Synthesis and Tautomerism of Porphyrin β-Ketoesters

Andrei N. Kozyrev, Alexander N. Nizhnik, and Andrei F. Mironov*
M. V. Lomonosov Institute of Fine Chemical Technology, Moscow 117571, USSR

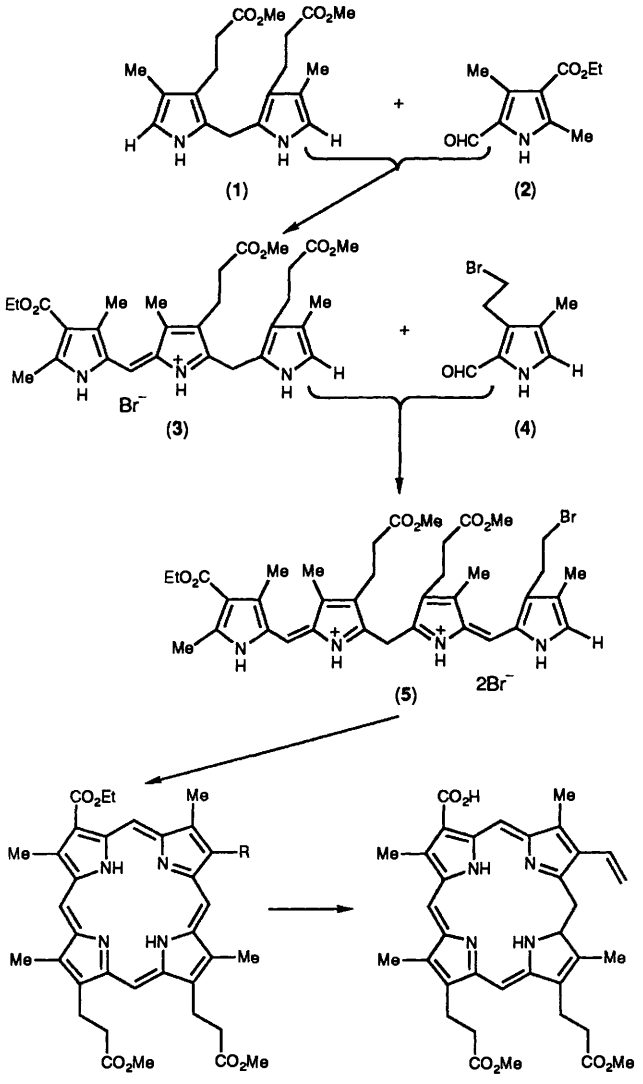
Deuteroporphyrin and cytodeuteroporphyrin β-ketoester derivatives have been prepared by condensation of the appropriate porphyrin acid chloride with ethyl t-butyl sodiomalonate or with the magnesium chelate of t-butyl β-oxopropionate. These porphyrins are enolised, and NMR results indicate that they consist of about 35% of the enol and 65% of the keto form.

Porphyrins bearing β-oxopropionate side chains have been of interest in recent years.[1–3] Porphyrins with reduced side chains (*i.e.* possessing α-hydroxypropionate groups) play an important role in the formation of the vinyl substituents in the biosynthesis of haem.[4] A porphyrin β-ketoester was used by Kenner and his colleagues in an elegant procedure in which a fused cyclopentane ring system was obtained by a photoinduced cyclisation of the thallium(III) enolate complex of the β-ketoester.[3] Intermediate benzyl β-oxopropionate porphyrins have been used in the synthesis of deoxophylloerythroaetioporphyrin and harderoporphyrin by an Australian group.[5] Our studies on pyrrole β-ketoesters have shown that this substituent can be useful for the attachment of the terpenoid side chain at the active methylene group of the β-ketoester substituent.[6a]

Synthesis of Deuteroporphyrin β-Ketoesters.—The initial synthetic plan had as its target molecule 3-carboxy-8-vinyldeuteroporphyrin IX dimethyl ester (**7**) which was to be used as a model porphyrin for the introduction of the β-oxopropionate side chain (Scheme 1). This porphyrin was chosen since it is related to a naturally occurring porphyrin and is easily available by a stepwise synthesis devised in our laboratory.[7] Condensation of equimolar quantities of the 5,5′-unsubstituted dipyrrolylmethane (**1**) with 3-ethoxycarbonyl-5-formyl-2,4-dimethylpyrrole (**2**) in a vigorously stirred solution in dry diethyl ether by slow addition of HBr gave the tripyrrene (**3**) in 96% yield. A second condensation with the formylpyrrole (**4**) was then achieved in acetic acid with an excess of HBr to give in 95% yield the biladiene-*a,c* (**5**). The latter compound was cyclised in the presence of a 2-fold excess of bromine and a 5-fold excess of iodine.[6b] The porphyrin (**6**) was obtained in 54% yield. This yield is regarded as satisfactory in view of the known difficulties in the cyclisation of linear tetrapyrroles possessing electron-withdrawing groups on the terminal ring.[7,8a]

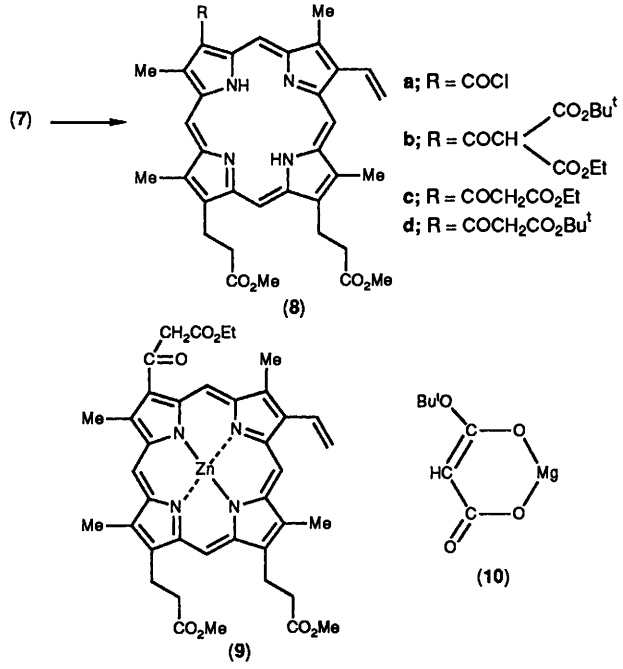
The product of cyclisation was subjected to HPLC using a reversed-phase column (Lichrosorb ODS, 10 μm) with acetonitrile as eluant (flow rate 2 ml/min) and was found to be a mixture of two porphyrins [with retention times (t_R) of 6.7 and 8.1 min (determined by absorbance at 400 nm)] in a ratio *ca.* 2:1. Mass spectrometry showed the presence of 8-(2-iodoethyl) derivative (**6b**) along with the required 2-bromoethyl substituted porphyrin (**6a**). A similar result had been obtained during the cyclisation of a biladiene-*a,c* bearing a 2-bromoethyl group on heating in *o*-dichlorobenzene with iodine as oxidant.[8b] The components were identified by treatment with sodium bromide in boiling chloroform, which led to the increase of one component at the expense of the other.

Porphyrins (**6a, b**) were used without separation for the synthesis of 3-carboxy-8-vinyldeuteroporphyrin IX (**7**) by treatment with KOH in boiling pyridine followed by esterification of the propionic acid groups with 3% sulphuric acid in methanol (86% yield). This porphyrin acid has been synthesised independently by the Australian group[9] using the bilene-*b* method although the total yield was lower.



Scheme 1.

In order to obtain the porphyrin β-ketoester the carboxyporphyrin (**7**) was treated with thionyl chloride and the resulting acid chloride (**8a**) was condensed with the sodium



Scheme 2.

Table. Percentages of the enol tautomer in the porphyrin β-ketoester (**8c**) in various solvents.[a]

Solvent	% Enol	
	0 °C	30 °C
$CDCl_3$–TFA (95:5, v/v)	85	75
C_6D_6	38	42
$CDCl_3$	33	40
$(CD_3)_2CO$	25	27
C_5D_5N	16	18

[a] The percentages were determined by integration of appropriate peaks in the 250 MHz ^1H NMR spectra.

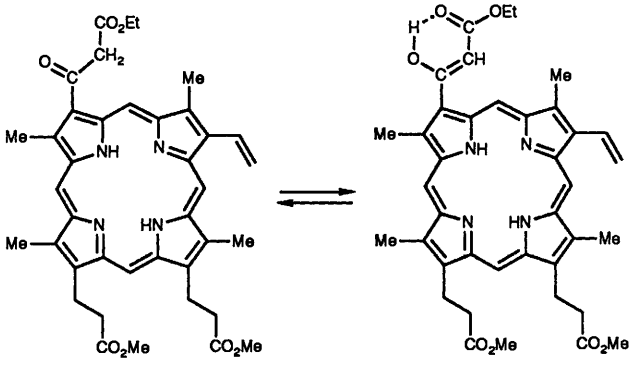
derivative of ethyl t-butyl malonate to yield the porphyrin (**8b**) (Scheme 2). The latter was treated with trifluoroacetic acid (TFA) to remove the t-butoxycarbonyl group and the required porphyrin (**8c**) with an ethyl β-oxopropionate side chain was obtained in 84% yield.

An alternative route to porphyrin β-ketoesters involved the condensation of the acid chloride (**8a**) with the magnesium enolate (**10**) to give the porphyrin (**8d**) bearing a t-butyl β-oxopropionate function in 73% yield. All the porphyrins obtained have been characterised by IR and NMR spectroscopy and by elemental analysis. Mass spectroscopy of porphyrin β-ketoesters by electron impact was unsuccessful because of the lability of the ester substituent.[10]

Interpretation of the NMR spectra of porphyrin β-ketoesters is complicated by keto–enol tautomerism and usually the spectra are not discussed.[9] We have examined 250 MHz NMR spectra and found that the porphyrin (**8c**) consists of 65% of the keto and 35% of the enol form based on area ratio. The distinctive singlet at δ *ca.* 13.5 was assigned to the enolic hydroxy proton and the singlet at δ *ca.* 6.0 to the olefinic hydrogen of the enol. The signal of the methylene group of the keto form was present at δ 4.6. The overlapping of the signals of *meso*-protons of both forms gave a complex pattern, but the 5-*meso*-proton, being closer to the tautomeric substituent, was observed clearly. The change in the ester function from ethyl [in (**8c**)] to t-butyl [in (**8d**)] did not affect the chemical shift values or the tautomeric ratio.

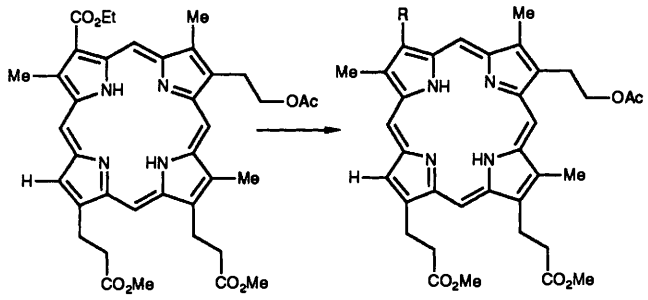
In contrast with these results, the NMR spectrum of the intermediate porphyrin (**8b**), which is in fact a β-ketoester substituted at the methylene group, exhibited no enolisation. Only the keto form was observed. It is of interest that the visible spectra of the porphyrins (**8b**) and (**8c**) exhibit clear differences. The spectrum of (**8b**) was of a typical etio-type whereas that of (**8c**) was more rhodified and showed a 3 nm bathochromic shift. The effect is attributed to the interruption of the conjugation with the porphyrin macrocycle by the bulky substituent of the porphyrin (**8b**). We tried to change the keto–enol equilibrium by insertion of a metal into the porphyrin ring, but the NMR spectrum of the zinc complex (**9**) showed the same ratio of tautomers. ^1H NMR spectroscopy appeared to be useful in the direct observation of the tautomerism of the β-ketoester (**8c**) tautomerism.

We studied this equilibrium (Scheme 3) under different conditions, and found (Table) that it depends on solvent and temperature. In non-polar solvents, *e.g.* hexadeuteriobenzene, the concentration of enol is higher than in polar solvents (*e.g.* hexadeuterioacetone). Increasing the temperature from 0 to 30 °C shifted the equilibrium towards the enol form in all solvents. The keto–enol tautomerism depended strongly on the presence of acids. Thus, in deuteriochloroform–TFA (95:5, v/v) at 0 °C the porphyrin (**8c**) is preferentially in the enol form (85%), whereas in pentadeuteriopyridine at 0 °C the keto-form prevails (84%) (Table).



Scheme 3.

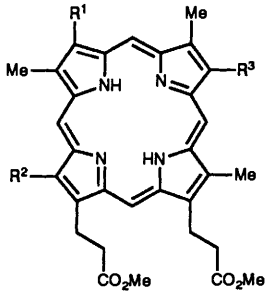
Synthesis of Cytodeuteroporphyrin β-Ketoesters.—Our plans included the synthesis of a formylcytodeuteroporphyrin β-ketoester derivative as a possible precursor of porphyrin *a* and related compounds. The synthesis of 8-(2-acetoxyethyl)-3-ethoxycarbonylcytodeuteroporphyrin dimethyl ester (**11**) by a stepwise route *via* an unsymmetrical dipyrrolylmethane has been described.[8] Porphyrin (**11**) contains a 2-acetoxyethyl group for conversion into a vinyl group and an unsubstituted position 18 for subsequent location of a formyl group. The β-ketoester substituent was planned to be utilised for the attachment of a terpenoid side chain. To obtain the porphyrin acid (**12a**) the starting compound (**11**) was treated with KOH in boiling pyridine followed by acetylation of the 2-hydroxyethyl substituent with acetic anhydride and methylation of the propionic acid side chains with 3% sulphuric acid in methanol. The β-ketoester derivative was obtained in a similar manner to that described for the model porphyrin (**8c**) by condensation of the acid chloride (**12b**) with sodium ethyl t-butyl malonate in tetrahydrofuran (THF) followed by treatment with TFA to yield the porphyrin β-ketoester (**12d**). The mass spectrum of porphyrin (**12d**) showed only fragmentation; the molecular ion (electron impact) was absent, a result typical for this sort of



(11) (12)

a; R = CO_2H
b; R = COCl
c; R = $COCH(CO_2Et)(CO_2Bu^t)$
d; R = $COCH_2CO_2Et$

Scheme 4.



(13)

a; $R^1 = CO_2Et$, $R^2 = CHO$, $R^3 = CH_2CH_2Br$
b; $R^1 = CO_2H$, $R^2 = CHO$, $R^3 = CH{=}CH_2$
c; $R^1 = COCl$, R^2 = 2-(1,3-dioxan-2-yl), $R^3 = CH{=}CH_2$
d; $R^1 = COCH(CO_2Bu^t)(CO_2Et)$, R^2 = 2-(1,3-dioxan-2-yl), $R^3 = CH{=}CH_2$
e; $R^1 = COCH_2CO_2Et$, R^2 = 2-(1,3-dioxan-2-yl), $R^3 = CH{=}CH_2$
f; $R^1 = COCH_2CO_2Et$, $R^2 = CHO$, $R^3 = CH{=}CH_2$

porphyrin.[10] The base peak at *m/z* 613 was assigned to the loss of the entire β-ketoester group, and another peak at *m/z* 655 was attributed to $M^+ - CO_2C_2H_5$. As for the model β-ketoester (**8c**) the NMR spectrum of the porphyrin (**12d**) showed enolisation, *ca.* 60% of keto form being present in chloroform at room temperature.

Attempts to introduce a formyl group into the unsubstituted 18 position by treatment of the copper(II) complex of the porphyrin (**12d**) with the Vilsmeier reagent [$POCl_3$–dimethylformamide (DMF)] failed because of the lability of the β-ketoester side chain. The use of dichloromethyl methyl ether–$SnCl_4$ as the formylating reagent[11] was also unsuccessful.

The problem of formylation can be solved by introducing this group before the β-ketoester group. This was achieved in our recent synthesis of 8-(2-bromoethyl)-3-ethoxycarbonyl-18-formylcytodeuteroporphyrin dimethyl ester (**13a**).[12,13] The formyl group was introduced by an intramolecular rearrangement at the stage of cyclisation of 1,19-dimethylbiladiene-*a,c* with the 18 position unsubstituted in DMF in the presence of $CuCl_2$ at room temperature.[13] After routine chemical transformation 3-carboxy-18-formyl-8-vinylcytodeuteroporphyrin dimethyl ester (**13b**) was achieved in good overall yield[13] by a simpler synthetic scheme than that employed by the Australian group.[14]

Porphyrin (**13b**) was protected as its acetal with 2-methylpentane-2,4-diol and was then treated with thionyl chloride to give the acid chloride (**13c**). The latter was condensed with ethyl t-butyl sodiomalonate followed by treatment with TFA to remove the t-butoxycarbonyl group and the protecting acetal, and the required porphyrin β-ketoester (**13f**) was obtained in 76% yield.

At 250 MHz the ^1H NMR spectrum of (**13f**) includes both keto (66%) and enol (34%) forms, as observed for the porphyrin β-ketoesters already described. A broadened OH signal at δ 13.5, a singlet due to the olefinic proton at δ *ca.* 6.1, and a singlet due to the enol tautomer were present. The signal of the CH_2 protons of the keto form was observed as a singlet at δ 4.56. Enolisation caused splitting of the formyl signal at δ 11.32 and of the *meso*-H signals so that it was difficult to interpret this part of the spectrum.

The synthesis of the formylcytodeuteroporphyrin β-ketoester (**13f**) opens the way to a study of synthetic approaches to porphyrin *a via* alkylation of the β-ketoester side chain. Our observations on the keto–enol tautomerism of porphyrin β-ketoesters using ^1H NMR spectroscopy could be useful in finding the experimental conditions for such alkylations.

Experimental

M.p.s were determined on a Kofler apparatus. UV–visible spectra were recorded for solutions in chloroform (porphyrins) and in 1% HBr in chloroform on a Hitachi EPS-3T spectrophotometer. IR spectra were recorded on a Perkin-Elmer 257 instrument. NMR spectra of porphyrins were recorded on Bruker-Physic WH 90 (90 MHz) and on Bruker-WM 250 (250 MHz) instruments for solutions in deuteriochloroform unless otherwise stated. Mass spectra were recorded on a Varian MAT-731 mass spectrometer (electron impact). HPLC of porphyrins was performed on a Spectra-Physics 8000 machine with SP 8310 detector.

17-(2-*Bromoethyl*)-2-*ethoxycarbonyl*-8,12-*bis*(2-*methoxycarbonylethyl*)-1,3,7,13,18-*pentamethyl*-10,24-*dihydro*-21H-*biline Hydrobromide* (**5**).—Tripyrrin hydrobromide[7] (**3**) (160 mg) and the formylpyrrole[13] (**4**) (62 mg) were stirred in ethanol (15 ml) and methanol (1.5 ml) with aqueous hydrobromic acid (40%, 0.2 ml) for 20 min at 20 °C. Dry diethyl ether (15 ml) was added dropwise and the precipitate was filtered off, washed with ether, and dried to yield the title *biladiene* (217 mg, 97%) as deep purple crystals, m.p. 268–270 °C (decomp.) (Found: C, 50.2; H, 5.2; N, 6.35. $C_{37}H_{44}BrN_4O_6 \cdot 2HBr$ requires C, 50.4; H, 5.2; N, 6.3%); ν_{max}(KBr) 3 190, 1 740, and 1 620 cm^{-1}; $\lambda_{max}(CHCl_3)$ (relative absorbance) 453 and 520 nm (1:2.8).

8-[2-*Bromo*(*iodo*)*ethyl*]-3-*ethoxycarbonyl*-13,17-*bis*(2-*methoxycarbonylethyl*)-2,7,12,18-*tetramethylporphyrin* (**6**).—A solution of the foregoing biline dihydrobromide (**5**) (100 mg), bromine (35 mg), and iodine (120 mg) in *o*-dichlorobenzene (100 ml) was heated under reflux for 20 min. After cooling to room temperature the solution was treated with triethylamine (0.5 ml) and filtered through an alumina column (60 × 20 mm diam.), which was washed with light petroleum and then with

chloroform to elute the product. The solvent was evaporated off and the residue was chromatographed on a silica column (150 × 15 mm diam.), with chloroform as eluant, to give the title porphyrin (**6a, b**) (48 mg, 54%), m.p. 203–206 °C (from chloroform–methanol); ν_{max}(KBr) 3 340, 1 730, and 1 700 cm^{-1}; λ_{max}($CHCl_3$) (relative absorbance) 409 (Soret), 507, 545, 574, and 621 nm (1.0:1.2:0.6:0.2); δ($CDCl_3$) 11.49 (1 H, s, *meso*-H), 11.40 (2 H, s, *meso*-H), 10.72 (1 H, s, *meso*-H), 4.98 (2 H, q, CH_2CH_3), 4.65 (2 H, t, CH_2CH_2Br), 4.45 (4 H, t, $CH_2CH_2CO_2$), 3.98 (2 H, t, CH_2CH_2Br), 3.66 (18 H, CH_3), 3.22 (4 H, m, $CH_2CH_2CO_2$), and 1.38 (3 H, t, CH_2CH_3); *m/z* (relative intensity) 792 (M^+, I, 2), 718 (M^+, ^{81}Br, 12), 716 (M^+, ^{79}Br, 10), 636 (59), 635 (36), 629 (42), 628 (31), 613 (18), 606 (33), 605 (28), 601 (14), 578 (32), and 574 (41).

3-*Carboxy*-13,17-*bis*(2-*methoxycarbonylethyl*)-2,7,12,18-*tetramethyl*-8-*vinylporphyrin* (**7**).—A solution of the foregoing porphyrin (**6**) (50 mg) in pyridine (50 ml) was heated under reflux under nitrogen for 5 min, diluted carefully with water (10 ml), and heated under reflux for a further 5 min. Aqueous KOH (3%; 10 ml) was added. The mixture was then heated under reflux for a further 2 h, aqueous acetic acid (30%; 10 ml) was added followed by water (75 ml), and the mixture was concentrated to 25 ml by evaporation. The precipitate formed was filtered off, washed with water, and dried. The precipitate was dissolved in methanolic sulphuric acid (3%; 100 ml) and the filtered solution was left overnight at room temperature. Water (200 ml) was added and the product was extracted with chloroform (3 × 100 ml). The combined extracts were washed with water (3 × 100 ml), dried (Na_2SO_4), and evaporated. The residue was purified by chromatography on a silica column (60 × 20 mm diam.) and then recrystallised from chloroform–benzene to give the porphyrin acid (**7**) (38 mg, 85%), m.p. > 300 °C (Found: C, 68.8; H, 5.8; N, 9.0. Calc. for $C_{35}H_{36}N_4O_6$: C, 69.1; H, 6.0; N, 9.2%); λ_{max}(relative absorbance) 410.5 (Soret), 510, 548, 577, and 633 nm (1.0:0.91:0.65:0.22) [lit.,[9] 410.5 (Soret), 510, 548, 578, and 635 nm (1.0:0.90:0.64:0.20)].

3-(2-*Ethoxycarbonyl*-1-*oxo*-2-*butyloxycarbonylethyl*)-13,17-*bis*(2-*methoxycarbonylethyl*)-2,7,12,18-*tetramethyl*-8-*vinylporphyrin* (**8b**).—The foregoing porphyrin acid (**7**) (30 mg) in $SOCl_2$ (5 ml) was stirred at room temperature in darkness for 1 h. The solution was evaporated and the residue was dissolved in dry tetrahydrofuran (THF) (25 ml). A solution of ethyl t-butyl sodiomalonate [from sodium hydride (220 mg) and ethyl t-butyl malonate (1.3 g)] in dry THF (20 ml) was added, the solution was stirred vigorously for 1 h at room temperature. Aqueous hydrochloric acid (0.01M; 200 ml) was added, and the porphyrin was extracted with chloroform (3 × 50 ml). The combined extracts were dried over Na_2SO_4 and evaporated. The residue was chromatographed on silica and then recrystallised from chloroform–light petroleum to give the title porphyrin (**8b**) (34 mg, 88%) as plates, m.p. 130–132 °C; ν_{max}(KBr) 3 325, 1 700, and 1 680 cm^{-1}; λ_{max}($CHCl_3$) (relative absorbance) 412 (Soret), 508, 543, 575, and 628 nm (1.0:0.85:0.62:0.21); δ($CDCl_3$) 10.60, 9.82, 9.80, 9.71 (each 1 H, s, *meso*-H), 8.23 (1 H, m, CH=CH_2), 6.28 (2 H, m, CH=CH_2), 4.95 (1 H, s, COCH), 4.36 (6 H, m, CH_2CH_3, $CH_2CH_2CO_2$), 3.68–3.54 (18 H, m, CH_3), 3.23 (4 H, t, $CH_2CH_2CO_2$), 1.56 (3 H, t, CH_2CH_3), and 1.40 (9 H, s, Me_3C).

3-(2-*Ethoxycarbonyl*-1-*oxoethyl*)-13,17-*bis*(2-*methoxycarbonylethyl*)-2,7,17,18-*tetramethyl*-8-*vinylporphyrin* (**8c**).—The foregoing porphyrin (**8b**) (30 mg) was treated with TFA (5 ml) at room temperature for 15 min. The excess of TFA was removed *in vacuo* and the residue was dissolved in chloroform (50 ml), washed with water (3 × 300 ml), dried over Na_2SO_4, and evaporated. The porphyrin was purified by column chromatography on silica to give the title *porphyrin* (**8c**) (25 mg, 92%) as purple plates, m.p. 251–252 °C (from chloroform–methanol) (Found: C, 68.7; H, 6.1; N, 7.9. $C_{39}H_{42}N_4O_7$ requires C, 69.0; H, 6.2; N, 8.2%); ν_{max}(KBr) 3 340, 1 720, and 1 680 cm^{-1}; λ_{max}($CHCl_3$) (relative absorbance) 413 (Soret), 511, 548, 578, and 634 nm (1.0:0.94:0.68:0.22); δ($CDCl_3$) 13.41 (s, OH), 10.61, 10.45, 9.96, 9.86, 9.78, 9.75 (4 H, m, *meso*-H), 8.20 (1 H, m, CH=CH_2), 6.30 (2 H, m, CH=CH_2), 6.07 (s, CH=C–OH), 4.60 (s, $COCH_2CO_2Et$), 4.34 (6 H, m, CH_2CH_3, $CH_2CH_2CO_2$), 3.66–3.52 (18 H, m, CH_3), 3.21 (4 H, m, $CH_2CH_2CO_2$), and 1.52 (3 H, t, CH_2CH_3).

13,17-*Bis*(2-*methoxycarbonylethyl*)-2,7,12,18-*tetramethyl*-3-(1-*oxo*-2-*t-butyloxycarbonylethyl*)-8-*vinylporphyrin* (**8d**).—In a similar manner to that described for (**8b**) the porphyrin acid (**7**) (20 mg) and t-butyl magnesiomalonate [prepared from Mg (200 mg) and t-butyl malonate (0.8 g)] gave the porphyrin β-oxoester (**8d**) (16 mg, 73%), m.p. 206–210 °C; ν_{max}(KBr) 3 340, 1 725, and 1 690 cm^{-1}; λ_{max}($CHCl_3$) (relative absorbance) 413 (Soret), 511, 548, 577, and 633 nm (1.0:0.92:0.67:0.2); δ($CDCl_3$) 13.6 (s, OH), 10.84, 10.74, 9.99 (m, *meso*-H), 8.28 (1 H, m, CH=CH_2), 6.4 (2 H, m, CH=CH_2), 6.03 (s, CH=C–OH), 4.66 (s, $COCH_2$), 4.32 (4 H, m, $CH_2CH_2CO_2$), 3.81–3.66 (18 H, m, CH_3), 3.23 (4 H, m, $CH_2CH_2CO_2$), and 1.41 (9 H, s, Me_3C).

3-(2-*Ethoxycarbonyl*-1-*oxoethyl*)-13,17-*bis*(2-*methoxycarbonylethyl*)-2,7,12,18-*tetramethyl*-8-*vinylporphyrinatozinc* (**9**).—A solution of the porphyrin β-ketoester (**8c**) (15 mg) in chloroform (15 ml) was refluxed with zinc acetate dihydrate for 10 min. The mixture was washed with water (3 × 50 ml), dried over Na_2SO_4, and chromatographed on silica to give the zinc complex (**9**) as pink plates, m.p. 268–270 °C (from chloroform–methanol); δ($CDCl_3$) 13.36 (s, OH), 9.95, 9.89, 9.16, 9.01, 8.90 (m. *meso*-H), 7.6 (1 H, m, CH=CH_2), 6.30 (2 H, m, CH=CH_2), 6.00 (s, CH=C–OH), 4.61 (s, $COCH_2$), 4.55–4.20 (6 H, m, CH_2CH_3, $CH_2CH_2CO_2$), 3.50–3.20 (18 H, m, CH_3), 2.9 (4 H, m, $CH_2CH_2CO_2$), and 1.68 (3 H, t, CH_2CH_3).

8-(2-*Acetoxyethyl*)-3-*carboxy*-13,17-*bis*(2-*methoxycarbonylethyl*)-2,7,12-*trimethylporphyrin* (**12a**).—In a manner similar to that described for the porphyrin (**7**) the porphyrin ester (**11**)[8b] (50 mg) was converted to the *porphyrin acid* (**12a**) (35 mg, 78%) and obtained as fine crystals (from chloroform–methanol), m.p. > 300 °C (Found: C, 65.9; H, 5.95; N, 8.5. $C_{36}H_{38}N_4O_8$ requires C, 66.2; H, 5.8; N, 8.6%); ν_{max}(KBr) 3 325, 1 700, and 1 680 cm^{-1}; λ_{max}(relative absorbance) 405 (Soret), 504, 539, 574, and 625 nm (1.0:0.89:0.53:0.2).

3-(2-*Ethoxycarbonyl*-1-*oxoethyl*)-13,17-*bis*(2-*methoxycarbonylethyl*)-2,7,12-*trimethylporphyrin* (**12d**).—The same procedure which was outlined for (**8c**) was used to convert the porphyrin acid (**12a**) (30 mg) to the *porphyrin* β-*ketoester* (**12d**) (27 mg, 79%), m.p. 142–143 °C (from chloroform–hexane) (Found: C, 66.8; H, 5.85; N, 7.7. $C_{40}H_{44}N_4O_9$ requires C, 66.5; H, 6.0; N, 7.7%); ν_{max}(KBr) 3 340, 1 720, and 1 680 cm^{-1}; λ_{max} 406 (Soret) 504, 540, 572, and 626 nm (1.0:0.94:0.6:0.18); δ($CDCl_3$) 13.48 (s, OH), 10.75, 10.61, 10.05 (m, *meso*-H), 9.18 (1 H, s, β-H), 6.12 (s, CH=C–OH), 4.69 (2 H, m, CH_2CH_3), 4.60 (s, CH_2CO), 4.48 (6 H, m, $CH_2CH_2CO_2$, CH_2CH_2OAc), 3.80–3.52 (15 H, m, CH_3), 3.31 (6 H, m, $CH_2CH_2CO_2$, CH_2CH_2OAc), 2.12 (3 H, s, OAc), and 1.78 (3 H, t, CH_2CH_3); *m/z* (relative intensity) 655 ($M^+ - CO_2C_2H_5$, 10%), 615 (30), 614 (80), 613 ($M^+ - COCH_2CO_2Et$, 100), 581 (10), 554 (14), 540 (34), 481 (14), 407 (10), and 397 (12).

3-(2-*Ethoxycarbonyl*-1-*oxoethyl*)13,17-*bis*(2-*methoxycarbonylethyl*)-2,7,12-*trimethyl*-8-*vinylporphyrin* (**13f**).—In a simi-

lar manner to that described for the porphyrin (**8c**), the porphyrin acid (**13b**) gave the β-ketoester (**13f**) (76%); ν_{max}(KBr) 3 335, 1 720, and 1 680 cm^{-1}; λ_{max}($CHCl_3$) (relative absorbance) 428 (Soret), 519, 554, 586, and 640 nm (1.0:0.79:0.57:0.22); δ($CDCl_3$) 13.50 (s, OH), 11.32 (1 H, d, CHO), 10.89, 10.77, 10.43 (m, *meso*-H), 8.19 (1 H, m, C*H*=CH_2), 6.36 (2 H, m, CH=CH_2), 6.06 (s, C*H*=C–OH), 4.62 (s, CH_2CO), 4.36–4.32 (6 H, m, CH_2CH_3, C$H_2CH_2CO_2$), 3.65–3.42 (15 H, m, CH_3), 3.22 (4 H, m, $CH_2CH_2CO_2$), and 1.67 (3 H, t, CH_2CH_3).

Acknowledgements

We are grateful to Professor R. Bonnett (Queen Mary College, London) for useful discussions and Mr. G. Coumbaradis (QMC) for the NMR spectra.

References

1 A. N. Kozyrev, A. F. Mironov, and R. P. Evstigneeva, Proceedings of III Conference on Porphyrin Chemistry (USSR), Samarkand, 1982, p. 37.
2 M. T. Cox, T. T. Howarth, A. H. Jackson, and G. W. Kenner, *J. Chem. Soc., Perkin Trans. 1*, 1974, 512.
3 G. W. Kenner, S. W. McCombie, and K. M. Smith, *J. Chem. Soc., Perkin Trans. 1*, 1974, 527.
4 I. A. Chaudhry, P. S. Clezy, and V. Diakiw, *Aust. J. Chem.*, 1977, **30**, 879.
5 I. A. Chaudhry, P. S. Clezy, and A. H. Mirza, *Aust. J. Chem.*, 1980, **33**, 1095.
6 (*a*) V. P. Zhestkov, A. F. Mironov, L. A. Ustyniuk, and R. P. Evstigneeva, *Bioorg. Khim.*, 1975, **1**, 1673; (*b*) V. P. Zhestkov, A. F. Mironov, and R. P. Evstigneeva, *ibid.*, 1975, 672.
7 A. F. Mironov, V. D. Rumyantseva, L. I. Fleiderman, and R. P. Evstigneeva, *Zh. Obsch. Khim.*, 1975, **45**, 1150.
8 (*a*) V. M. Bayramov, A. S. Kaledin, G. M. Isaeva, A. F. Mironov, and R. P. Evstigneeva, *Zh. Org. Khim.*, 1978, **14**, 857; (*b*) G. M. Isaeva, V. M. Bayramov, A. F. Mironov, and R. P. Evstigneeva, *Bioorg. Khim.*, 1979, **5**, 1544.
9 P. S. Clezy and C. J. R. Fookes, *Aust. J. Chem.*, 1981, **34**, 871.
10 M. T. Cox, T. T. Howarth, A. H. Jackson, and G. W. Kenner, *J. Am. Chem. Soc.*, 1969, **91**, 1232.
11 G. M. Isaeva and A. F. Mironov, in ref. 1, p. 33.
12 A. N. Nizhnik, A. N. Kozyrev, and A. F. Mironov, Proceedings of XII Mendeleev meeting on Pure and Applied Chemistry (USSR), 1981, p. 688.
13 A. N. Nizhnik, A. N. Kozyrev, and A. F. Mironov, *Bioorg. Khim.*, 1985, **11**, 692.
14 P. S. Clezy and V. Diakiw, *Aust. J. Chem.*, 1975, **28**, 2703.

Paper 9/02448D
Received 9*th June* 1989
Accepted 30*th October* 1989