring during 20 min (after 22 min, no colouration with starch–iodide paper was observed). The solvent was removed *in vacuo* at room temperature to give an orange semi-solid which was triturated with ether to give the *product* as prisms (2·8 g, 87%), m.p. 129·5—131·5° (decomp.). Recrystallisation from methylene chloride–petroleum (b.p. 40—60°) raised the m.p. to 131·5—133° (decomp.) (Found: C, 51·3; H, 6·05; N, 10·7. $C_{11}H_{15}ClN_2O_3$ requires C, 51·1; H, 5·8; N, 10·8%), τ ($CDCl_3$) −1·16br (NH), 5·10 (CH_2Cl), 6·14 (OMe), 6·88 (NMe_2), and 7·71 (4-Me), $\nu_{max.}$ (Nujol) 1590 and 1700 cm^{-1}, *m/e* 258 (M^+).

Methyl 5-Dimethylcarbamoyl-4-methyl-2-(pyridiniomethyl)-pyrrole-3-carboxylate Chloride.—The foregoing pyrrole (21·9 g) in chloroform (100 ml) and ether (100 ml) was treated with pyridine (8 ml) in chloroform (10 ml). The solution was left at 0° during 3 h, during which time a purple oil separated and crystallised. The solid was filtered off, washed with ether, and recrystallised from methanol–ether to give the *product* (19·9 g, 70%), m.p. 208—209° (decomp.) (Found: C, 56·9; H, 6·1; N, 12·2. $C_{16}H_{20}ClN_3O_3$ requires C, 56·9; H, 5·9; N, 12·4%), τ (D_2O) 1·3 and 3·70 ($C_5H_5N^+$·-CH_2), 6·03 (OMe), 6·71 (NMe_2), and 7·64 (4-Me), $\nu_{max.}$ (Nujol) 1625 and 1680 cm^{-1}.

t-Butyl 2-Benzyloxycarbonyl-4-ethyl-3-methylpyrrole-5-carboxylate (19c).—2-Benzyloxycarbonyl-4-ethyl-3-methylpyrrole-5-carboxylic acid (25 g) was dissolved in thionyl chloride (80 ml) and left at room temperature during 45 min. The solvent was removed *in vacuo* to give an off-white solid

which was used without further purification. (The i.r. spectrum was identical with that of an authentic sample of 2-benzyloxycarbonyl-4-ethyl-3-methylpyrrole-5-carbonyl chloride.[11]) To the crude acid chloride were added dry t-butyl alcohol (43 ml) and freshly distilled *NN*-dimethylaniline (29 ml) and the solution was heated at 70° during 2 h, then set aside at room temperature overnight. Methylene chloride (250 ml) was added and the solution was washed with 6N-sulphuric acid (4 × 200 ml), aqueous 10% sodium carbonate solution (200 ml), and water. After drying ($MgSO_4$), evaporation gave a blue oil which crystallised from petroleum (b.p. 40—60°). The off-white solid was filtered off (25·2 g) and recrystallised from petroleum (b.p. 40—60°) to give the *pyrrole* (22·8 g, 81%) as chunky prisms, m.p. 89—89·5° (Found: C, 69·8; H, 7·4; N, 4·2. $C_{20}H_{25}NO_4$ requires C, 69·95; H, 7·3; N, 4·1%), τ ($CDCl_3$) 0·66br (NH), 2·65 and 4·70 ($PhCH_2$), 7·32 (q) and 8·92 (t) (Et), 7·75 (3-Me), and 8·45 (Bu^t), $\nu_{max.}$ (Nujol) 1675 and 1695 cm^{-1}, *m/e* 343 (M^+).

3-Ethyl-4-methyl-2-t-butoxycarbonylpyrrole-5-carboxylic Acid (20).—The foregoing pyrrole (11·6 g) in tetrahydrofuran (120 ml) and triethylamine (6 drops) containing 10% palladised charcoal (1·16 g) was hydrogenated at room temperature and atmospheric pressure until uptake ceased (30 min). Filtration and evaporation gave the *product* (8·1 g, 94%) which crystallised from benzene–light petroleum (b.p. 60—80°) as prisms, m.p. 181° (decomp.) (Found: C, 61·75; H, 7·4; N, 5·5. $C_{13}H_{19}NO_4$ requires C, 61·6; H, 7·6; N, 5·5%), τ ($CDCl_3$) 0·58br (NH), 7·27 (q) and 8·88 (t) (Et), 7·68 (4-Me), and 8·41 (Bu^t), $\nu_{max.}$ (Nujol) 1660 and 1695 cm^{-1}.

Pyrroketones

Benzyl 3-Ethyl-4′-methoxycarbonyl-3′,4,5′-trimethylpyrroketone-5-carboxylate (4a).—Benzyl 2-dimethylcarbamoyl-3-ethyl-4-methylpyrrole-5-carboxylate[11] (15 g) in 1,2-dichloroethane (80 ml) was stirred in a flask fitted with a nitrogen gas inlet, a dropping funnel, and a reflux condenser equipped with guard tube. Phosphoryl chloride (4·93 ml, 1 equiv.) was added rapidly and the resulting solution was heated under reflux during 5 h. After cooling, the apparatus was flushed with nitrogen, and a slow stream of the gas was passed for the remainder of the reaction. Methyl 2,4-dimethylpyrrole-3-carboxylate[21] (7·3 g) in 1,2-dichloroethane (20 ml) was added to the mixture during *ca.* 15 min and the solution was then heated under reflux during 6 h. After this time, the absorption at *ca.* 400 nm had reached a maximum, so sodium carbonate (30 g) in water (300 ml) was added and the mixture was heated under reflux during 45 min with stirring. The *product* (18·1 g) crystallised overnight from the organic layer; recrystallisation from chloroform–petroleum (b.p. 40—60°) gave needles (14·1 g, 70%), m.p. 211—212° (Found: C, 68·0; H, 6·1: N, 6·5. $C_{24}H_{26}N_2O_5$ requires C, 68·2; H, 6·2; N, 6·6%), τ ($CDCl_3$) −0·16br and 0·66br (2NH), 2·58 and 4·64 ($PhCH_2$), 6·17 (OMe), 7·32 (q) and 8·94 (t) (Et), and 7·48, 7·68, and 7·82 (3Me), $\nu_{max.}$ (Nujol) 1570 and 1690 cm^{-1}, $\lambda_{max.}$ ($CHCl_3$) 303 (ε 13,600) and 339 nm (22,200), *m/e* 422 (M^+).

Benzyl 5′-Chloromethyl-3-ethyl-4′-methoxycarbonyl-3′,4-dimethylpyrroketone-5-carboxylate (4c).—The foregoing pyrroketone (6·0 g) in tetrahydrofuran (180 ml) and dry ether (180 ml) was stirred during the addition of sulphuryl chloride (1·27 ml, 1·1 equiv.) in carbon tetrachloride (20 ml) over 50 min. The solvents were evaporated off at room temperature and the semi-solid residue was triturated with ether (40 ml). The pink solid (4·4 g) was filtered off and recrystallised from methylene chloride–petroleum (b.p. 40—60°) to give the *product* as fluffy needles (4·1 g, 63%), m.p. 175·5—176° (decomp.) (Found: C, 63·4; H, 5·4; N, 5·9. $C_{24}H_{25}ClN_2O_5$ requires C, 63·1; H, 5·5; N, 6·1%), τ ($CDCl_3$) −0·05br and 0·75br (2NH), 2·48 and 4·57 ($PhCH_2$), 4·95 (CH_2Cl), 6·08 (OMe), 7·38 (q) and 8·90 (t) (Et), and 7·63 and 7·72 (2Me), $\nu_{max.}$ (Nujol) 1580, 1690, and 1700 cm^{-1}, *m/e* 456 (M^+).

Pyrromethanes

Benzyl 5′-Dimethylcarbamoyl-3-ethyl-3′-methoxycarbonyl-4,4′-dimethylpyrromethane-5-carboxylate.—To methyl 5-dimethylcarbamoyl-4-methyl-2-pyridiniomethylpyrrole-3-carboxylate chloride (12·4 g) in formamide (30 ml) was added a solution of 5-benzyloxycarbonyl-3-ethyl-4-methylpyrrole-2-carboxylic acid (10·5 g) and lithium methoxide (1·4 g) in formamide (100 ml). The solution was heated at 100° during 80 h under nitrogen before pouring into water, and the emulsion was extracted with ethyl acetate. A yellow solid which separated at the interface was filtered off and recrystallised from aqueous methanol to give yellow needles (1·2 g, 14%), m.p. >300°, shown to be *1,2-bis-(5-dimethylcarbamoyl-3-methoxycarbonyl-4-methylpyrrol-2-yl)-ethylene* (Found: C, 59·3; H, 6·4; N, 12·3. $C_{22}H_{28}N_4O_6$ requires C, 59·4; H, 6·4; N, 12·6%), τ ($CF_3{\cdot}CO_2H$) 1·92 (CH:CH), 5·92 (2OMe), 6·58 ($2NMe_2$), and 7·58 (2Me), $\lambda_{max.}$ (95% EtOH) 262 (ε 19,800) and 372 nm (16,100).

The ethyl acetate extract was dried ($MgSO_4$) and evaporated to dryness. After chromatography the required *pyrromethane* was recrystallised from chloroform–petroleum (b.p. 60—80°) to give needles (0·85 g, 5%), m.p. 174—175° (Found: C, 66·8; H, 6·6; N, 9·0. $C_{26}H_{31}N_3O_5$ requires C, 67·1; H, 6·7; N, 9·0%), τ ($CDCl_3$) −1·25br and −0·2br (2NH), 2·53 and 4·65 ($PhCH_2$), 5·86 (CH_2), 6·14 (OMe), 7·65 (q) and 9·01 (t) (Et), 6·91 (NMe_2), and 7·71 and 7·75 (2Me), $\nu_{max.}$ (Nujol) 1610 and 1710 cm^{-1}.

Benzyl 5′-Dimethylcarbamoyl-4′-ethyl-3-methoxycarbonyl-3′,4-dimethylpyrromethane-5-carboxylate (16).—(*a*) Benzyl 2-chloromethyl-3-methoxycarbonyl-4-methylpyrrole-5-carboxylate (6·42 g) in pyridine (6 ml) was added to a solution of 2-dimethylcarbamoyl-3-ethyl-4-methylpyrrole-5-carboxylic acid[11] (4·47 g) and lithium methoxide (0·76 g) in formamide (15 ml). The resulting solution was heated at 100° during 16 h under nitrogen, during which time a brown oil separated. After cooling, the solution was decanted and the oil was dissolved in methylene chloride and washed with 2N-hydrochloric acid (2 × 100 ml), aqueous 10% sodium carbonate (2 × 50 ml), and water, dried ($MgSO_4$), and evaporated. The residual brown gum crystallised from ether as pink needles (2·35 g), m.p. 194·5—198·5°. The *product* was recrystallised from methylene chloride–petroleum (b.p. 40—60°) to give fluffy needles (1·95 g, 21%), m.p. 203·5—204·5° (Found: C, 66·8; H, 6·75; N, 8·9. $C_{26}H_{31}N_3O_6$ requires C, 67·1; H, 6·7; N, 9·0%), τ ($CDCl_3$) 0·08br (2NH), 2·72 and 4·80 ($PhCH_2$), 5·82 (CH_2), 6·18 (OMe), 7·01 (NMe_2), 7·49 and 8·03 (2Me), and 7·55 (q) and 8·94 (t) (Et), $\nu_{max.}$ (Nujol) 1580 and 1695 cm^{-1}, *m/e* 465 (M^+).

Evaporation of the mother liquors gave minute prisms, shown by i.r. to be 2-dimethylcarbamoyl-3-ethyl-4-methylpyrrole (0·68 g, 19%).

[21] R. Fletcher, A. H. Jackson, and G. W. Kenner, unpublished results.

(*b*) To a solution of sodium acetate (1·26 g) in glacial acetic acid (80 ml) were added 2-dimethylcarbamoyl-3-ethyl-4-methylpyrrole [10] (2·5 g) and benzyl 2-chloromethyl-3-methoxycarbonyl-4-methylpyrrole-5-carboxylate (3·6 g), and the mixture was heated at 110° during 30 min. After slight cooling, the solution was poured into water (250 ml) and the resulting emulsion was extracted with chloroform (2 × 100 ml), which was then washed with water, dried ($MgSO_4$), and evaporated. The residual oil was triturated with ether. The product was filtered off and recrystallised from methylene chloride–petroleum (b.p. 60—80°) to give fluffy needles (3·34 g, 64%), m.p. 203—204°, identical (t.l.c., i.r.) with the material synthesised in (*a*).

The ethereal mother liquors yielded a second product, *benzyl 2-acetoxymethyl-3-methoxycarbonyl-4-methylpyrrole-5-carboxylate* (0·48 g, 13%), m.p. 173·5—174° (Found: C, 62·4; H, 5·6; N, 4·1. $C_{18}H_{19}NO_6$ requires C, 62·6; H, 5·6; N, 4·1%), τ ($CDCl_3$) 0·5br (NH), 2·63 and 4·67 ($PhCH_2$), 4·77 and 7·89 ($CH_2O{\cdot}COMe$), 6·18 (OMe), and 7·43 (4-Me), $\nu_{max.}$ (Nujol) 1675, 1710, and 1730 cm^{-1}.

Benzyl 5′-Dimethylcarbamoyl-3′-methoxycarbonyl-3-(2-methoxycarbonylethyl)-4,4′-dimethylpyrromethane-5-carboxylate (18).—This compound was prepared as described in the foregoing method (*b*), from anhydrous sodium acetate (1·85 g), glacial acetic acid (180 ml), benzyl 4-(2-methoxycarbonylethyl)-3-methylpyrrole-2-carboxylate [12] (6·3 g), and methyl 2-chloromethyl-5-dimethylcarbamoyl-4-methylpyrrole-3-carboxylate (5·44 g). Recrystallisation from benzene–petroleum (b.p. 60—80°) gave *needles* (4·39 g, 40%), m.p. 136—137° (Found: C, 64·4; H, 6·25; N, 7·8. $C_{28}H_{33}N_3O_7$ requires C, 64·2; H, 6·35; N, 8·0%), τ ($CDCl_3$) −0·66br and 0·03br (2NH), 2·67 and 4·75 ($PhCH_2$), 5·88 (CH_2), 6·23 (OMe), 6·35 (s) and 7·4 (m) ($MeO_2C{\cdot}CH_2{\cdot}CH_2$), 7·00 ($NMe_2$), and 7·76 and 7·79 (2Me), $\nu_{max.}$ (Nujol) 1610, 1700, 1725, and 1755 cm^{-1}, *m/e* 523 (M^+).

t-Butyl 5′-Benzyloxycarbonyl-3′,4-diethyl-3,4′-dimethylpyrromethane-5-carboxylate (17b).—2-t-Butoxycarbonyl-3-ethyl-4-methylpyrrole-5-carboxylic acid (10·12 g) and lithium methoxide (1·52 g) were dissolved in formamide (80 ml) and treated with the pyridinio-derivative of benzyl 2-bromomethyl-3-ethyl-4-methylpyrrole-5-carboxylate (16·6 g). The solution was heated at 100° during 15 h under nitrogen, during which time a dark oil separated; this was dissolved in methylene chloride after decantation. After washing well with water, the methylene chloride solution was dried ($MgSO_4$) and evaporated to dryness, and the residue was chromatographed, eluting first with petroleum (b.p. 60—80°) and then with 1 : 1 benzene–petroleum (b.p. 60—80°). A pale orange gum was obtained by evaporation of the eluate shown by t.l.c. (pink colouration with bromine vapour) to contain pyrromethane. Crystallisation from petroleum (b.p. 60—80°) gave the *product* (7·7 g, 41%) as prisms, m.p. 133—135° (Found: C, 72·6; H, 7·75; N, 6·1. $C_{28}H_{36}N_2O_4$ requires C, 72·4; H, 7·8; N, 6·0%), τ ($CDCl_3$) 1·03br and 1·33br (2NH), 2·68 and 4·74 ($PhCH_2$), 6·18 (CH_2), 7·31 (q), 7·61 (q), 8·91 (t), and 8·98 (t) (2Et), 7·72 and 8·06 (2Me), and 8·50 (Bu^t), $\nu_{max.}$ (Nujol) 1670 and 1700 cm^{-1}, *m/e* 464 (M^+).

Benzyl 3′,4-Diethyl-5-formyl-3,4′-dimethylpyrromethane-5′-carboxylate (17c).—The foregoing pyrromethane (0·5 g) in trifluoroacetic acid (10 ml) was set aside during 15 min before being evaporated to dryness. The residual oil was dissolved in methylene chloride (50 ml) and washed with aqueous 10% sodium carbonate solution (100 ml) and then water (2 × 50 ml). The solution was dried ($MgSO_4$) and evaporated and the residue, in dry methylene chloride (10 ml) was treated with the phosphoryl chloride complex of dimethylformamide (*ca.* 700 mg) in dry methylene chloride (10 ml) during 20 min. Aqueous 10% sodium carbonate (50 ml) was then added and the mixture was heated under reflux with stirring during 1 h. The organic layer was separated, washed with water, and dried ($MgSO_4$). The solvent was removed *in vacuo* and the residual oil crystallised from ether as cream prisms. The *product* was recrystallised from methylene chloride–petroleum (b.p. 60—80°) to give needles (0·21 g, 48%), m.p. 163—164° (Found: C, 73·3; H, 7·0; N, 7·0. $C_{24}H_{28}N_2O_3$ requires C, 73·4; H, 7·2; N, 7·1%), τ ($CDCl_3$) −1·00br and −0·38br (2NH), 0·58 (CHO), 2·76, and 4·78 ($PhCH_2$), 6·21 (CH_2), 7·37 (q), 7·54 (q), 8·86 (t), and 8·98 (t) (2Et), and 7·73 and 7·99 (2Me), $\nu_{max.}$ (Nujol) 1635 and 1690 cm^{-1}.

t-Butyl 3′-(2-Acetoxyethyl)-5′-benzyloxycarbonyl-4-ethyl-3,4′-dimethylpyrromethane-5-carboxylate (28a).—2-t-Butoxycarbonyl-3-ethyl-4-methylpyrrole-5-carboxylic acid (3·21 g) and lithium methoxide (0·48 g) dissolved in formamide (30 ml) were treated with benzyl 3-(2-acetoxyethyl)-4-methyl-2-pyridiniomethylpyrrole-5-carboxylate bromide (6·0 g).[19] The solution was heated at 100° during 20 h, during which time a brown oil separated, which was decanted, and dissolved in methylene chloride (200 ml). The solution was washed with N-hydrochloric acid, aqueous 10% sodium carbonate (100 ml), and water, dried ($MgSO_4$), and evaporated, and the residual gum was chromatographed. Elution with benzene gave a pale yellow gum (3·5 g, 62%) which could not be induced to crystallise. T.l.c. showed the product to be one component and its structure was confirmed by n.m.r.: τ ($CDCl_3$) 0·11br and 0·70br (2NH), 2·74 and 4·76 ($PhCH_2$), 6·14 (CH_2), 6·00 (t), 7·32 (m), and 8·04 (s) ($CH_2{\cdot}CH_2{\cdot}O{\cdot}COMe$), 7·32 (m) and 8·91 (t) (Et), 7·72 and 8·06 (2Me), and 8·52 (Bu^t).

Oxobilanes

Dibenzyl 2,6,7-Triethyl-4-methoxycarbonyl-1,3,5,8-tetramethyl-a-oxobilane-1′,8′-dicarboxylate (3).—Benzyl 5′-chloromethyl-3-ethyl-4′-methoxycarbonyl-3′,4-dimethylpyrroketone-5-carboxylate (1·0 g) in pyridine (1·8 ml) was treated with a solution of 5′-benzyloxycarbonyl-3,3′-diethyl-4,4′-dimethylpyrromethane-5-carboxylic acid [22] (0·89 g) and lithium methoxide (0·085 g) in formamide (45 ml). The resulting solution was heated at 100° under nitrogen during 5 h, during which time a brown oil separated. The solution was allowed to cool and left overnight. The supernatant was decanted from the brown gum, which was washed with formamide (2 × 50 ml) and water (2 × 100 ml). The gum was dissolved in methylene chloride (50 ml) and washed with water several times; the solution was dried ($MgSO_4$) and evaporated. The residual oil crystallised from ether–methanol (1 : 2). Recrystallisation from methylene chloride–methanol gave yellow *prisms* (0·813 g, 48%), m.p. 166—168° (Found: C, 71·8; H, 6·6; N, 6·95. $C_{47}H_{52}N_4O_7$ requires C, 71·9; H, 6·7; N, 7·1%), τ ($CDCl_3$) 0·87br and 1·2br (4NH), 2·69, 2·78, 4·76, and 4·96 ($2PhCH_2$), 5·98 and 6·27 ($2CH_2$), 6·27 (OMe), 7·65 (6H, m) and 9·04 (9H, m) (3Et), and 7·77, 7·78, 7·89, and 8·06 (4Me), $\nu_{max.}$ (Nujol) 1575, 1660, and 1690 cm^{-1}, $\lambda_{max.}$ ($CHCl_3$) 288 (ε 29,700) and 338 nm (20,800), *m/e* 784 (M^+).

[22] T. T. Howarth, Ph.D. Thesis, Liverpool, 1967; M. J. Broadhurst, R. Grigg, and A. W. Johnson, *J. Chem. Soc.* (*C*), 1971, 3681.

Dibenzyl 4,6,7-*Triethyl*-2-*methoxycarbonyl*-1,3,5,8-*tetramethyl*-b-*oxobilane*-1′,8′-*dicarboxylate* (13a).—Benzyl 5′-dimethylcarbamoyl-4′-ethyl-3-methoxycarbonyl-3′,4-dimethylpyrromethane-5-carboxylate (3·72 g) was dissolved in phosphoryl chloride (19 ml) and warmed at 50° during 1 h before evaporation; the last traces of phosphoryl chloride were removed by adding ethylene dibromide and repeated evaporation to dryness.

Meanwhile, 5′-benzyloxycarbonyl-3,3′-diethyl-4,4′-dimethylpyrromethane-5-carboxylic acid [22] (3·3 g) was heated *in vacuo* at 180° during 1 h, after which time the evolution of carbon dioxide had ceased. The colourless oil was dissolved in methylene chloride (10 ml) and added to the phosphoryl chloride complex in methylene chloride (15 ml), and a slow stream of nitrogen was passed through the mixture for the remainder of the reaction. After 18 h at 40° the unsubstituted pyrromethane obtained from a further 3·3 g of pyrromethanecarboxylic acid was added, and the reaction was continued for 16 h. The mixture was diluted with methylene chloride (65 ml) and washed with water (2 × 100 ml). After drying ($MgSO_4$) the solution was evaporated to dryness and the oil was chromatographed. Elution with 1 : 4 ethyl acetate–benzene removed most of the non-polar by-products and the required imine salt ($\lambda_{max.}$ 410 nm) was eluted with ethyl acetate–benzene (1 : 3) and finally methanol. The solvents were removed *in vacuo* and the residual deep yellow oil was dissolved in methylene chloride (70 ml), to which was added aqueous 10% sodium carbonate (100 ml). The mixture was heated under reflux during 1·5 h, after which time the absorption at 410 nm had disappeared. The organic layer was separated, washed with water (2 × 100 ml), dried ($MgSO_4$), and evaporated. The resulting brown foam (3·8 g) could not be induced to crystallise. T.l.c. indicated that it was essentially one component and the u.v. spectrum [$\lambda_{max.}$ (CH_2Cl_2) 352 nm] was consistent with a *b*-oxobilane. This material was used in subsequent experiments without further purification.

Dibenzyl 5,7-*Diethyl*-3-*methoxycarbonyl*-2-(2-*methoxycarbonylethyl*)-1,4,6,8-*tetramethyl*-b-*oxobilane*-1′,8′-*dicarboxylate* (24b).—Benzyl 5′-dimethylcarbamoyl-3′-methoxycarbonyl-3-(2-methoxycarbonylethyl)-4,4′-dimethylpyrromethane-5-carboxylate (4·72 g) was dissolved in phosphoryl chloride (30 ml) and warmed at 50° during 45 min. The solvent was removed *in vacuo* (' chasing ' with ethylene dibromide).

Meanwhile, t-butyl 5′-benzyloxycarbonyl-3′,4-diethyl-3,4′-dimethylpyrromethane-5-carboxylate (4·58 g) was dissolved in methylene chloride (20 ml) and treated with trifluoroacetic acid (60 ml). A slow stream of nitrogen was passed through the solution, which was kept at room temperature during 1 h. The solvents were removed *in vacuo* and the residual oil was dissolved in methylene chloride (100 ml). The solution was washed with aqueous 10% sodium carbonate (2 × 50 ml) and then water (2 × 50 ml), dried ($MgSO_4$), and evaporated. The residue was taken up in methylene chloride (15 ml) and added to the phosphoryl chloride complex; nitrogen was passed through this mixture at 40° during 15 h before the solution was diluted with methylene chloride (85 ml) and washed with water (3 × 100 ml). After drying ($MgSO_4$) the solution was evaporated to dryness and the dark oil was chromatographed. By-products and starting materials were eluted with ethyl acetate–benzene (1 : 4); elution with methanol then gave the imine salt ($\lambda_{max.}$ 402 nm) as a bright yellow oil. The oil was taken up in methylene chloride (100 ml), treated with aqueous 10% sodium carbonate (100 ml), and then stirred with heating under reflux during 3·5 h, after which time the absorption at 402 nm had disappeared. The methylene chloride layer was separated, washed with water (2 × 100 ml), and dried ($MgSO_4$). Removal of the solvent *in vacuo* gave a brown oil which was chromatographed, the product being eluted with ethyl acetate–benzene (1 : 9) to give a pale brown oil (3·1 g, 42%) which could not be induced to crystallise. T.l.c. confirmed that the product was one component and this material was used without further purification in subsequent reactions.

Dibenzyl 7-(2-*Acetoxyethyl*)-5-*ethyl*-3-*methoxycarbonyl*-2-(2-*methoxycarbonylethyl*)-1,4,6,8-*tetramethyl*-b-*oxobilane*-1′,8′-*dicarboxylate* (24e).—This compound was prepared from benzyl 5′-dimethylcarbamoyl-3′-methoxycarbonyl-3-(2-methoxycarbonylethyl)-4,4′-dimethylpyrromethane-5-carboxylate (3·18 g) and t-butyl 3′-(2-acetoxyethyl)-5′-benzyloxycarbonyl-4-ethyl-3,4′-dimethylpyrromethane-5-carboxylate (3·5 g) under conditions similar to those for (24b). The product was obtained as a pale brown oil (2·4 g, 39%).

4,6,7-*Triethyl*-2-*methoxycarbonyl*-1,3,5,8-*tetramethyl*-b-*oxobilane*-1′,8′-*dicarboxylic Acid* (13c).—Dibenzyl 4,6,7-triethyl-2-methoxycarbonyl-1,3,5,8-tetramethyl-*b*-oxobilane-1′,8′-dicarboxylate (1·7 g) in tetrahydrofuran (30 ml) and triethylamine (2 drops) was hydrogenated at room temperature and atmospheric pressure over 10% palladised charcoal (0·3 g) until uptake had ceased (3 h). The catalyst was filtered off; after evaporation, trituration with ether gave the dicarboxylic acid (0·92 g, 70%) as an amorphous solid which was not further purified.

5,7-*Diethyl*-3-*methoxycarbonyl*-2-(2-*methoxycarbonylethyl*)-1,4,6,8-*tetramethyl*-b-*oxobilane*-1′,8′-*dicarboxylic Acid* (24c).—This compound, prepared in an analogous manner from the corresponding dibenzyl ester (24b) (3·1 g), was obtained as a pale yellow oil (2·3 g, 95%).

7-(2-*Acetoxyethyl*)-5-*ethyl*-3-*methoxycarbonyl*-2-(2-*methoxycarbonylethyl*)-1,4,6,8-*tetramethyl*-b-*oxobilane*-1′,8′-*dicarboxylic Acid* (24f).—Prepared in a similar manner, this was obtained in 95% yield (1·8 g) from the corresponding dibenzyl ester (2·4 g).

Porphyrins

2,6,7-*Triethyl*-4-*methoxycarbonyl*-1,3,5,8-*tetramethylporphin* (2).—(a) *Reduction of dibenzyl* 2,6,7-*triethyl*-4-*methoxycarbonyl*-1,3,5,8-*tetramethyl*-a-*oxobilane*-1′,8′-*dicarboxylate* (3) *with diborane*. The *a*-oxobilane (2·82 g, 3·6 mmol) in dry tetrahydrofuran (105 ml) and ethyl acetate (105 ml) was reduced externally with diborane generated from sodium borohydride (1·75 g) in bis-(2-methoxyethyl) ether (64 ml) and boron trifluoride–ether complex (17·52 ml) in bis-(2-methoxyethyl) ether (48 ml). The reduction was followed spectroscopically as described in earlier parts of this series, and after 6 h the absorption at 338 nm had disappeared. The solution was evaporated to dryness and the residual gum was used directly in the next step.

(b) *Catalytic debenzylation*. The foregoing residue, in dry methanol (78 ml), was diluted with dry tetrahydrofuran (75 ml) and 15% triethylamine in tetrahydrofuran (5 drops) and then hydrogenated over palladised charcoal (10%; 1·56 g) at room temperature and atmospheric pressure during 12 h. The catalyst was filtered off on ' Hiflo ' under nitrogen and the residue obtained on evaporation was dissolved in dry peroxide-free ether, which was then evaporated off (to remove traces of methanol and tetrahydrofuran).

(c) *Oxidation with t-butyl hypochlorite*. The foregoing

bilanedicarboxylic acid dissolved in dry tetrahydrofuran (150 ml) was diluted with dry peroxide-free ether (450 ml). The flask was flushed with nitrogen and a slow stream of nitrogen was passed for the remainder of the reaction. The stirred solution was cooled to −15° and t-butyl hypochlorite (0·432 ml, 3·6 mmol) was added during 75 min in the dark. After a further 10 min the solution gave a negative test with starch–iodide paper. It was allowed to warm to room temperature, and the solvents were removed *in vacuo* to give a red solid (1·94 g), which exhibited the expected absorption at 525 nm.

(d) *Macrocycle formation and oxidation to porphyrin.* The foregoing bilene hydrochloride (1·92 g) in methylene chloride (614 ml) and trimethyl orthoformate (6·66 ml) was added to a solution of trichloroacetic acid (30·08 g) in methylene chloride (614 ml) and the flask was flushed with oxygen. The mixture was stirred overnight in the dark, washed with aqueous 10% sodium carbonate (3 × 450 ml) and water (3 × 450 ml), dried ($MgSO_4$), and evaporated. The residue was chromatographed, with methylene chloride as eluant. Evaporation of the porphyrin eluates gave a red solid (564 mg), which crystallised from methylene chloride–petroleum (b.p. 60—80°) to give the *porphyrin* (544 mg, 30%) as purple needles, m.p. 335° (birefringence lost at 310°) (Found: C, 75·8; H, 7·2; N, 10·8. $C_{32}H_{36}N_4O_2$ requires C, 75·5; H, 7·15; N, 11·0%), τ (0·07M in $CDCl_3$) −1·03, −0·05, 0·11, and 0·12 (4 *meso*-H), 5·66 (OMe), 6·0 (6H, m) and 8·2 (9H, m) (3Et), 6·17, 6·40, 6·48, and 6·56 (4Me), and 14·0br (2NH), τ ($CF_3{\cdot}CO_2H$) −1·73, −1·13, −0·94, and −0·88 (4 *meso*-H), 5·38 (OMe), 5·78 (6H, m) and 8·18 (9H, m) (3Et), 5·91 (3-Me), 6·24 (1-, 5-, and 8-Me), and 14·0br (NH), $\lambda_{max.}$ ($CHCl_3$) 404 (ε 187,000), 510 (9750), 548 (15,100), 575 (8390), and 633 nm (1580), $\lambda_{max.}$ ($CHCl_3$–HCl) 422 (ε 207,000), 563 (12,600), and 611 nm (10,900), $\nu_{max.}$ (KBr) 1695 cm^{-1}, *m/e* 508 (M^+).

β-*Acetoxy*-4,6,7-*triethyl*-2-*methoxycarbonyl*-1,3,5,8-*tetramethylporphin* (12b).—To 4,6,7-triethyl-2-methoxycarbonyl-1,3,5,8-tetramethyl-*b*-oxobilane-1′,8′-dicarboxylic acid (0·241 g) in methylene chloride (40 ml) was added freshly dried trichloroacetic acid (3·94 g) in methylene chloride (24 ml). Methylene chloride (96 ml) and then trimethyl orthoformate (0·852 ml) were added and the solution was then stirred in the dark during 7 days. During this time a peak at 420 nm appeared in the visible spectrum and this had reached a maximum after *ca.* 5 days. Pyridine (2 ml) was added and the green solution was evaporated *in vacuo*. To the residue were added pyridine (56 ml) and acetic anhydride (16 ml) and after 2 h the solvents were removed *in vacuo*. The residue was dissolved in methylene chloride (100 ml); the solution was washed with water (2 × 50 ml), dried ($MgSO_4$), and evaporated to dryness. Chromatography of the residue (elution with methylene chloride) gave a red solid. Recrystallisation from methylene chloride–methanol gave the *porphyrin* (45 mg, 21%) as red-brown fluffy needles, m.p. 267—269° (Found: C, 72·0; H, 7·0; N, 9·8. $C_{34}H_{38}N_4O_4$ requires C, 72·1; H, 6·8; N, 9·9%), τ (0·08M in $CDCl_3$) −0·90, 0·42, and 0·91 (3 *meso*-H), 5·73 (OMe), 6·3 (6H, m) and 8·3 (9H, m) (3Et), 6·46 (1-Me), 6·67, 6·71, and 7·04 (3-, 5-, and 8-Me), 7·15 (Ac), and 14·25br (2NH), $\lambda_{max.}$ ($CHCl_3$) 410 (ε 224,000), 512 (12,600), 549 (12,500), 580 (7120), and 637 nm (1150), $\lambda_{max.}$ ($CHCl_3$–HCl) 421 (ε 245,000), 558 (16,200), and 604 nm (9400), *m/e* 566 (M^+).

β-*Acetoxy*-2,4-*diethyl*-6-*methoxycarbonyl*-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethylporphin* (25a).—To 5,7-diethyl-2-(2-methoxycarbonylethyl)-3-methoxycarbonyl-1,4,6,8-tetramethyl-*b*-oxobilane-1′,8′-dicarboxylic acid (2·5 g) in methylene chloride (300 ml) was added trichloroacetic acid (29·43 g) in methylene chloride (180 ml). Methylene chloride (720 ml) and trimethyl orthoformate (6·39 ml) were then added and the solution was stirred in the dark during 2 h ($\lambda_{max.}$ 510 nm at this point) before addition of pyridine (15 ml). After stirring for a further 16 h, the green ($\lambda_{max.}$ 396, 630, and 690 nm) solution was evaporated to dryness and the residue was treated with pyridine (56 ml) and acetic anhydride (16 ml). The red solution was set aside for 2 h and was then evaporated to dryness; a solution of the residue in methylene chloride (200 ml) was washed with water (2 × 200 ml), dried ($MgSO_4$), and evaporated and the residue was chromatographed, with methylene chloride as eluant. The resulting red solid was crystallised from methylene chloride–methanol to give the *porphyrin* (1·126 g, 50%) as red-brown fluffy needles, m.p. 220—222° (Found: C, 69·1; H, 6·3; N, 8·9. $C_{36}H_{40}N_4O_6$ requires C, 69·2; H, 6·45; N, 9·0%), τ (0·08M in $CDCl_3$) −0·53, 0·42, and 0·84 (3 *meso*-H), 5·63 (6-CO_2Me), 6·05 (m), 8·28 (t), and 8·32 (t) (2Et), *ca.* 6·1 (m), 6·9 (m), and 6·42 (s) ($CH_2{\cdot}CH_2{\cdot}CO_2Me$), 6·30 (5-Me), 6·59 (3-Me), 6·88 (1- and 8-Me), 7·16 (COMe), and 13·83br (2NH), $\lambda_{max.}$ ($CHCl_3$) 407 (ε 190,000), 510 (12,000), 547 (9550), 579 (6740), and 633 nm (1470), $\lambda_{max.}$ ($CHCl_3$–HCl) 430 (ε 244,000), 567 (11,900), and 610 nm (9310), *m/e* 624 (M^+).

β-*Acetoxy*-2-(2-*acetoxyethyl*)-4-*ethyl*-6-*methoxycarbonyl*-7-(2-*methoxycarbonylethyl*)-1,3,5,7-*tetramethylporphin* (25b).—This compound, prepared in an identical manner to (25a) from 7-(2-acetoxyethyl)-5-ethyl-3-methoxycarbonyl-2-(2-methoxycarbonylethyl)-1,4,6,8-tetramethyl-*b*-oxobilane-1′,8′-dicarboxylic acid (1·8 g), was obtained from chloroform–methanol with m.p. 238—240° as red fluffy *needles* (0·865 g, 51%) (Found: C, 66·6; H, 6·25; N, 8·3. $C_{38}H_{42}N_4O_8$ requires C, 66·8; H, 6·2; N, 8·2%), τ (0·08M in $CDCl_3$) −0·49, 0·46, and 1·01 (3 *meso*-H), 5·64 (6-CO_2Me), *ca.* 6·1 (m), 6·93 (m), and 6·43 (s) ($CH_2{\cdot}CH_2{\cdot}CO_2Me$), *ca.* 6·2 (m), 5·47 (t), and 8·04 (s) ($CH_2{\cdot}CH_2{\cdot}O{\cdot}COMe$), 6·31 (5-Me), 6·58 (3-Me), 7·00 and 7·05 (1- and 8-Me) 7·14 (COMe), and 14·4br (2NH), $\lambda_{max.}$ ($CHCl_3$) 410 (ε 228,000), 511 (13,100), 548 (11,700), 579 (7520), and 634 nm (1420), $\lambda_{max.}$ ($CHCl_3$–HCl) 430 (ε 256,000), 568 (12,700), and 616 nm (10,600).

2,4-*Diethyl*-6-*methoxycarbonyl*-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethylporphin* ('*Rhodoporphyrin*-XV *Dimethyl Ester*') (1a).—β-Acetoxy-2,4-diethyl-6-methoxycarbonyl-7-(2-methoxycarbonylethyl)-1,3,5,8-tetramethylporphin (300 mg) in tetrahydrofuran (240 ml) containing triethylamine (3 drops) and 10% palladised charcoal (300 mg) was hydrogenated at room temperature and atmospheric pressure duriug 4 h, after which time the solution was colourless. {During the hydrogenation the solution changed from red to blue [$\lambda_{max.}$ (tetrahydrofuran) 390, 570, and 605 nm; $\lambda_{max.}$ (tetrahydrofuran–HCl) 430 and 715 nm] and then to colourless.} The catalyst was filtered off and the solution was diluted with tetrahydrofuran (500 ml) and pyridine (15 ml) before a stream of air was passed through for 24 h. The solvents were evaporated off and the residue was chromatographed on alumina, with methylene chloride as eluant. The resulting red solid crystallised from methylene chloride–petroleum (b.p. 60—80°) as lustrous prisms (216 mg, 79%), m.p. 266—268° (lit.,[23] 268°). A mixed m.p. determination with a purified authentic sample (Fluka) of rhodoporphyrin-XV dimethyl ester showed no depression (Found: C, 72·0; H, 6·8; N, 9·7. Calc. for $C_{34}H_{38}N_4O_4$: C, 72·1; H, 6·8; N,

[23] Ref. 3. p. 535.

9·9%), τ (0·04M in $CDCl_3$) −0·81, 0·12, 0·29, and 0·33 (4 *meso*-H), 5·64 (6-CO_2Me), 5·79 (t), 6·81 (t), and 6·39 (s) (CH_2·CH_2·CO_2Me), 6·18 (q) and 8·24 (t) (2Et), 6·24 (5-Me), 6·54, 6·56, and 6·63 (3Me), and 14·1br (2NH), $\lambda_{max.}$ ($CHCl_3$) 404 (ε 179,000), 508 (10,000), 547 (13,400), 574 (7780), and 632 nm (2000), $\lambda_{max.}$ ($CHCl_3$–HCl) 424 (ε 208,000), 562 (12,400), and 612 nm (9660), *m/e* 566 (M^+).

Oxidation of the foregoing porphyrinogen, in methylene chloride, with 0·0002M-iodine in aqueous 5% w/v sodium acetate solution gave (1a) in *ca.* 60% yield.

2-(2-*Acetoxyethyl*)-4-*ethyl*-6-*methoxycarbonyl*-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethylporphin* (1c).—Prepared in an identical manner to the analogue (1a) from the corresponding *meso*-acetoxyporphyrin (200 mg), this *product* (122 mg, 66%) crystallised from chloroform–petroleum (b.p. 60—80°) as purple prisms, m.p. 273·5—275° (Found: C, 69·2; H, 6·45; N, 9·1. $C_{36}H_{40}N_4O_6$ requires C, 69·2; H, 6·45; N, 9·0%), τ (0·09M in $CDCl_3$) −0·89, 0·02, 0·16, and 0·26 (4 *meso*-H), 5·61 (6-CO_2Me), 5·75 (t), 5·24 (t), and 7·94 (s) (CH_2·CH_2·O·COMe), 5·75 (t), 6·74 (t), and 6·36 (s) (CH_2·CH_2·CO_2Me), 6·15 (5-Me), 6·42, 6·48, and 6·56 (3Me), 6·16 (q) and 8·18 (t) (Et), and 14·1br (2NH), $\lambda_{max.}$ ($CHCl_3$) 407 (ε 216,000), 511 (10,700), 549 (16,600), 574 (8800), and 632 nm (1500), $\lambda_{max.}$ ($CHCl_3$–HCl) 422 (ε 241,000), 563 (13,500), and 611 nm (10,800), *m/e* 624 (M^+).

4-*Ethyl*-2-(2-*hydroxyethyl*)-6-*methoxycarbonyl*-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethylporphin* (1d).—The foregoing porphyrin (80 mg) in 5% w/v sulphuric acid in methanol was left in the dark during 16 h. The solution was poured into sodium acetate (6 g) in water (100 ml), and the precipitated porphyrin was extracted into methylene chloride (100 ml). The solution was washed with aqueous 10% sodium carbonate (2 × 50 ml), water (2 × 50 ml), then dried ($MgSO_4$), and evaporated. The *porphyrin* crystallised from tetrahydrofuran–petroleum (b.p. 60—80°) to give shiny purple prisms (70 mg, 93%), m.p. 264—266° (Found: C, 70·0; H, 6·7; N, 9·4. $C_{34}H_{38}N_4O_5$ requires C, 70·1; H, 6·6; N, 9·6%), τ (CF_3·CO_2H) −1·84, −1·14, −0·99, and −0·94 (4 *meso*-H), 5·40 (6-CO_2Me), 5·4 (CH_2-CH_2OH), 5·92 (5-Me), 6·24 (3Me), 5·4 (t), 6·65 (t), and 6·24 (s) (CH_2·CH_2·CO_2Me), 5·73 (q) and 8·18 (t) (Et), $\lambda_{max.}$ ($CHCl_3$) 407 (ε 197,000), 510 (10,000), 548 (15,200), 574 (8250), and 632 nm (1580), $\lambda_{max.}$ ($CHCl_3$–HCl) 422 (ε 233,000), 562 (13,100), and 610 nm (9700).

2-(2-*Chloroethyl*)-4-*ethyl*-6-*methoxycarbonyl*-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethylporphin* (1e).—The foregoing porphyrin (70 mg) in pyridine (6·6 ml) was treated with mesyl chloride (1·89 ml) and then warmed under nitrogen during 35 min. Water (75 ml) was added and the precipitated porphyrin was extracted into methylene chloride (4 × 50 ml). The extract was washed with water, dried ($MgSO_4$), and evaporated, and the *product* crystallised from chloroform–petroleum (b.p. 60—80°) to give shiny purple needles (55 mg, 75%), m.p. 272—273° (Found: C, 67·9; H, 6·4; N, 9·1. $C_{34}H_{37}ClN_4O_4$ requires C, 67·9; H, 6·2; N, 9·3%), τ (CF_3·CO_2H) −1·81, −1·11, −1·00, and −0·92 (4 *meso*-H), 5·41 (6-CO_2Me), 5·4 (m) and 5·7 (m) (CH_2·CH_2Cl), 5·4 (m), 6·65 (t), and 6·23 (s) (CH_2·CH_2·CO_2Me), 5·8 (m) and 8·21 (t) (Et), 5·92 (5-Me), and 6·23 (3Me), $\lambda_{max.}$ ($CHCl_3$) 408 (ε 221,000), 508 (11,100), 546 (17,500), 574 (9580), and 631 nm (1750), $\lambda_{max.}$ ($CHCl_3$–HCl) 424 (ε 230,000), 562 (13,100), and 611 nm (11,600), *m/e* 600 (M^+)

4-*Ethyl*-6-*methoxycarbonyl*-7-(2-*methoxycarbonylethyl*)-1,3,5,8-*tetramethyl*-2-*vinylporphin* (' 2-*Vinylrhodoporphyrin*-XV *Dimethyl Ester* ') (1b).—The foregoing porphyrin (55 mg) in methylene chloride (11 ml) was treated with a saturated solution of zinc acetate in methanol (23 ml) and the solution was warmed at 50° during 5 min. Chloroform (100 ml) and saturated sodium acetate solution were added, and the organic layer was separated and washed with water. After drying ($MgSO_4$), the solvent was removed *in vacuo* and the residue was dried at 50° under high vacuum during 2 h. The solid residue was dissolved in dry tetrahydrofuran (15 ml) and M-potassium t-butoxide in t-butyl alcohol (40 ml) was added. The solution was stirred during 3 h under nitrogen before being poured into 2N-sulphuric acid (25 ml) and extracted with ethyl acetate; the extract was washed well with water and evaporated *in vacuo*. The addition of ethyl acetate and its evaporation was repeated twice more to remove the last traces of water. The residue, in 5% w/v sulphuric acid in methanol (50 ml), was kept in the dark for 16 h before being poured into 2N-ammonium hydroxide, and the pH was adjusted to *ca.* 7 with 2N-hydrochloric acid. The porphyrin was extracted into methylene chloride; the solution was washed with water, dried ($MgSO_4$), and then evaporated to dryness. The residue was taken into methylene chloride (50 ml) and treated with an excess of ethereal diazomethane at 0° during 1 h. The solution was washed with dilute acetic acid, aqueous 10% sodium carbonate (2 × 50 ml), and finally water. After drying ($MgSO_4$), the solution was evaporated and the residue was chromatographed, with methylene chloride as eluant. The resulting red solid crystallised from chloroform–petroleum (b.p. 60—80°) as lustrous needles (20 mg, 40%), m.p. 272—274° (lit.,[24] 276°). T.l.c. showed only one spot, R_F identical with that of an authentic sample of 2-vinylrhodoporphyrin-XV dimethyl ester, and a mixed m.p. determination with an authentic sample (m.p. 267—269°) showed no depression (Found: C, 72·2; H, 6·3; N, 10·0. Calc. for $C_{34}H_{36}N_4O_4$: C, 72·3; H, 6·4; N, 9·9%), τ (0·04M in $CDCl_3$) −0·67, 0·27, 0·28, and 0·48 (4 *meso*-H), 1·94 (m) and 3·92 (m) (2-CH:CH_2), 5·62 (6-CO_2Me), 5·81 (t), 6·86 (t), and 6·39 (s) (CH_2·CH_2·CO_2Me), 6·26 (5-Me), 6·27 (q) and 8·30 (t) (Et), and 6·59, 6·62, and 6·64 (3Me), $\lambda_{max.}$ ($CHCl_3$) 408 (ε 190,000), 514 (9600), 554 (17,900), 579 (11,300), and 635 nm (1920), $\lambda_{max.}$ ($CHCl_3$–HCl) 427 (ε 200,000), 568 (11,700), and 618 nm (11,800), *m/e* 564 (M^+.)

[3/1969 *Received*, 25*th September*, 1973]

[24] Ref. 3, p. 538.