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ORIENTATION OF NUCLEOPHILIC SUBSTITUTION IN π-CATION RADICALS OR π-DICATIONS FROM *MESO*-SUBSTITUTED METALLOPORPHYRINS

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(Dedicated to Prof. Dr. HANS HERLOFF INHOFFEN on the occasion of his 70th birthday)

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Abstract—Treatment of *meso*-substituted metalloporphyrins [*meso*-substituent = $OCOCF_3$, $OCOCH_3$, OMe, CHO, CN, Cl; metal = Zn(II) or Cd(II)] with thallium(III) trifluoroacetate, followed by an acidic work-up, gives the corresponding β-substituted α-oxophlorins which were either characterised as such or else further derivatised. In all cases the major (or only) disubstitution product has the αβ orientation at the *meso* positions, indicating that the existing *meso* substituent directs the incoming one (trifluoroacetate) into the flanking, rather than opposite, *meso* position of the intermediate π-cation radical or π-dication. In contradistinction, *meso* substituted zinc(II) porphyrins which are able to lose protons (e.g. α-oxophlorins or α-aminoporphyrins) react with thallium(III) trifluoroacetate, and after a work-up with HCl the corresponding γ-chloro-α-oxophlorin or γ-chloro-α-aminoporphyrin is obtained.

Several studies of the orientation of disubstitution products from electrophilic substitution at the *meso*-positions of porphyrins and metalloporphyrins have been reported. Thus, nitration of octaethylporphyrin gave[1] a mixture of αβ and αγ disubstitution products, but chlorination afforded[2] only the αγ-dichloro derivative. On the other hand, nitration of α-nitroporphin has been reported[3] to give only αβ-dinitroporphin, but nitration of zinc(II) octaethylporphyrin under less acidic conditions gave[4] αγ as the only disubstitution product; Vilsmeier formylation of the copper(II) complex similarly afforded[4] the αγ-diformylporphyrin. More recently, Vilsmeier formylation of nickel(II) octaethyloxophlorin gave[5] the γ-formyl-α-oxophlorin in good yield.

In this paper we report straightforward routes to several β-substituted oxophlorins and derivatives, as well as more limited methods for preparing γ-chloro-α-oxophlorins or γ-chloro-α-aminoporphyrins. The approach is a development of our earlier synthesis of oxophlorins employing[6] the treatment of zinc(II) porphyrins with thallium(III) trifluoroacetate (TTFA). We had envisaged the mechanism of this useful transformation as involving abstraction of two electrons from the metalloporphyrin (to give the π-dication) by the thallium reagent, followed by nucleophilic attack of trifluoroacetate and then loss of a proton. Hydrolysis and demetallation then affords oxophlorin in very good yield. An alternative mechanism might also be proposed in which attack by trifluoroacetate precedes abstraction of the second electron, that is that the metalloporphyrin π-cation radical is the species upon which nucleophilic attack occurs. The former mechanism was preferred on account of statements[7] to the effect that metalloporphyrin π-cation radicals are unreactive towards nucleophiles; indeed, this view which has been generalised from the case of methanol, has even been restated recently with some force.[8] However, solutions of metalloporphyrin π-cation radicals do react with nitrite[9] as well as several other common nucleophiles,[10,11] but not with methanol. Thus, the reactions described in this paper are assumed to follow a mechanism involving abstraction of one electron from the *meso*-substituted metalloporphyrin to give the π-cation radical which reacts with trifluoroacetate before loss of a second electron and a proton. The usual acid/SO_2 work-up[6] then affords the *meso*-substituted oxophlorin. Nevertheless we accept that a mechanistic delineation between initial one or two electron abstraction is very difficult, particularly since disproportionation of the π-cation radical could afford π-dication.

RESULTS AND DISCUSSION

Results from the reaction of TTFA with metal complexes of *meso* substituted octaethylporphyrins and/or aetioporphyrins-I are given below. The *meso*-substituted porphyrins were prepared by literature methods as indicated in the Experimental. In the main, orientations of the disubstituted products were determined by ^1H and/or ^{13}C NMR spectroscopy, and thus it is not possible to detect small quantities of minor isomers, should they be present. In order to provide a double check, the products were usually derivatised (e.g. by preparing the enol acetate of the oxophlorin).

In an earlier paper,[12] we described the synthesis and transformations of β-hydroxy-α-oxophlorins (**1**), obtained as by-products in the synthesis of oxophlorins from zinc(II) porphyrins.[6] We deduced[12] that the zinc(II) αβ-bis(trifluoroacetoxy)porphyrins (**2**) were intermediates in the formation of **1**, and this appeared to indicate that the existing trifluoroacetoxy substituent (at α) was directing the incoming trifluoroacetate to the adjacent (β) rather than opposite (γ) *meso*-position. However, another by-product from the oxophlorin synthesis is the αγ-dioxoporphodimethene (**3**) which can be readily obtained[5,12] from the corresponding oxophlorin during the chromatographic work-up. The possibility also existed that **3** might be produced from an αγ-bis(trifluoroacetoxy)porphyrin via the semi-quinone (**4**) [an isomer of **1**] and thus be considered as evidence against preferential αβ disubstitution in the TTFA reaction. However, treatment of zinc(II) *meso*-acetoxyporphyrins

(**5**) with TTFA, followed by acidic work-up gave exclusively the β-acetoxy-α-oxophlorin (**6**) which could be hydrolysed to give the β-hydroxy-α-oxophlorin (**1**), or treated with acetic anhydride in pyridine to give the $\alpha\beta$-bis(acetoxy)porphyrin (**7**). The identical compound (**7**) could also be obtained by treatment of **1** with acetyl chloride in pyridine, and the ^{13}C NMR spectrum of **7**, which showed eight resolved side-chain methyl or methylene carbons, added confirmation to our assignment of it (and therefore of compound **1** also) as an $\alpha\beta$ rather than $\alpha\gamma$ disubstituted macrocycle.

Treatment of zinc(II) *meso*-methoxyporphyrins (**8**) [obtained from the corresponding zinc(II) oxophlorin by treatment with carbonate and methyl iodide] with TTFA gave a product which was demetallated with HCl to give a good yield of the β-hydroxy-α-oxophlorin (**1**). Cleavage of the methyl ether was unexpected because the substituent remains intact when **8** is treated under similar conditions with HCl; however, oxophlorins are stronger bases than porphyrins[13] and the demethylation might proceed as indicated in structure **9**.

Zinc(II) *meso*-formyloctaethylporphyrin (**10**; R=Et) reacted with TTFA, and after work-up gave a stable oxophlorin with a sharp NMR spectrum.[†] The product was $\alpha\beta$ disubstituted as attested by the sharp equal intensity *meso* proton signals (τ 2.52, 3.21). Furthermore, the structures (**11**; R=Et) (or the tautomeric mesomeric dipolar forms) for the formyl-oxophlorin were indicated by the existence of the low-field aldehydic proton as an equal intensity doublet (τ −0.50, −0.01), and by the infrared spectrum which did not show a normal aldehyde band. In the aetioporphyrin—I series the formyl-oxophlorin displayed similar NMR data (*meso* protons τ 2.73, 3.45; aldehyde −0.40, −0.34 ($\frac{1}{2}$H) and 0.16, 0.26 ($\frac{1}{2}$H)) indicating the presence of the expected *two* $\alpha\beta$ disubstituted products (rather than only one which is possible with the $\alpha\gamma$ orientation of substituents). The zinc(II) complex, unlike the free base (**11**) showed a strong aldehyde band in the infrared (1690 cm^{-1}) and reacted with acetic anhydride in pyridine to give the zinc(II) α-acetoxy-β-formylporphyrin (**12**; R=Et) which showed non-equivalent *meso*-protons in the ^1H NMR (τ 0.24, 0.38) and in the ^{13}C NMR the γ and δ *meso*-carbons appeared at 105.25 and 102.25 ppm and hence the molecule is not symmetrically substituted.

Zinc(II) *meso*-cyano-octaethylporphyrin or the aetioporphyrin—I analogue failed to react with TTFA. This is probably due to the cyano group (which unlike the CHO group is linear and able to conjugate fully with the porphyrin macrocycle[14]) withdrawing electrons from the porphyrin ligand and thereby raising the oxidation potential of the zinc(II) cyanoporphyrin above the reduction potential of thallium(III) in TTFA. However, cadmium(II) *meso*-cyanoporphyrins (**13**) reacted smoothly with TTFA to give, after work-up, a stable oxophlorin. Infrared (strong band 2180 cm^{-1}) indicated that the cyano function had been retained and asymmetry in the ^1H NMR resonances for the side-chains indicated the product to be (**14**); the *meso*-protons were observed as an inconclusive broad singlet (**14**; R=Et, τ 2.13). The orientation was shown to be largely[‡] $\alpha\beta$ by conversion into the *meso*-benzoyloxy derivative (**15**; R=Me) or *meso*-acetoxy derivative (**16**; R=Et), each of which showed the *meso* protons as equal intensity doublets.

Zinc(II) *meso*-nitro and *meso*-chloro octaethylporphyrins failed to react with TTFA, as did cadmium (II) *meso*-nitro-octaethylporphyrin. However, cadmium(II) *meso*-chloro-octaethylporphyrin (**17**; R=Et) gave a low yield of an unstable oxophlorin when treated with TTFA and submitted to an acidic work-up. It was not possible to purify or characterise the product, to which we assign the structure (**18**; R=Et); it was clearly different from the very stable γ-chloro-α-oxophlorin (**19**) described below.

There is abundant evidence to show[15] that oxophlorins and *meso*-aminoporphyrins behave anomalously compared wtih other *meso*-substituted porphyrins. This circumstance might also be expected to extend to the reaction of their zinc(II) complexes with TTFA, and such is indeed the case. Treatment of zinc(II) octaethyloxophlorin (**20**; R=Et) with TTFA, followed by work-up using hydrochloric acid gave a good yield of the γ-chloro-α-oxophlorin (**19**; R=Et), a stable compound which gave a sharp NMR spectrum. The ^1H NMR spectrum appeared at first to suggest $\alpha\beta$ disubstitution (*meso* protons τ 3.25, 4.74), as did the very complex ^{13}C NMR spectrum. However, the ^1H and ^{13}C NMR spectra of the derived enol acetate gave no doubt, from their symmetry, that the product was indeed $\alpha\gamma$ disubstituted (i.e. **21**; R=Et). We therefore ascribe the asymmetry of the oxophlorin spectra to a specific aggregate. The isomer **19** (R=Et) is presumably more stable than **18** (R=Et) because the main pathway for decomposition of oxophlorins is by reaction at the *meso* position opposite to the carbonyl in the radical; in compound **19** (R=Et) this position is blocked by the Cl atom. We envisage that the reaction proceeds by initial formation of the metallo-oxophlorin π-cation radical which is able to lose a proton to form the corresponding radical. In the absence of oxygen this radical is stable, but a chlorine is inserted (obtained from HCl) during the work-up. The generality of this reaction, and the form in which the chlorine is inserted (i.e. atom or anion) are under investigation.

In a completely analogous fashion, treatment of zinc(II) *meso*-amino-octaethylporphyrin (**22**; R=Et) with TTFA followed by work-up with HCl gave a good yield of the α-amino-γ-chloro-octaethylporphyrin (**23**; R=Et) (*meso*-H, τ 0.39). Again, the initially formed zinc(II) aminoporphyrin π-cation radical is able to lose a proton to afford the radical, from which, during the work-up the product **23** (R=Et) is obtained. Both oxophlorin and aminoporphyrin radicals are known[12,15,16] to react through the γ-position.

EXPERIMENTAL

M.ps were measured on a hot-stage apparatus. Except where otherwise stated, neutral alumina (Brockmann Grade III) was used for chromatographic separations. Electronic absorption spectra (in $CHCl_3$ soln) were measured using a Unicam SP 800 spectrophotometer, and NMR spectra with a Varian XL-100 (^1H or ^{13}C) or HA-100 (^1H) instrument (solns in $CDCl_3$ with TMS as internal standard). Mass spectra were determined with an AEI MS 12 spectrometer (at 50 μA and 70 eV; direct insertion probe; source temps 200–220°).

Octaethylporphyrin was a generous gift from Professor H. H. Inhoffen, to whom this paper is dedicated. Aetioporphyrin—I was

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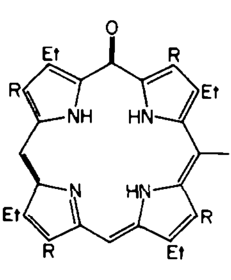
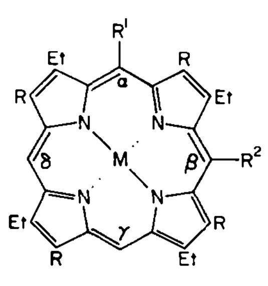
[†] Oxophlorin free bases do not normally show sharp NMR spectra; Fuhrhop[5] has shown this to be due to the presence of small amounts of the corresponding radical. Sharp spectra were obtained here presumably owing to the electron-withdrawing formyl group raising the oxidation potential of the oxophlorin (**11**).

[‡] It is possible that small quantities of the $\alpha\gamma$ disubstitution products were present in these samples; a small peak, slightly downfield from the *meso* proton doublet was observed in each case (**15**; R = Me) and (**16**; R = Et).

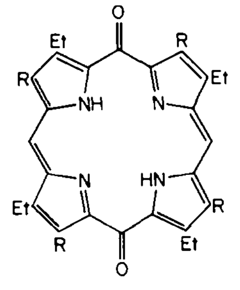




R = Me or Et

1: R^1 = OH
6: R^1 = OCOCH$_3$
14: R^1 = CN
18: R^1 = Cl
22: R^1 = NH$_2$

2: R^1 = R^2 = OCOCF$_3$; M = Zn
7: R^1 = R^2 = OCOCH$_3$; M = 2H
12: R^1 = OCOCH$_3$; R^2 = CHO; M = Zn
15: R^1 = OCOPh; R^2 = CN; M = 2H
16: R^1 = OCOCH$_3$; R^2 = CN; M = 2H



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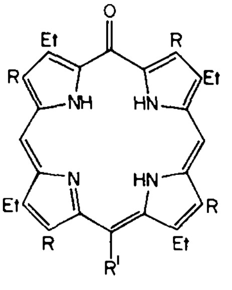
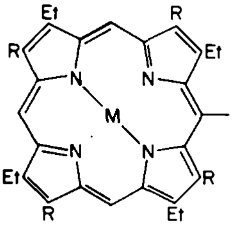
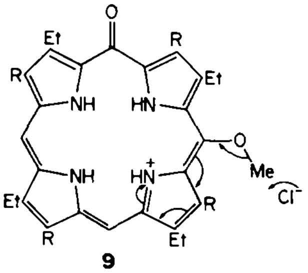


4: R^1 = OH
19: R^1 = Cl



5: R^1 = OCOCH$_3$, M = Zn
8: R^1 = OMe; M = Zn
10: R^1 = CHO; M = Zn
13: R^1 = CN; M = Cd
17: R^1 = Cl; M = Cd
20: R^1 = OH; M = Zn



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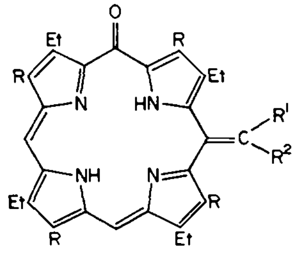
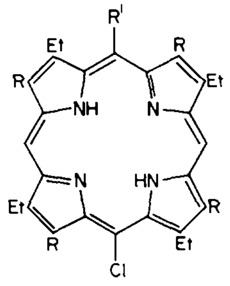


11: R^1 = H; R^2 = OH
or R^1 = OH; R^2 = H



21: R^1 = OAc
23: R^1 = NH$_2$

prepared using a convenient modification of an existing procedure,[17] as follows:

Aetioporphyrin—I. A soln of Br$_2$ (31.2 ml) in HOAc (140 ml) was added to a stirred soln of t-butyl 4-ethyl-3,5-dimethylpyrrole-2-carboxylate[18] (44.6 g) in HOAc (150 ml) (Caution: HBr given off!) and the mixture was set aside overnight. After filtration, the purple and orange-brown crystals were washed with petrol (b.p. 60–80°) and dried in a vacuum oven. The kryptopyrromethene was heated under reflux in 98% formic acid (100 ml) during 3 hr. Evaporation of the solvent gave a residue which was dissolved in CHCl$_3$ (350 ml), washed with H$_2$O (2 × 200 ml), 10% NaHCO$_3$ aq, then H$_2$O (200 ml), and dried (Na$_2$SO$_4$). The solution was evaporated and the residue treated with CH$_2$Cl$_2$ (50 ml) and MeOH (300 ml) before being filtered and the crystals washed with MeOH until clear. Recrystallisation from CHCl$_3$–MeOH gave purple microneedles (5.0–7.2 g; 21–30%), m.p. >300°. (Found: C, 80.54; H, 7.93; N, 11.98. Calc. for C$_{32}$H$_{38}$N$_4$: C, 80.29; H, 8.00; N, 11.71%), λ_{max} 400 (ϵ 172,700), 496 (14,200), 528 (10,400), 560 (6800) and 610 nm (5300).

Zinc(II) meso-*methoxyoctaethylporphyrin* (**8**; R=Et). Anhydrous K$_2$CO$_3$ (3.0 g) was suspended in dry MeOH (50 ml) for 10 min under a N$_2$ atmosphere with stirring. A soln of zinc(II) octaethyloxophlorin (300 mg) in dry THF (100 ml) was added and the colour changed from red to green (anion). MeI (40 ml) was added and the mixture was heated at 60° for 2 hr before being poured into CH$_2$Cl$_2$ (250 ml) and washed with H$_2$O (3 × 400 ml), dried (Na$_2$SO$_4$), and evaporated. The residual solid was chromatographed (elution with CH$_2$Cl$_2$) and the red-pink eluates were evaporated to give a residue which was crystallised from CH$_2$Cl$_2$-n-hexane to give the *methoxyporphyrin* (86 mg; 28%), m.p. >300°. (Found: C, 70.87; H, 7.15; N, 9.00; Zn, 10.65. C$_{37}$H$_{46}$N$_4$OZn requires: C, 70.75; H, 7.38; N, 8.92; Zn, 10.41%), λ_{max} 407 (ϵ 430,400), 531 (18,500), 564 nm (12,000); τ, 0.00 (2H), 0.24 (1H) *meso*-H; 5.64 (3H) OMe; 5.8–6.2 (16H, m), 8.0–8.3 (24 H, m) $C\underline{H}_2C\underline{H}_3$·*m*/*e* 626 (100%), 611 (41) and 313 (16).

Reaction of **8** (R=Et) *with TTFA*. The foregoing zinc(II) complex (60 mg) in dry THF (30 ml) and CHCl$_3$ (60 ml) was flushed with N$_2$ for 10 min before addition of a soln of TTFA (57 mg; 1.1 equiv) in dry THF (25 ml); the mixture was stirred under N$_2$ for 10 min. SO$_2$ gas was bubbled through the mixture for 30 sec and then conc HCl (1 ml) in THF (20 ml) was added and the mixture was stirred for 5 min. It was poured into CHCl$_3$ (200 ml) and washed with H$_2$O (3 × 400 ml), dried (Na$_2$SO$_4$), and evaporated. Chromatography (elution with CHCl$_3$) gave meso-*methoxyoctaethylporphyrin*, crystallised from CH$_2$Cl$_2$–MeOH as red needles (14 mg) m.p. 237–239°. (Found: C, 78.27; H, 8.49; N, 10.13. C$_{37}$H$_{48}$N$_4$O requires: C, 78.68; H, 8.56; N, 9.92%), λ_{max} 407 (ϵ 189,400), 501 (14,500), 533 (5100), 578 (5900) and 618 nm (1600), τ, 0.00 (2H), 0.17 (1H) *meso*-H; 5.64 (3H) OMe; 5.8–6.2 (16H, m), 8.0–8.3 (24 H, m) $C\underline{H}_2C\underline{H}_3$. Further elution gave the required **1** (R=Et; 11 mg; 20%) identical with a sample prepared earlier.[12]

When the same reaction was carried out using zinc(II) *meso*-methoxyaetioporphyrin—I (**8**; R=Me) a 27% yield of **1** (R=Me) was obtained, and this was satisfactorily identified with an authentic sample.[12]

Zinc(II) *complex of β-hydroxy-α-oxophlorin* (**1**; R=Me). Compound **1** (R=Me; 50 mg) in CH$_2$Cl$_2$ (50 ml) was refluxed with a soln of zinc(II) acetate (70 mg) in MeOH (10 ml) during 10 min, after which time the mixture was evaporated to low volume. The *zinc*(II) *complex* (52 mg; 93%) was filtered off as dark green prisms, m.p. >300°. (Found: C, 66.95; H, 5.99; N, 9.73; Zn, 11.33. C$_{32}$H$_{36}$N$_4$O$_2$Zn requires: C, 66.96; H, 6.32; N, 9.76; Zn, 11.39%). λ_{max} 392 (ϵ 24,300), and 587 nm (5900). The compound was extremely insoluble and a NMR spectrum could not be obtained.

Zinc(II) meso-*formylaetioporphyrin—I* (**10**; R=Me). *meso*-Formylaetioporphyrin—I[18] (130 mg) in CH$_2$Cl$_2$ (30 ml) was treated with a soln of zinc(II) acetate (150 mg) in MeOH (20 ml). After refluxing for a few min the green soln was evaporated to low volume (*ca*. 25 ml) when the *zinc*(II) *complex* crystallised as red microneedles (139 mg; 95%), m.p. >300°. (Found: C, 69.63: H, 6.31; N, 9.77; Zn, 11.32. C$_{33}$H$_{36}$N$_6$OZn requires: C, 69.53; H, 6.37; N, 9.83; Zn, 11.47%), λ_{max} 403 (ϵ 191,500), 534 (11,500), 572 (14,000), and 636 nm (2750).

Zinc(II) meso-*formyloctaethylporphyrin* (**10**; R=Et). This compound was similarly prepared in 95% yield from *meso*-formyloctaethylporphyrin.[19] It had m.p. >300°. (Found: C, 70.97; H, 7.03; N, 8.99; Zn, 10.40. C$_{37}$H$_{44}$N$_4$OZn requires: C, 70.97; H, 7.08; N, 8.95; Zn, 10.44%).

β-Formylaetio-α-oxophlorin—I (**11**; R=Me). Zinc(II) complex (**10**; R=Me; 100 mg) was dissolved in dry THF (30 ml) and CHCl$_3$ (100 ml) and then flushed for 10 min with N$_2$. To the stirred soln was added a soln of TTFA (105 mg) in dry THF (20 ml) and the mixture was left stirring for 10 min. SO_2 was bubbled through the soln for 30 sec before addition of conc. HCl (1 ml) in THF (10 ml) and stirring for 10 min. $CHCl_3$ (150 ml) was added and the organic phase was washed with H_2O (3 × 300 ml), dried (Na_2SO_4), and evaporated to give a blue residue which was chromatographed. Elution of the alumina with $CHCl_3$ gave first a red band which yielded **10** (R=Me; 13 mg from CH_2Cl_2–MeOH), and then a blue band (aetio-oxophlorin—I[6], 4 mg from CH_2Cl_2–MeOH). Further elution of the column with $CHCl_3$–MeOH (50:1) gave the *formyloxophlorin* (38 mg; 41%) from ether–n-hexane, m.p. 212–214°. (Found: C, 75.98; H, 7.50; N, 10.81. $C_{33}H_{38}N_4O_2$ requires: C, 75.83; H, 7.33; N, 10.72%). λ_{max} 392 (ϵ 58,700), 589 (15,700), and 638 nm (19,800). τ, −0.40, −0.34 ($\frac{1}{2}$H), 0.16, 0.26 ($\frac{1}{2}$H) CHO; 2.73, 3.45 (each 1H) *meso*-H; 6.0–8.0 (20 H, m) $C\underline{H}_2CH_3$ and Me; 8.0–9.2 (12 H, m) $CH_2C\underline{H}_3$·*m/e* 522 (0.5%) and 494 (100). ν_{max} (KBr) 3380 (NH), 3130 (OH) and 1590 (C=O) cm^{-1}.

β-Formyloctaethyl-α-oxophlorin (**11**; R=Et). This compound was similarly prepared from **10** (R=Et) in 49% yield. It was crystallised from ether–n-hexane and had m.p. 195–196°. (Found: C, 76.21; H, 8.04; N, 9.57. $C_{37}H_{46}N_4O_2$ requires: C, 76.51; H, 8.33; N, 9.53%). λ_{max} 399 (ϵ 58,200), 588 (11,600), and 638 nm (15,100), τ, −0.50 ($\frac{1}{2}$H), −0.01 ($\frac{1}{2}$H) CHO; 2.52, 3.21 (each 1H) *meso*-H; 5.9–8.0 (16 H, m), 8.0–9.2 (24 H, m) $C\underline{H}_2C\underline{H}_3$·*m/e* 578 (3%), 550 (100).

Zinc(II) *β-formylaetio-α-oxophlorin*—I. Compound **11** (R=Me; 35 mg) in CH_2Cl_2 (25 ml) was heated for 5 min with a soln of zinc(II) acetate (40 mg) in MeOH (20 ml). The mixture was washed with H_2O (25 ml), dried (Na_2SO_4), and evaporated to give a residue which was crystallised from CH_2Cl_2–n-hexane to give the *zinc complex* (37 mg; 95%) as fluffy red needles, m.p. >300°. (Found: C, 67.90; H, 6.33; N, 9.78; Zn, 11.41. $C_{33}H_{36}N_4O_2Zn$ requires: C, 67.63; H, 6.19; N, 9.56; Zn, 11.15%). λ_{max} 403 (ϵ 166, 600), 533 (10,500), 568 (7500) and 658 nm (2700). The compound was not sufficiently soluble in $CDCl_3$ for its NMR spectrum to be measured. *m/e* (^{64}Zn), 584 (10%), 556 (100). ν_{max} (KBr) 3540 (OH), 1690 (C=O) cm^{-1}.

Zinc(II) *β-Formyl-α-methoxyaetioporphyrin*—I. A suspension of K_2CO_3 (3 g) in dry MeOH (40 ml) was flushed with N_2 for 10 min before addition to the stirred soln of the foregoing zinc(II) complex (200 mg) in dry THF (50 ml). The colour of the soln immediately turned green (anion formation) and MeI (20 ml) was added to the mixture which was heated to 60° under reflux for 1 hr. The red–brown mixture was poured into H_2O (250 ml) and extracted into $CHCl_3$ (250 ml) which was washed with H_2O (2 × 250 ml) before being dried (Na_2SO_4) and evaporated to give a solid residue. Chromatography (elution with $CHCl_3$) gave *meso*-methoxyaetioporphyrin—I (13 mg from $CHCl_3$–MeOH). Further elution with $CHCl_3$–MeOH (50:1) gave, after evaporation of the appropriate eluates, the *formyl-methoxy-porphyrin complex* (26 mg; 13%) as red needles, m.p. >300°. (Found: C, 68.23; H, 6.08; N, 9.58; Zn, 10.85. $C_{34}H_{38}N_4O_2Zn$ requires: C, 68.05; H, 6.38; N, 9.34; Zn, 9.34%). λ_{max} 402 (ϵ 225, 700), 533 (11,400), 573 (13,900) and 632 nm (4100). The compound was not soluble enough in $CDCl_3$ for its NMR spectrum to be measured. *m/e* 598 (93%), 583 (52), 570 (100), 299 (15), 285 (22). ν_{max} (KBr) 1690 (C=O) cm^{-1}.

Zinc(II) *α-acetoxy-β-formyloctaethylporphyrin* (**12**; R=Et). Zinc(II) β-formyloctaethyl-α-oxophlorin (70 mg) (prepared by insertion of zinc as described above for **11** (R = Me)) was heated at 80° in pyridine (10 ml) and freshly distilled Ac_2O (3 ml) for 1 hr. The mixture was evaporated to dryness, using toluene to chase out last traces of pyridine. The residue was chromatographed on alumina (Grade V) (elution with $CHCl_3$). A minor red forerun was discarded and the green eluates were collected and evaporated to give a residue which was recrystallised from $CHCl_3$–n-hexane to afford the *zinc porphyrin* (38 mg; 50%) as green prisms, m.p. >300°. (Found: C, 68.42; H, 7.00; N, 8.13; Zn, 9.73. $C_{39}H_{46}N_4O_3Zn$ requires: C, 68.46; H, 6.78; N, 8.19; Zn, 9.55%). λ_{max} 410 (ϵ 226, 300), 536 (11,000), 570 (9900) and 632 nm (4800), τ, −2.22 (1H) CHO; 0.24, 0.38 (each 1H) *meso*-H; 6.0–6.5 (16H, m), 8.0–8.5 (24 H, m) $C\underline{H}_2C\underline{H}_3$; 7.31 (3H) COMe. ^{13}C NMR, δ ppm,† α and β-pyrrole carbons 163.44, 161.41, 149.17, 148.85, 147.42, 146.76, 145.32, 145.21, 145.03, 144.80, 143.02; γ and δ *meso* carbons 105.25, 102.25; side-chain methyls and methylenes, 25.54, 24.89, 24.60, 22.77, 22.70, 22.40, 21.90, 21.72, 21.63, 21.26, 21.07, 20.72, 20.11 and 19.47. *m/e* 682 (66%), 654 (37), 640 (69), 612 (100), ν_{max} 1760, 1595 (C=O) cm^{-1}.

Zinc(II) meso-*cyano-aetioporphyrin*—I. *meso*-Cyano-aetioporphyrin—I[18] (115 mg) in $CHCl_3$ (25 ml) was heated under reflux with zinc(II) acetate (120 mg) in MeOH (20 ml) containing HOAc (0.5 ml) for 20 min. The mixture was evaporated to low volume whereupon the *zinc porphyrin* (119 mg; 92%) crystallised as purple needles, m.p. >300°. (Found: C, 70.17; H, 6.13; N, 12.35. $C_{33}H_{35}N_5Zn$ requires: C, 69.90; H, 6.22; N, 12.35%). λ_{max} 406 (ϵ 171,000), 546 (8600) and 600 nm (18,300). The compound was not sufficiently soluble in $CDCl_3$ for its NMR spectrum to be obtained. It also failed to react with TTFA (see text).

β-Cyano-octaethyl-α-oxophlorin (**14**; R=Et). Compound **13** (R=Et; 230 mg; obtained in 98% yield by treatment of *meso*-cyano-octaethylporphyrin with cadmium(II) acetate in hot MeOH and CH_2Cl_2 during 10 min with work-up as described above for the zinc(II) analogue) was dissolved in dry THF (50 ml) and CH_2Cl_2 (100 ml) and flushed with N_2 for 10 min. To this soln was added a soln of TTFA (205 mg) in THF (30 ml) and the mixture was stirred for 10 min before SO_2 was bubbled through it for 30 sec. Conc. HCl (2 ml) in THF (20 ml) was added and the mixture was stirred for 5 min before being poured into CH_2Cl_2 (200 ml) and washed with H_2O (3 × 400 ml) and dried (Na_2SO_4). Evaporation gave a solid which was chromatographed (elution with CH_2Cl_2). The first band eluted afforded *meso*-cyano-octaethylporphyrin (116 mg; crystallised from CH_2Cl_2–MeOH), and this was followed by a blue band which afforded the *cyano-oxophlorin* (34 mg; 17% or 44% based on consumed starting material) as red prisms from CH_2Cl_2–n-hexane, m.p. 225–227°. (Found: C, 77.23; H, 7.76: N, 12.30. $C_{37}H_{45}N_5O$ requires: C, 77.18; H, 7.88; N, 12.16%). λ_{max} 404 (ϵ 123,200), 572 (11,100), and 613 nm (15,600). τ, 2.13 (2 H, br) *meso*-H; 6.5–7.1 (16 H, m), 8.4–8.9 (24 H, m) $C\underline{H}_2C\underline{H}_3$·*m/e* 575 (100%), 560 (5), 550 (12), 287.5 (17). ν_{max} (KBr) 2190 (CN), 1575 (C=O) cm^{-1}. When the initial mixture was left for 1 hr the absolute yield was raised to 21%.

β-Cyano-aetio-α-oxophlorin—I (**14**; R=Me). This compound was similarly prepared from cadmium(II) *meso*-cyano-aetioporphyrin—I (190 mg) in 30% yield (30 mg). Chromatography allowed recovery of 45 mg unconsumed *meso*-cyano-aetioporphyrin—I.

α-Benzoyloxy-β-cyano-aetioporphyrin—I (**15**; R=Me). The foregoing cyano-oxophlorin (39 mg) in dry pyridine (10 ml) was stirred with benzoyl chloride (2 ml) for 5 min before evaporation of the mixture to dryness. The residue was chromatographed (elution first with toluene and then CH_2Cl_2) and the red eluates were evaporated to give a residue which was crystallised from CH_2Cl_2–MeOH to give the *porphyrin* (38 mg; 81%) as red prisms, m.p. 170–172°. (Found; C, 76.61; H, 6.74; N, 11.53. $C_{40}H_{41}N_5O_2$ requires: C, 77.02; H, 6.63; N, 11.23%). λ_{max} 406 (ϵ 124,800), 508 (10,700), 543 (10,500), 575 (6600), and 624 nm (7700), τ, 0.28, 0.48 (each 1H) *meso*-H; 1.34 (2H, m), 2.24 (3H, m) Ph; 5.7–6.4 (8H, m) $C\underline{H}_2C\underline{H}_3$; 6.49, 6.66, 6.73, 6.86 (each 3H) 4 × Me; 8.2–8.7 (12H, m) $CH_2C\underline{H}_3$. A peak at τ 0.22 indicated possible contamination with the $\alpha\gamma$ isomer or starting *meso*-cyano-aetioporphyrin—I; TLC showed one spot. *m/e* 623 (56%), 589 (14), 518 (100), and 503 (43).

α-Acetoxy-β-cyano-octaethylporphyrin (**16**; R=Et). Compound **14** (R=Et; 20 mg) in dry pyridine (5 ml) was heated with freshly distilled Ac_2O (2 ml) at 70° for 10 min. The mixture was evaporated to dryness and the residue was chromatographed on silicagel (MFC) (elution with CH_2Cl_2). Evaporation of the red eluates and crystallisation from CH_2Cl_2–n-hexane gave the *porphyrin* (19 mg; 89%) as purple microneedles, m.p. 214–215°. (Found: C, 75.51; H, 7.54; N, 11.35. $C_{39}H_{47}N_5O_2$ requires: C, 75.81; H, 7.67; N, 11.34%). λ_{max} 410 (ϵ 155,800), 512 (11,100), 547 (11,400), 580 (6100), and 628 nm (7300). τ, 0.02, 0.16 (each 1H) *meso*-H; 5.5–6.5 (16H, m), 8.0–8.3 (24 H, m) $C\underline{H}_2C\underline{H}_3$; 7.15 (3H) COMe; (a very small peak at τ −0.12 indicated possible contamination with the $\alpha\beta$ isomer, or starting *meso*-cyanoporphyrin; TLC showed one spot). *m/e* 617 (50%), 575 (100).

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†At this stage in the development of ^{13}C NMR in porphyrins, the precise assignments are unknown. The intention here is to provide evidence of a lack of symmetry in the molecule, i.e. $\alpha\beta$ disubstitution.

γ-Chloro-octaethyl-α-oxophlorin (**19**; R=Et). Compound **20** (R=Et;[6] 260 mg) in dry THF (50 ml) and CH_2Cl_2 (100 ml) was flushed with N_2 for 10 min before addition of a soln of TTFA (254 mg) in dry THF (50 ml). After 10 min stirring the colour had changed from red to yellow-brown, so conc. HCl (4 ml) in THF (10 ml) was added (colour change to green). SO_2 was bubbled through the soln for 30 sec and the mixture was poured into CH_2Cl_2 (200 ml) and washed with H_2O (3 × 400 ml). The mixture was dried (Na_2SO_4), evaporated to dryness, and the residual solid was chromatographed (elution with CH_2Cl_2). A forerun afforded αγ-dioxo-octaethylporphodimethene[12] (10 mg, from CH_2Cl_2–n-hexane, m.p. 268–270°). Further elution and evaporation of the green eluates gave the *chloro-oxophlorin* (148 mg; 60%) as black-green prisms from CH_2Cl_2–n-hexane, m.p. >300°. (Found: C, 73.95; H, 7.48: N, 9.40; Cl, 6.11. $C_{36}H_{45}ClN_4O$ requires: C, 73.88; H, 7.75; N, 9.57; Cl, 6.06%), λ_{max} 461 (20,100), and 603 nm (8100). τ, 3.25, 4.74 (each 1H) *meso*-H; 7.0–8.0 (16 H, m), 8.5–9.2 (24 H, m) $C\underline{H}_2C\underline{H}_3$. *m/e* 586 (0.5%), 584 (1), 550 (100), ν_{max} (KBr) 3340 (NH), 1600 (C=O) cm^{-1}.

α-Acetoxy-γ-chloro-octaethylporphyrin (**21**; R=Et). The foregoing chloro-oxophlorin (90 mg) in $CHCl_3$ (50 ml) was heated at 65° for 30 min with a mixture of acetyl chloride (3 ml) in dry pyridine (20 ml) (prepared by dropwise addition of the former into the latter at 0°). The mixture was then poured into $CHCl_3$ (250 ml), washed with H_2O (3 × 400 ml), dried (Na_2SO_4) and evaporated to give a red oil. This was chromatographed (elution first with toluene and then with $CHCl_3$) and the red eluates were evaporated to give a residue which was crystallised from CH_2Cl_2–MeOH to give the *porphyrin* (31 mg; 32%) as red prisms, m.p. 196–197°. (Found: C, 72.71; H, 7.39; N, 8.70; Cl, 5.90. $C_{38}H_{47}ClN_4O_2$ requires: C, 72.76; H, 7.55; N, 8.93; Cl, 5.65%), λ_{max} 410 (ε 194,600), 506 (16,100), 536 (4600), 575 (6500) and 624 nm (1800). τ, −0.08 (2H) *meso*-H; 5.8–6.3 (16H, m) $C\underline{H}_2CH_3$; 7.15 (3H) COMe; 8.18 (24 H, t) $CH_2C\underline{H}_3$. ^{13}C NMR, δ ppm, 172.21 (C=O), α and β pyrrole carbons 145.04, 144.21, 143.78, 142.00, 141.52, 140.81, 140.03, 139.38; β,δ *meso*-C 111.07; side-chain methyl and methylene carbons, 22.80, 22.02, 21.59, 19.82, 19.63, 18.39, 17.00, 16.84 and 16.61. *m/e* 628 (15%), 626 (30), 584 (56), 550 (100). ν_{max} (KBr) 1755 (C=O) cm^{-1}.

γ-Chloro-aetio-α-oxophlorin—I (**19**; R=Me). This compound was prepared in the same manner as the analogue (**19**; R=Et) described above in 61% yield, with m.p. >320°, crystallised from CH_2Cl_2–MeOH as black-green prisms. (Found: C, 72.76; H, 6.98; N, 10.74; Cl, 6.79. $C_{32}H_{37}ClN_4O$ requires: C, 72.64; H, 7.05; N, 10.59; Cl, 6.70%), λ_{max} 412 (ε 20,500) and 610 nm (7800). τ, 3.30, 3.28 (each 1H, br) *meso*-H; 7.0–8.0 (20H, br m) $C\underline{H}_2CH_3$ and Me; 8.2–9.2 (12H, br m) $CH_2C\underline{H}_3$·*m/e* 530 (7%), 528 (20%), 494 (100). ν_{max} (KBr) 3350 (NH), 1600 (C=O) cm^{-1}.

α-Benzoyloxy-γ-chloro-aetioporphyrin—I. The foregoing oxophlorin (80 mg) in dry THF (30 ml) and dry pyridine (5 ml) was treated with benzoyl chloride (5 ml) and heated under reflux for 10 min before being poured into 10% NaOAc aq (100 ml) and extracted with CH_2Cl_2 (150 ml). The organic extract was dried (Na_2SO_4) and evaporated to give a red oil which was chromatographed (Grade II alumina, elution first with toluene and then with CH_2Cl_2). The red eluates were evaporated to give a residue which was crystallised from CH_2Cl_2–n-hexane to give the *porphyrin* (44 mg; 46%) as red prisms, m.p. 293–294°. (Found: C, 73.99; H, 6.49; N, 8.92; Cl, 5.88. $C_{39}H_{41}ClN_4O_2$ requires: C, 73.97; H, 6.53; N, 8.85; Cl, 5.60%), λ_{max} 407 (ε 202,000), 503 (17, 500), 534 (3900), 573 (6000) and 625 nm (970). τ, 0.00 (2H) *meso*-H; 2.25 (2H, m), 3.28 (3H, m) Ph; 5.9–6.4 (8H, m) $C\underline{H}_2CH_3$; 6.34, 6.41, 6.45, 6.70 (each 3H) Me; 9.1–9.5 (12H, m) $CH_2\underline{H}_3$. *m/e* 634 (5%), 532 (10), 598 (8), 527 (33), 508 (100), ν_{max} (KBr) 1740 (C=O) cm^{-1}.

meso-*Amino-octaethylporphyrin*. *meso*-Nitro-octaethylporphyrin[9] (210 mg) in formic acid (75 ml) containing 5% Pd–C (50 mg; caution during addition of charcoal to formic acid!) was hydrogenated at room temp and atmospheric pressure for 5 min. (Use of 10% Pd–C and longer reaction times cause formation of large amounts of octaethylporphyrin). The mixture was filtered through Celite, poured into $CHCl_3$ (250 ml), washed with H_2O (300 ml), 10% K_2CO_3 aq (300 ml), then H_2O again, and dried (Na_2SO_4). Evaporation gave a solid residue which was chromatographed (elution with CH_2Cl_2). The purple eluates were evaporated to give a residue which was crystallised from CH_2Cl_2–n-hexane to give the porphyrin (170 mg; 85%) as purple needles, m.p. >300° (soft at 269°), (Lit.[1] 258–259°). (Found: C, 78.43; H, 8.43; N, 12.91. Calc. for $C_{36}H_{47}N_5$: C, 78.64; H, 8.62; N, 12.74%). λ_{max} 416 (ε 197,900), 421 inf (181,500), 515 (12,200), 551 (5600), 583 (3700), and 636 nm (6400), *m/e* 549 (100%), 534 (16), 274.5 (14).

α-Amino-γ-chloro-octaethylporphyrin (**23**; R=Et). The foregoing aminoporphyrin was converted into its zinc(II) complex in 97% yield by treatment of it in CH_2Cl_2 with zinc(II) acetate in methanol. Zinc(II) *meso*-amino-octaethylporphyrin (**22**; R=Et) (100 mg) in dry THF (50 ml) and $CHCl_3$ (100 ml) was flushed with N_2 for 10 min before treatment of the stirred soln with TTFA (98 mg) in dry THF (50 ml). After stirring for a further 5 min, SO_2 was passed through the soln for 30 sec and conc. HCl (2 ml) in THF (30 ml) was added. $CHCl_3$ (200 ml) was added and the mixture was washed with H_2O (3 × 400 ml), dried (Na_2SO_4), and evaporated. The residue was chromatographed (elution with CH_2Cl_2) and the purple eluates were collected. Evaporation gave a residue which was crystallised from CH_2Cl_2–MeOH to give the *porphyrin* (51 mg; 53%) as purple needles, m.p. >300°. (Found: C, 74.15; H, 8.06; N, 12.02. $C_{36}H_{46}ClN_5$ requires: C, 74.00; H, 7.94; N, 11.99%), λ_{max} 422 (ε 167,800), 524 (11,400), 561 (7400), 595 (3300), and 651 nm (6800). τ, 0.39 (2H) *meso*-H; 3.76 (2H, br) NH_2; 6.0–6.5 (16H, m), 8.0–8.4 (24H, m) $C\underline{H}_2C\underline{H}_3$. ^{13}C NMR, δ ppm, α and β pyrrole carbons 146.24, 145.41, 145.29, 141.14, 140.47, 139.42, 138.15, 136.42; β,δ *meso*-carbons 105.30; side-chain methyl and methylene carbons, 22.48, 21.70, 19.61, 19.32, 18.41, 18.15, 16.87, 15.55. *m/e* 585 (1), 583 (2), 549 (100), 504 (10%).

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