NMR Spectra of the Porphyrins. Part 42.[1] The Synthesis and Aggregation Behaviour of Some Chlorophyll Analogues

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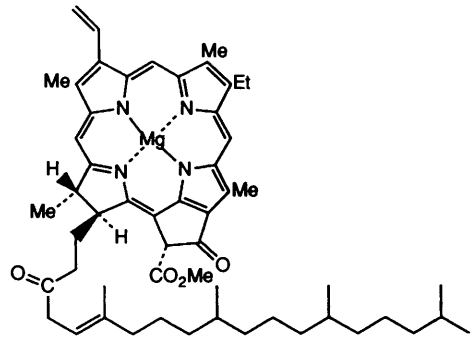
The synthesis of three analogues of pyrochlorophyll a with the selective removal of the carbonyl functions is described; 7-despropionate-7-propyl-mesopyrochlorophyllide a (DPC), methyl 9-desoxo-mesopyrochlorophyllide a (DOC) and 9-desoxo-7-despropionate-7-propyl-mesopyrochlorophyllide a (DODPC), were prepared from methyl mesopyropheophorbide a by the extension of known preparative methods. A detailed study of the aggregation of these compounds in solution, using the NMR shifts observed upon dissociation of the aggregates formed in $CDCl_3$ solution by the addition of [$^2H_4$]methanol, together with the application of the ring current theory of the porphyrin ring is given. In DPC the observed aggregation shifts can be given a precise explanation in terms of a sandwich type dimer with an interplanar separation of *ca.* 4.2–4.7 Å. All the dimer models considered allow for coordination between the C-9 keto group and the magnesium atom of the adjoining molecule, probably *via* a bridging water molecule. In DOC the calculated dimer shifts based on the sandwich type dimers also give a reasonable explanation of the observed shifts, although now it is the C-7c carbonyl group which is positioned so as to complex with the magnesium atom of the adjacent porphyrin molecule, with a smaller interplane separation of *ca.* 3.7–3.9 Å, which may imply direct coordination of the carbonyl and the magnesium atom. In DODPC, in which no carbonyl function is present, there is no evidence of any aggregation in solution. Thus in this metallochlorin there is no π–π attractive interaction, in complete contrast to the analogous metalloporphyrins.

The tendency of porphyrins and chlorins to aggregate in solution is of considerable interest, both practically in terms of obtaining reproducible NMR chemical shifts, and also more fundamentally the reactions of these molecules both *in vitro* and *in vivo* may be determined by their state of aggregation. Indeed the phenomenon of photosynthesis, without which virtually all life on this planet would cease, relies upon interactions between chlorophyll molecules in some antenna systems and also in the bacterial reaction centre.[2–4]

In chlorophylls the determining interaction in solution is the complexation of the coordinatively unsaturated Mg atom with a donor atom of a neighbouring molecule, and as chlorophyll a (Chl; **1**) has three keto/ester groups capable of coordinating to the Mg atom, a variety of aggregate structures are possible.

Early NMR and IR studies by Katz and co-workers[5–7] identified the C_9 keto oxygen as the major coordinating atom, probably bound to Mg *via* a water molecule (the Shipman model). This was later contested by Fong[8] who suggested that the dimer structure involved the C_{10} ester group. This model however cannot explain the virtually identical aggregation behaviour of chlorophyll and pyrochlorophyll in which the C_{10} ester group is removed. Other proposed dimer structures are the Strouse model,[9] the skew model[10] and two novel structures (the piggy-back and back-to-back models), proposed in previous parts of this Series.[11,12] In our earlier investigations[11,12] the structure of the chlorophyll dimer was deduced by first obtaining the NMR complexation shifts for the ^1H nuclei in the molecule, and then using a refined ring current model to calculate these complexation shifts for any given dimer geometry. The complexation shifts themselves were obtained by titrating the chlorophyll solution in $CDCl_3$ with aliquots of [$^2H_4$]-methanol or [$^2H_5$]-pyridine. These weak nucleophiles preferentially bind to the Mg atom and dissociate the chlorophyll aggregates. Back titration from the known assignments of the disaggregated ^1H spectrum gave the assignments in the aggregate and aggregate shifts.



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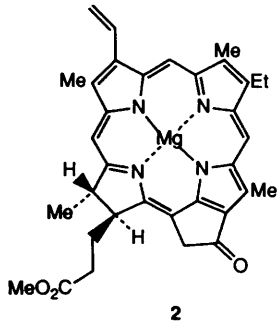

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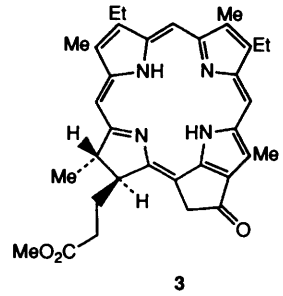

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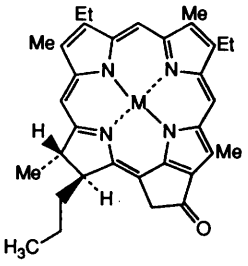
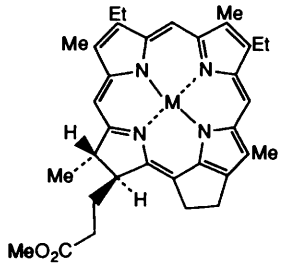
This technique was performed for both chlorophyll a (Chl; **1**)[11] and methyl pyrochlorophyllide a (MeP; **2**).[12] The latter investigation showed conclusively that the C_{10} ester group and the phytyl side chain are not involved in the dimer formation. Furthermore, on the basis of the more complete data set obtained for MeP it was suggested that both the C_9

keto group and the C_7 ester group may be involved in the dimer geometry, *via* a hydrogen bonding network involving a water molecule. The C_7 ester group had not previously been implicated in the dimer geometry. All these studies have been reviewed recently.[3]

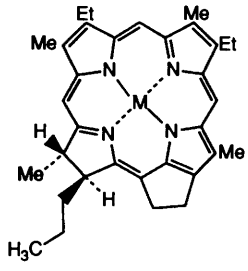
It was felt that a similar investigation on MeP analogues in which the complexing keto groups were selectively replaced by methylenes would be of some interest in positively identifying the role of each keto group. Furthermore, as there is no evidence from any of the dilution studies of the involvement of the C-2 vinyl group in chlorophyll a being implicated in the dimer geometry, for practical reasons the corresponding C-2 ethyl ('meso') derivatives were synthesised, using as starting material the available chlorin methyl mesopyropheophorbide **3**. Here we give the preparations and results of a detailed NMR investigation on the complexing behaviour of 7-despropionate-7-propyl-mesopyrochlorophyllide a (DPC; **4**), methyl 9-desoxo-mesopyrochlorophyllide a (DOC; **5**) and 9-desoxo-7-despropionate-7-propyl-mesopyrochlorophyllide a (DODPC; **6**).



4A M = 2 H
4 M = Mg



5A M = 2 H
5 M = Mg

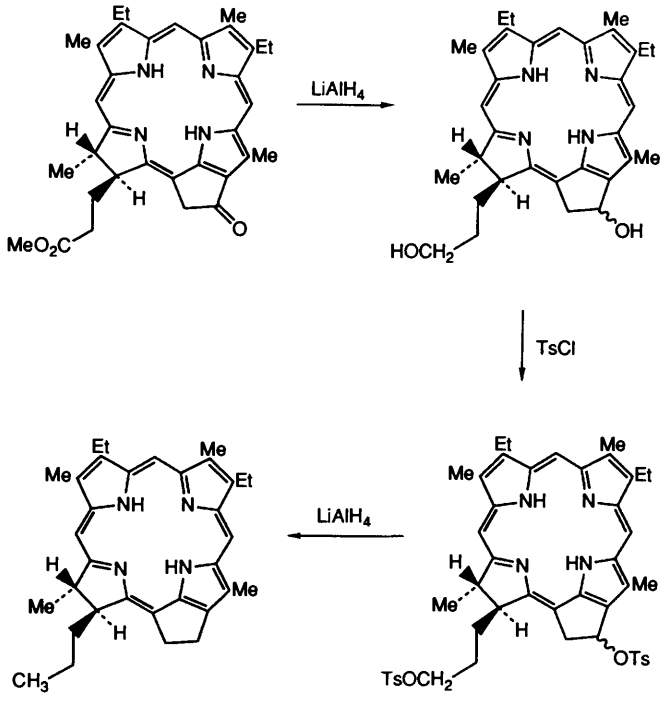


6A M = 2 H
6 M = Mg

Synthetic Studies.—The necessary starting material for these syntheses was methyl pyropheophorbide a **3** which was obtained[13] by acetone extraction of chlorophyll a from *Spirilina maxima* algae. This is a particularly convenient source of the chlorophyll a series because it contains no chlorophyll b.

A. *Methyl 9-desoxomesopyropheophorbide a.* The first chlorophyll a derivative prepared was methyl 9-desoxomesopyropheophorbide a **5A**. Following the method of Gribble[14] the 9-carbonyl was converted to the corresponding methylene group. This procedure involved treatment with sodium borohydride in the presence of TFA. Thus, sodium borohydride in the form of a pellet was added to dry trifluoroacetic acid. Chlorin **3** was also dissolved in TFA and added to the NaBH–TFA mixture. Monitoring the reaction by UV–VIS spectroscopy determined the reaction to be complete within 3 h (blue-shift of the long wavelength absorption maximum from 656 nm to 638 nm). A normal aqueous workup and purification gave the required compound **5A** without any detectable reduction of the 7-methyl propionic ester.

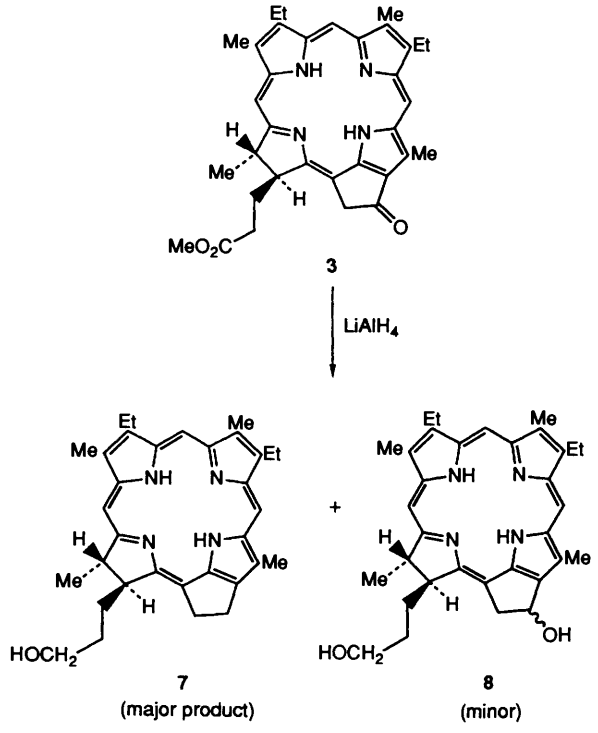
B. *9-Desoxo-7-propyl derivative.* The second chlorophyll a derivative prepared was the 9-desoxo-7-propyl compound **6A**.

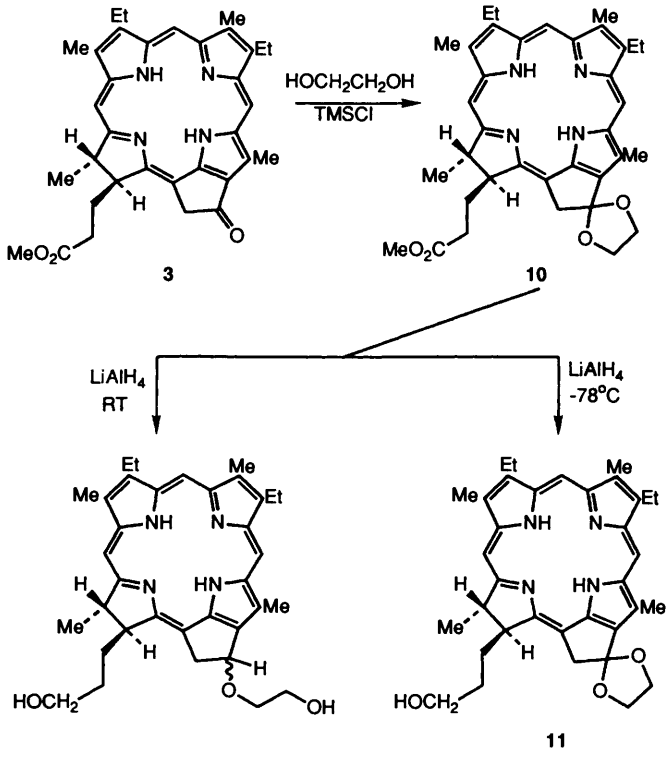


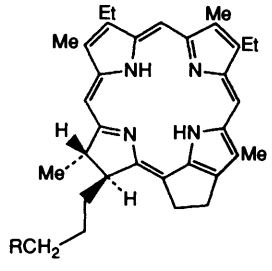
Scheme 1 Initial strategy for removal of carbonyl functions

The initial strategy for preparation of this material was to reduce the 9-keto and 7-ester functions to their corresponding hydroxy functions, then convert them to the toluene-*p*-sulfonates and subsequently displace the leaving group with a second lithium aluminium hydride treatment. See Scheme 1. Conversion of a methyl propionate side chain to its corresponding propyl side chain using this type of strategy was successfully accomplished by Verne-Mismer *et al.*[15] in the preparation of a petroporphyrin. Thus, methyl mesopyropheophorbide **3** was treated with excess $LiAlH_4$ in dry diethyl ether at 0 °C. Monitoring the course of the reaction by TLC indicated a faster than expected spot had appeared as the reaction proceeded and would not react further. It was thought initially that this was simply unreduced ester. However, this spot was much less mobile on the TLC than the starting material, but not nearly as slow as expected based on the mobility of other dihydroxy chlorins. The UV–VIS spectrum showed that the long-wavelength absorption maximum had blue-shifted from 656 nm to 638 nm as expected for the decrease in conjugation with the 9-carbonyl based on the results obtained for **5A** above. After an aqueous workup and chromatography, the NMR spectrum of the main band showed that the propionic ester had indeed been reduced to the corresponding hydroxy propyl, but there was only one hydroxy group in the molecule. Surprisingly, the 9-carbonyl had been reduced completely to methylene. The proton NMR spectrum showed a very complicated multiplet centred at 4.85 ppm, corresponding to the 10-CH_2 and another multiplet at 4.09 ppm corresponding to the 9-CH_2. The resonance expected for an aryl proton which is geminal to a hydroxy (such as the expected 9-H) is expected to be usually between 6.0 ppm and 7.0 ppm, but there was no peak present near this region showing that this major product was not a 9-hydroxy compound. The structure was therefore determined to be **7**. The hydroxy group was destined to be reduced to methylene in any case, so this provided a shortcut to the desired product. Depending on the length of time the reaction was allowed to proceed, varying amounts of 9-hydroxy-7-hydroxypropyl diastereoisomers **8** were obtained in low yield.

The next step was to convert the hydroxy group of **7** into a good leaving group so that treatment with a hydride reagent could accomplish eventual complete reduction to propyl. This







9A R = OTs
9B R = OMs

was initially attempted *via* the tosyl derivative **9A**, but reduction of this compound with excess $LiAlH_4$ resulted in a poor yield of the desired product **6A**. The mesyl derivative **9B** provided a satisfactory avenue. The methanesulfonate was prepared by the method of Crossland and Servis[16] which involved stirring the hydroxypropyl compound **7** in dry CH_2Cl_2 with methanesulfonyl chloride (mesyl chloride) in the presence of triethylamine. In this case only three equivalents of mesyl chloride were used. The reaction was very fast, even at 0 °C, to give an 88% yield of product. This was a significant improvement in yield compared to 53% for the toluene-*p*-sulfonate. Treatment of methanesulfonate **9B** with $LiAlH_4$ proceeded without formation of large quantities of baseline material this time to give 59% of the 7-propyl-9-desoxo compound **6A**.

C. *9-Oxo-7-propyl derivative.* The third target molecule to be prepared was **4A**, the 9-oxo-7-propyl compound. It was envisioned that protection of the 9-keto group, followed by reduction of the propionate side chain as discussed above, and then removal of the protecting group would give the desired material. One of the most common ways of protecting carbonyl compounds is to form an acyclic or a cyclic ketal (acetal).[17] Such protected groups are stable toward organometallic reagents and they are easily removed by acidic hydrolysis.

In 1983, Chan and co-workers[18] prepared a series of 1,3-dioxolanes by treatment of carbonyl compounds with ethylene glycol and trimethylsilyl chloride (TMSCl). Following this precedent, methyl mesopyropheophorbide a (**3**) was dissolved in CH_2Cl_2 and ethylene glycol was added. Although two phases were evident at this stage, addition of TMSCl gave a completely miscible solution. After stirring for two hours at room temperature, TLC showed the reaction to be complete, and the desired ketal **10** was obtained in 87% yield. Recovered starting material accounted for the remainder of the mass balance, so the yield based on recovered starting material is virtually quantitative.

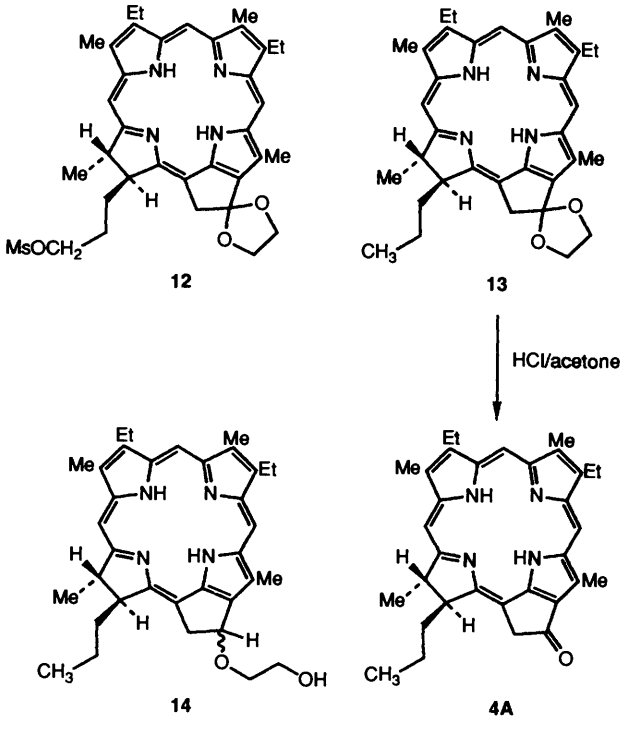
With the protected ketone **10** in hand, the next step required reduction of the 7-methyl propionate ester to propyl. Essentially the same strategy as employed for preparation of **6A** was carried out for this conversion. The first step was reduction with $LiAlH_4$ of the propionate ester to the corresponding hydroxypropyl substituent. Initially this reaction was attempted at room temperature, but this caused ring opening of the 1,3-dioxolane; when the reduction was done at −78 °C **11** was obtained in 90% yield. Conversion of the hydroxypropyl compound **11** to the methanesulfonate was carried out as discussed above with a small excess of methanesulfonyl chloride. Again the reaction was very fast, and a quantitative yield of the methanesulfonate derivative **12** was obtained.

The next required reaction was to convert the 7-(3-mesyloxypropyl) substituent into 7-propyl. Using $LiAlH_4$ at room temperature was not attempted for fear of ring-opening the ketal protecting group. When the reaction was done at −78 °C, however, the methanesulfonate was not displaced. Warming to −23 °C (dry ice–CCl_4) and then −15 °C (dry ice–ethylene glycol) still gave no product. Warming still further, to 0 °C caused ketal ring-opening to occur about as fast as displacement of the methanesulfonate group. Optimum conditions were achieved by doing the reaction with an ice-salt bath at −7 °C. Even at this temperature considerable amounts of ketal-opened product were obtained. Thus, **12** was dissolved in ether and treated with $LiAlH_4$ under N_2. Carefully monitoring the reaction by TLC indicated that maximum product formation occurred after about 20 minutes; the relative ratio of starting material to product stopped changing and formation of the desired product **13** was accompanied by conversion to **14**. However, the desired product **13** was obtained in 52% yield. Removal of the protecting group was accomplished by trans-

Table 1 Titration of DPC **4** in $CDCl_3$ with [$^2H_4$]-methanol[a]

	Ligand/mol																	
Proton	0	0.4	0.7	1.1	1.6	2.0	2.5	3.5	4.9	5.8	8.0	10.0	19.1	28.0	36.9	54.3	87.1	141.1
Meso β	8.95	9.28	9.31	9.34	9.36	9.38	9.38	9.39	9.40	9.41	9.42	9.42	9.44	9.44	9.44	9.44	9.44	9.43
α	8.72	8.93	8.97	8.99	8.99	9.02	9.02	9.02	9.03	9.03	9.03	9.03	9.04	9.03	9.04	9.02	9.00	9.00
δ	8.07	8.14	8.16	8.18	8.18	8.20	8.20	8.21	8.21	8.21	8.21	8.21	8.21	8.21	8.21	8.20	8.19	8.19
10-CH a	—	—	—	—	—	—	4.50	4.60	4.66	4.70	4.76	4.80	4.92	4.98	5.02	5.08	5.13	5.15
b	—	—	—	—	—	—	4.26	4.29	4.42	4.46	4.53	4.58	4.72	4.80	4.85	4.95	4.95	5.00
8-H	4.23	4.39	4.39	4.46	4.46	4.49	4.49	4.50	4.49	4.49	—	4.49	4.49	4.47	4.47	4.47	4.46	4.46
7-H	—	—	4.00	4.05	4.06	4.09	4.09	4.10	4.11	4.11	—	4.12	4.13	4.13	4.14	4.13	4.12	4.12
5-Me	—	—	2.83	2.79	2.78	2.76	2.76	2.81	2.87	2.91	3.00	3.10	3.24	3.33	3.39	3.52	3.58	3.58
3-Me	3.16	3.22	3.24	3.26	3.26	3.27	3.27	3.27	3.27	3.27	3.27	3.27	3.27	3.26	3.26	3.25	3.25	3.25
1-Me	3.05	3.12	3.14	3.16	3.17	3.17	3.17	3.17	3.18	3.18	3.18	3.18	3.17	3.17	3.17	3.16	3.15	3.15
8-Me	—	—	—	1.82	1.83	1.83	1.84	1.84	1.84	1.84	1.83	1.83	1.81	1.80	1.79	1.78	1.77	1.77
4b-Me	—	—	—	1.77	1.77	1.78	1.78	1.78	1.78	1.78	1.77	1.77	1.74	1.73	1.73	1.71	1.70	1.70
2b-Me	—	—	—	1.67	1.68	1.68	1.69	1.68	1.69	1.69	1.69	1.69	1.69	1.68	1.68	1.68	1.67	1.67
7d-Me	—	—	—	1.62	1.03	1.04	1.05	1.06	1.05	1.05	1.05	1.05	1.03	1.02	1.01	1.01	1.01	1.01

[a] Initial concentration = 3.4×10^{-2} mol dm^{-3} (9.0 mg, in 0.5 cm^3) in $CDCl_3$.



ketalisation in acetone and dilute aqueous HCl[19] to give the 9-oxo-7-propyl product **4A** in 83% yield.

The magnesium was inserted into the three free base chlorins **4A**, **5A**, **6A** using Eschenmoser's procedure,[20,21] which utilises the bromomagnesium salt of 2,6-di-*tert*-butyl-4-methylphenol (BHT), to give the required products **4**, **5**, **6**.

Results and Discussion

NMR Studies

(*a*) *DPC* **4**.—Table 1 gives the titration measurements and Fig. 1 some illustrative spectra. The spectrum obtained with an excess of [$^2H_4$]-methanol is that typical of a monomeric species characterised by sharp well-resolved resonances [Fig. 1(*c*)]. The assignment of this monomer was relatively straightforward due to its similarity with MeP.[12] The 7-propyl methyl is clearly visible as a triplet at 1.00 ppm. The only ambiguities were the assignments for the meso and β-methyl protons. These were resolved by NOE experiments. Irradiation of the methyl resonance at 3.19 ppm clearly caused an enhancement at the δ meso proton at 8.19 ppm confirming it as the 1-Me resonance. Irradiation of the 5-Me resonance at 3.59 ppm caused an enhancement of the downfield signal at 9.43 ppm, confirming it as the β meso proton, and the signal at 9.00 ppm as the α meso proton. The latter assignment was confirmed by an enhancement upon irradiation of the 3-M at 3.25 ppm. The effect of the replacement of the 2-vinyl substituent in MeP by ethyl is an upfield shift of about 0.2 ppm for both the α and 1-Me protons. The full assignments of the monomeric species of DPC in $CDCl_3$ with excess CD_3OD, [$^2H_6$]-acetone and those of the monomeric MeP are shown in Table 2. Having assigned the spectra of the monomeric species, the aggregation was analysed by back titration. The spectrum of the aggregate was again very broad; however the meso proton resonances were just distinguished. As methanol was added these resonances appeared to show a slight downfield shift. At 0.7 mol equiv. of methanol the 5-Me resonance was sufficiently sharp to be observed [Fig. 1(*a*)]. As the disaggregation continued this resonance remained relatively stationary (a slight upfield shift of 0.07 ppm) until approximately 2–2.5 mol equiv. had been added [Fig. 1(*b*)]. Upon further additions of ligand this resonance dramatically moved downfield crossing the 3-Me and 1-Me resonances. The only other resonance which showed a large aggregation shift was that of the 10-CH_2 protons which moved downfield across the 8-H and 7-H resonances. The remaining resonances showed very little or no aggregation shift after the addition of 2 mol equiv. The initial addition of methanol up to 2.0 mol equiv. would appear to be breaking up larger aggregates into dimers and the shifts seen upon further addition are due to the dissociation of the dimer. Thus the dimer aggregation shifts are taken as the difference between the disaggregate shifts and the shifts at 2.0 mol equiv. This gives a $\Delta\delta$ of 0.82 for the 5-Me resonance and 0.65 and 0.74 for the two 10-CH_2 protons. One would expect these protons to have large aggregation shifts due to their proximity to the C-9 keto function. The $\Delta\delta$s for all the protons are shown in Table 2 as well as those for MeP. It can be clearly seen that the shifts are different to MeP implying a different dimer geometry. The most obvious difference is that there are no $\Delta\delta$s for the 8 H and 7 H protons. This implies that with the removal of the C-7 propionate group, the ring D is no longer involved in the aggregation mechanism. In the case of MeP the C-7 ester function must pull this ring into the area of overlap.

Analysis of the titration curve for the 5-Me resonance, using the previously described equilibria[12] gave excellent agreement

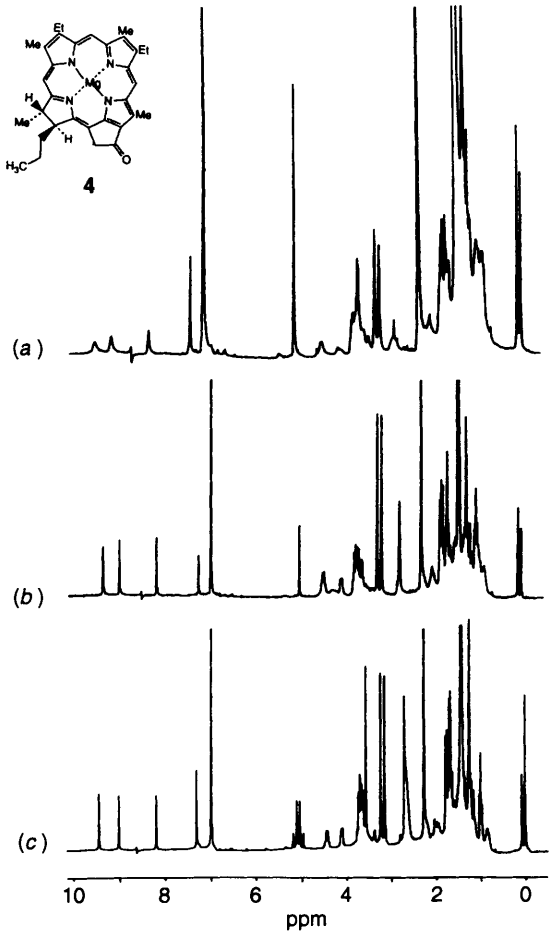


Fig. 1 ^{1}H NMR spectra of DPC **4** upon disaggregation with [$^2H_4$]-methanol: (*a*) 0.7 mol equiv.; (*b*) 2.0 mol equiv.; (*c*) 141 mol equiv.

Table 2 Observed ^{1}H NMR chemical shifts and complexation shifts for DPC **4** and methylpyrochlorophyllide a (MeP)

Proton	DPC[a]	DPC[b]	MeP[c]	DPC[d]	MeP[d]
β	9.617	9.432	9.55	0.06	0.15
α	9.186	9.002	9.29	−0.01	0.08
δ	8.405	8.187	8.30	0.00	0.09
10-CH a	5.051	5.153	5.15	0.65	0.95
b	4.908	5.003	5.03	0.74	1.25
8-H	4.537	4.555	4.40	−0.02	0.23
7-H	4.243	4.125	4.18	−0.04	0.33
4a-H	3.819	3.729	3.75	—	0.02
2a-H	3.757	3.694	—	—	—
5-Me	3.554	3.576	3.65	0.82	0.66
3-Me	3.273	3.246	3.25	−0.02	0.01
1-Me	3.193	3.155	3.33	−0.02	0.01
7a-CH	obscured	obscured	—	—	
7b-CH		1.994	—	—	
8-Me	1.772	1.775	1.72	−0.06	0.10
4b-Me	1.689	1.701	1.70	−0.08	0.02
2b-Me	1.681	1.674	—	−0.02	—
7c-Me	0.990	1.001		−0.04	—

[a] Solution in [$^2H_6$]-acetone (6.3 × 10^{-3} mol dm^{-3}). [b] Solution in $CDCl_3$ with excess [$^2H_4$]-methanol (3.4 × 10^{-2} mol dm^{-3}). [c] Solution in $CDCl_3$ with excess [$^2H_5$]-pyridine (ref. 12). [d] Complexation shifts.

for a value of $K = 0.17$ (Fig. 2). This is of interest when compared to the K values obtained for MeP and Chl a titrated with methanol.[12] For the latter K values of 13.0 and 7.0 were obtained. The value for the DPC is two orders of magnitude lower indicating a much weaker aggregation. Again the importance of the 7-ester function in Chl is confirmed, since it significantly enhances the aggregation.

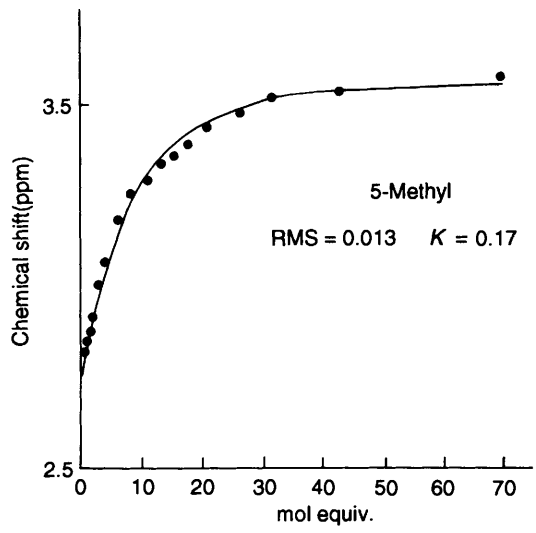


Fig. 2 Titration of DPC **4** in $CDCl_3$ with [$^2H_4$]-methanol. Observed points and calculated curve.

Table 3 Observed and calculated complexation shifts (Δδ) for DPC **4**

	Obs.	*a*	*b*	*c*	*d*	*e*
Meso β	0.06	−0.04	0.02	0.08	0.01	0.21
α	−0.01	0.40	−0.06	−0.06	−0.07	−0.01
δ	0.00	−0.06	−0.07	−0.06	−0.08	0.01
10-CH_{trans}	0.65	0.36	0.63	0.65	0.61	0.45
10-CH_{cis}	0.74	0.48	0.74	0.72	0.75	0.80
8-H	−0.02	−0.10	−0.09	−0.06	0.11	−0.05
7-H	−0.04	−0.02	0.07	0.02	−0.05	0.00
5-Me	0.82	0.58	0.83	0.82	0.80	0.52
3-Me	−0.02	−0.04	−0.06	−0.05	−0.07	0.02
1-Me	−0.02	0.27	−0.05	−0.06	−0.06	0.01
8-Me	−0.06	−0.12	0.02	−0.09	0.01	−0.01
4b-Me	−0.08	—	0.00	−0.09	−0.01	—
2b-Me	−0.02	—	−0.05	−0.05	−0.05	—
7c-Me	−0.04	—	—	—	—	—
rms		0.213	0.059	0.039	0.059	0.089

Displacement coordinates: [a] Strouse Model, $x = -4.00, y = 6.50, z = -4.00$ Å, no rotation. [b] Shipman Model, $x = -4.60, y = -6.05, z = -4.60$ Å, rotated 110°. [c] Piggy-back Model, $x = 4.20, y = -6.50, z = 4.70$ Å, rotated 185.00°. [d] Back-to-back Model, $x = 2.55, y = -7.85, z = 4.15$ Å, rotated −55.0°. [e] Skew Model, $x = 3.20, y = -9.0, z = 0.0$ Å, orthogonal.

The dimer geometry. Using the same ring current model as described earlier,[12,22] the dimer geometry was investigated. Unlike MeP, where only three models needed to be examined due to its similarity to Chl a, this molecule has a completely unknown dimer geometry. Consequently all the previously proposed models for Chl have to be reexamined to see if a fit can be obtained between the calculated and the observed. The first model investigated was that of Strouse.[9] The geometry of this aggregate model[9,12] is such that only the exocyclic ring E overlaps, with the C-9 keto function under ring A of the neighbouring molecule ideally placed for co-ordination to the Mg of the other chlorin. However, optimisation of the geometry gave a solution with an rms of 0.213, with coordinates of $x = 4.00$ Å, $y = 6.50$ Å, $z = 4.00$ Å, no rotation. The C-9 keto function has coordinates, −0.87, 0.63 and −4.25 Å, ideally positioned for coordination *via* a water molecule to the Mg above it. Unfortunately the calculated shifts do not reproduce the observed values. Although the largest complexation shifts are calculated for 10-CH_2 and 5-Me, large values are also calculated for the α and 1-Me protons [Table 3(*a*)]. Although

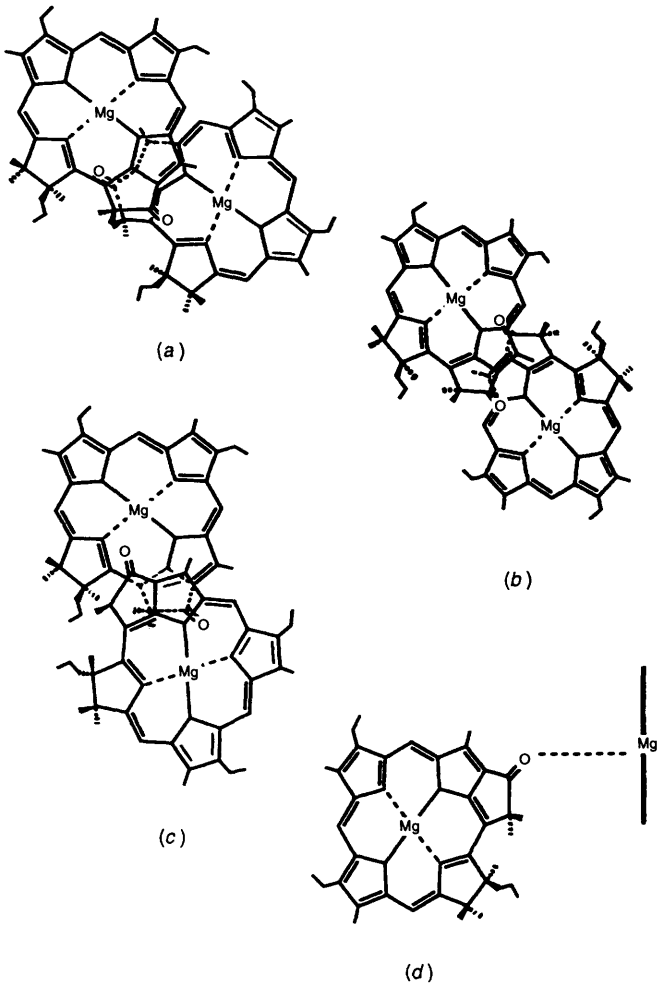


Fig. 3 Calculated dimer geometries for DPC **4**: (*a*) Shipman model; (*b*) piggy-back model; (*c*) back-to-back model; (*d*) skew model

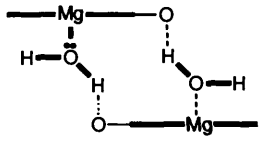


Fig. 4 H-bonding network

the geometry of this dimer appears to reflect a binding mechanism involving just the C-9 keto function, the calculated shifts clearly dismiss this model as that being present in the aggregate solution.

The next model examined was the Shipman model.[11] In contrast to the previous calculation an excellent solution was obtained, with a dimer displacement geometry of $x = 4.60, y = 6.05, z = 4.60$ Å. One molecule is rotated by 110° with respect to the other [Fig. 3(*a*)]. The calculated shifts are all within experimental error with an rms of 0.059. The 2-Me and 4-Me geometries were subsequently optimised using this dimer geometry. The calculated shifts for these protons, are also very similar to those observed. Examination of the geometry reveals that the C-9 carbonyl has coordinates $x = 0.01, y = 1.57, z = 4.6$ Å, clearly ideally placed beneath the Mg of the other chlorin.

The two models proposed for MeP, the piggy-back and back-to-back model[11,12] were both reexamined. Again excellent agreement was obtained for both models. In the case of the piggy-back model a dimer geometry of $x = 4.20, y = 6.50, z = 4.70$ Å, rotated by 185°, was obtained, with an rms error between calculated and observed of 0.039 [Fig. 3(*b*), Table 3(*c*)]. This solution had excellent agreement for all shifts. The displacement coordinates for the carbonyl (2.08, 0.41, 4.70 Å) again place this functional group below the Mg of the other chlorin. In the case of the back-to-back model the rms was only slightly higher, 0.059 with coordinates $x = 2.55, y = 7.85, z = 4.15$ Å, rotated by 55°. Examination of the calculated shifts revealed good correlations for all the shifts except for 8-H, which has an error of 0.13 ppm. The geometry of the carbonyl being 0.75, 2.33, 4.15 Å slightly further away from the Mg of the other chlorin molecule.

All the sandwich type dimer geometries have a similar interplane separation of approximately 4.15–4.70 Å. This distance is much smaller than that in MeP, which varied from 5.6 to 5.9 Å. This larger interplane distance in MeP can be accounted for by the presence of the 7-propionate function which is sandwiched in between both planes forcing them apart. In this 9-oxo-7-propyl derivative this functional part is absent and the planes of the chlorins can approach much closer. In all cases the carbonyl of one molecule sits below the Mg of the other. The interplane distance of 4.15–4.70 is ideal for an aggregation mechanism involving a water molecule (Fig. 4).

In addition to these sandwich type dimers, the skew model[10] was also examined. In this case one molecule is orthogonal to the other. Analysis of the geometry gave the best solution with coordinates $x = 3.20, y = 9.00, z = 0.0$ Å [Fig. 3(*d*)]. The rms value of 0.089 is slightly higher than those obtained previously. The shifts, however, do show a quantitative agreement. (This calculation could not be computationally iterated, due to the conditions of the program.) Despite the rms value which just borders on the experimentally acceptable, this solution cannot be outrightly dismissed. In this molecule only one carbonyl involved in the binding path; however in the case of the other geometries both carbonyl functions are placed such that both could contribute to the aggregate mechanism.

(b) *DOC* **5**.—In this molecule as in DPC, an ethyl replaces the vinyl group at carbon C-2 in MeP. In addition, the C-9 ketone function has been reduced to CH_2. Unlike DPC the 7-position still possesses the propionate function. It was seen earlier that the removal of the 7-propionate appears to weaken the aggregate compared to MeP. It is of interest, therefore, to see what geometry is preferred with only this functional group present and how strongly it holds the aggregate together.

A solution of DOC was titrated, as before, with [$^2H_4$]-methanol (Table 4). The spectra again showed the standard features upon disaggregation, going from broad aggregate spectra [Fig. 5(*d*)] to a characteristic sharp monomeric spectrum [Fig. 5(*a*)]. The effect of removing the C-9 keto function upon the chlorin ring current has been previously discussed by Abraham *et al.*[22] The predominant downfield shifts observed upon going from a C-9 keto function in MeP were accounted for by an increase in the chlorin ring current of 10%. In addition to this increase there is also the effect of the removal of the anisotropic influence of the carbonyl which deshields both the 10-CH_2 and 5-Me protons [Table 5(*e*) shows the observed $\Delta\delta$ on going from MeP keto to MeP ketal]. The 10-CH_2 and 5-Me protons were observed to experience an overall shielding effect and were shifted upfield. Knowing these effects and the previous assignments for the DPC **4** we can easily assign the ^1H spectra of this molecule.

The increase in ring current should affect all the meso protons equally and hence their relative assignments remain the same. It is interesting to note that the observed $\Delta\delta$ for the β meso proton is smaller than that seen before and that for the α meso proton rather larger. These differences illustrate the long-range effects of the C-9 keto function. The four methyl resonances can also be easily assigned. The downfield resonance at 3.52 ppm is that of the ester. The methyl furthest upfield at 3.33 ppm is that of the

Table 4 Titration of DOC **5** with [$^2H_4$]-methanol[a]

Proton	Ligand (mol equiv.) 0.0	0.2	0.4	0.7	0.9	1.2	1.5	2.0	3.1	4.6	6.7	13.6	27.4	48.0	68.7
Meso β	9.57	9.57	9.56	9.56	9.56	9.57	9.57	9.57	9.57	9.57	9.58	9.58	9.58	9.58	9.58
α	9.47	9.49	9.50	9.51	9.51	9.52	9.52	9.52	9.53	9.53	9.53	9.53	9.53	9.53	9.53
δ	8.77	8.70	8.65	8.60	8.59	8.57	8.57	8.56	8.56	9.56	8.56	8.57	8.57	8.57	8.58
10-CH_{cis}	4.19	4.24	4.35	4.46	4.49	4.54	4.57	4.60	4.63	—	—	—	—	—	4.75
10-CH_{trans}															4.60
8-H	—	—	4.32	4.35	4.42	4.46	4.48	4.51	4.54	4.56	4.57	4.58	4.58	4.59	4.59
7-H	—	—	4.04	4.12	4.22	4.28	4.31	4.34	4.37	4.39	4.40	4.40	4.41	4.41	4.41
2a-CH	3.95	3.93	3.92	—	—	—	3.91	—	3.90	3.91	3.91	3.91	3.91	3.91	3.91
4a-CH	3.85	3.86	3.86	—	—	—	3.87	—	3.87	3.88	3.88	3.88	3.88	3.88	3.88
1-Me	3.55	3.48	3.42	3.39	3.37	3.35	3.35	3.34	3.33	3.33	3.33	3.33	3.33	3.33	3.33
5-Me	3.42	3.42	3.42	3.42	3.42	3.42	3.42	3.43	3.43	3.43	3.43	3.43	3.43	3.43	3.43
3-Me	3.38	3.39	3.39	3.41	3.41	3.42	3.43	3.43	3.44	3.44	3.44	3.44	3.44	3.44	3.44
2b-Me	1.81	1.78	1.77	1.76	1.75	1.74	—	—	1.74	1.74	1.74	1.74	1.74	1.74	1.74
4b-Me	1.70	1.72	1.72	1.73	1.74	1.74	—	—	1.75	1.76	1.76	1.76	1.76	1.76	1.76
7d-OMe	—	2.04	2.38	2.58	2.84	2.98	3.06	3.15	3.24	3.30	3.33	3.42	3.48	3.50	3.52
8-Me	1.59	1.63	1.68	1.68	1.71	1.73	—	—	1.76	1.77	1.77	1.78	1.79	1.79	1.80

[a] Initial concentration = 0.05 mol dm^{-3}.

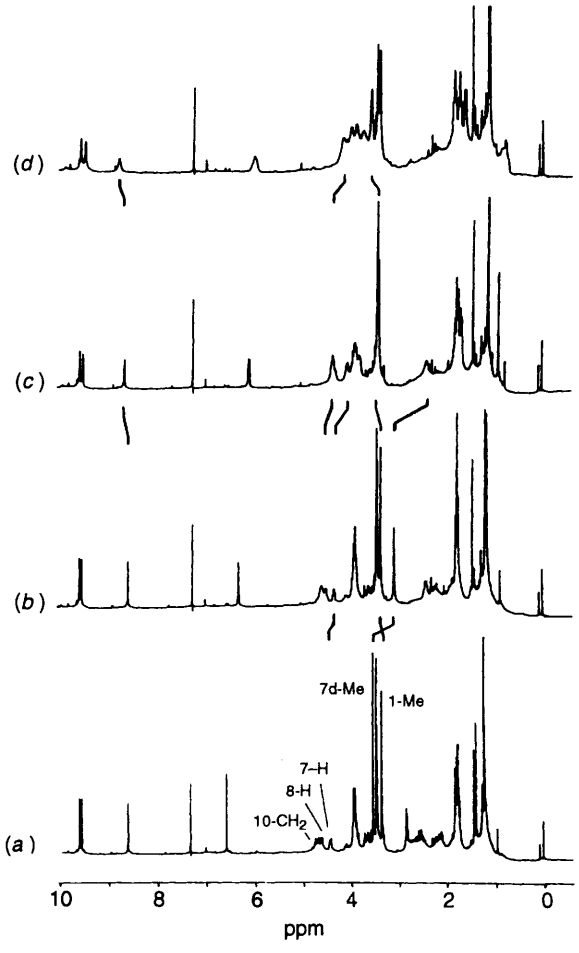


Fig. 5 ^1H NMR spectra of DOC upon disaggregation with [$^2H_4$]-methanol: (*a*) 68.7 mol equiv.; (*b*) 1.5 mol equiv.; (*c*) 0.4 mol equiv.; (*d*) 0.0 mol equiv.

C-1 methyl. This methyl is always upfield of the others due to the influence of the adjacent saturated ring D. The remaining two methyls are those of the 5-Me and 3-Me at 3.4 ppm. At 400 MHz, an expansion of this region of the spectrum reveals that the upfield resonance of these two peaks is actually a triplet with a fine coupling of 1.2 Hz [Fig. 6(*b*)]. Consequently, this

Table 5 Proton chemical shifts of DOC **5** and analogues

	a	*b*	*c*	*d*	*e*
Meso β	9.58	9.58	9.43	0.15	0.30
α	9.53	9.55	9.00	0.53	0.24
δ	8.58	8.65	8.19	0.29	0.30
10-CH a	4.75	4.75	5.15	(−0.40)	−0.09
b	4.60	4.63	5.00	(−0.37)	
9-CH a	—	≃3.8	—	—	—
b	—	≃3.8	—	—	—
8-H	4.59	4.65	4.55	0.04	—
7-H	4.41	4.43	4.12	0.29	—
2-CH	3.91	3.90	3.73	0.28	—
4-CH	3.88	3.88	3.69	0.19	0.13
3-Me	3.44	3.41	3.25	0.19	0.14
5-Me	3.43	3.40	3.58	−0.15	−0.05
1-Me	3.33	3.31	3.15	0.18	0.13
2b-Me	1.74	1.73	1.67	0.07	—
4b-Me	1.76	1.74	1.70	0.06	0.05
7d-OMe	3.52	3.52	—	—	—
8-Me	1.80	1.78	1.77	0.03	0.01

[a] Monomeric solution in $CDCl_3$ with excess [$^2H_4$]-methanol (concentration = 0.05 mol dm^{-3}). [b] Monomeric solution in [$^2H_4$]-acetone (concentration = 0.045 mol dm^{-3}). [c] Monomeric solution of DPC **4**. [d] Observed $\Delta\delta(b - c)$. [e] Observed $\Delta\delta$ on going from MeP ketal to MeP ref. 22.

resonance must be that of the 5-Me coupling to the 9-CH_2 protons.

The 10-CH_2 protons no longer exhibit a simple AB quartet, but couple to both C-9 protons. Expansion of the spectra at 400 MHz reveals a first order pattern [Fig. 6(*a*)]. The upfield part of the ABXY is partially covered by the 8-H resonance at 4.65 ppm with 7-H at 4.43 ppm. Analysis of this part of the spectrum enables all the couplings to be obtained for the 7, 8 and 10 proton resonances, to give $J_{10a,10b}$ = 15.7 Hz, $J_{10a,9a}$ = 7.4 Hz, $J_{10a,9b}$ = 3.7 Hz, and $J_{10b,9a}$ = 3.2 Hz, $J_{10b,9b}$ = 7.4 Hz. The 8-H proton couples to both the 8-Me $J_{8a,8Me}$ = 7.6 Hz, and to 7 H $J_{8H,7H}$ = 2.2 Hz. The 7-H proton couples to 8-H, 7$_a$ $J_{7,7a}$ = 8.4 Hz, and 7a′ $J_{7,7a'}$ = 2.6 Hz. Having assigned the disaggregated spectra [Table 5 (*a*), (*b*)] the complexation shifts can be obtained by back titration.

The most prominent change upon disaggregation is the large

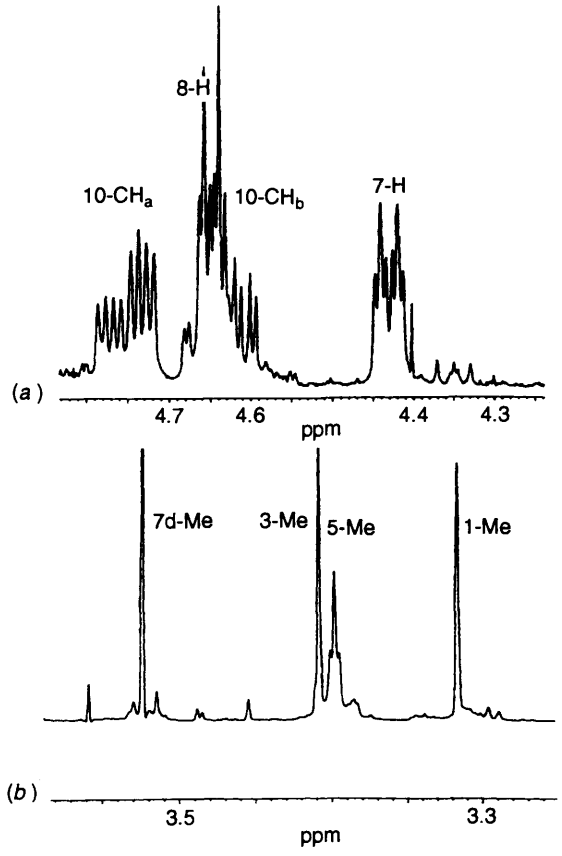


Fig. 6 Expansion of the δ 3.3–3.5 and δ 4.3–4.8 regions of the ^{1}H NMR spectrum of DOC **5**, 0.05 mol dm^{-3} in $CDCl_3$ with excess [$^2H_4$]-methanol

Table 6 Observed and calculated complexation shifts for DOC **5**

		Calculated	
Proton	Observed	*a*	*b*
Meso β	0.01	−0.09	−0.08
α	0.06	−0.13	−0.11
δ	−0.20	−0.08	−0.06
10-CH_{cis}	(0.40)	0.39	0.38
10-CH_{trans}	(0.56)	0.51	0.59
8-H	0.55	0.57	0.50
7-H	0.78	0.72	0.74
1-Me	−0.22	−0.10	−0.09
3-Me	0.07	−0.07	−0.07
5-Me	0.01	0.11	0.06
8-Me	0.20	0.20	0.33
7d-OMe	2.07	—	—
rms		0.096	0.105

[a] Back-to-face displacement coordinates $x = -4.15$, $y = -6.85$, $z = 3.65$, rotated 240°. [b] Back-to-back displacement coordinates $x = -5.50$, $y = -6.00$, $z = 3.90$, rotated 20°.

downfield shift of the 7d-OMe resonance which moves across the three other methyl resonances (Fig. 5). The 10-CH_2, 8-H and 7-H protons all move downfield implying their proximity to the aggregation site. In contrast to previous molecules, the 5-Me resonance hardly moves; clearly, it is not near the site of aggregation. In contrast to these downfield shifts both the 1-Me and δ-meso protons have an upfield complexation shift. This means that they are situated at the side of the other chlorin molecule. The assignment of the 10-CH_2 protons is not unambiguous. It is clear that one proton has a larger shift than the other, since in the aggregate, their relative chemical shifts are similar and not until disaggregation occurs does the ABXY pattern appear, as the difference in their relative chemical shift increases. It can be seen in Fig. 5(*d*) and (*c*) that a resonance appears slightly upfield of 2a and 4a-CH_2, which, as disaggregation occurs, moves downfield and disappears under these resonances. This is assigned to the 9-CH_2. The complete set of $\Delta\delta$s was obtained by a plot against the 1-Me resonance (Table 6).

Analysis of the equilibrium, using the shifts for the 1-Me resonance gives a good correlation (rms = 0.022) for a K value of 170 dm^3 mol^{-1}. This value is about ten times that observed for MeP and Chl a, clearly indicating the strong binding power of this propionate group. In turn, comparison with the K value for DPC (K = 0.13) suggests that the main binding of the MeP and Chl a aggregate is actually *via* the 7-propionate function.

The dimer geometry. The dimer geometry of this molecule was investigated using the ring current model previously discussed,[22] and the observed complexation shifts. The dipole equivalents used in the ring current model were increased by 10% from $\mu_p = 14.6$, $\mu_h = 16.5$ to $\mu_p = 16.1$ and $\mu_h = 18.1$, in order to account for the removal of the C-9 ketone. The dimer geometry can be considered to be one of three possibilities, a back-to-face dimer, a back-to-back dimer and a face-to-face dimer. The latter can be discarded since in this model both 7-propionate functions are exo to the dimer. Hence only two sandwich type dimer geometries need to be considered.

The first model considered was that of the back-to-face model in which one 7-propionate function is endo and the other is exo to the dimer. The x, y, z coordinates were varied over a large region using the complexation shifts of the fixed protons including the (10-CH_2 protons). The resulting solution had displacement coordinates $x = -4.15$, $y = -6.85$, $z = +3.65$ Å rotated 240°, with an rms of 0.096. The calculated shifts for this solution are in excellent agreement for all the protons with a large $\Delta\delta$s (8-H, 7-H, 10-CH_2, 8-Me, 1-Me, δ) (Table 6a). Examination of the other shifts reveals small errors for the α proton and the 3-Me and 5-Me protons.

The second dimer model investigated was that of the back-to-back model in which both ester functions are endo to the dimer. The calculated solution [Table 6(*b*)] had one molecule displaced $x = -5.50$, $y = -6.00$, $z = 3.90$ Å and rotated 20.0° with respect to the other. The rms error between the observed and calculated shifts was 0.105. Examination of the shifts reveals reasonable agreement with again errors for the 3-Me, 8-Me and α meso protons. The dimer geometries obtained are shown in Fig. 7. Both the calculated back-to-back and face-to-back dimer geometries are similar. It is very encouraging that in both cases one C-7c carbonyl is ideally positioned to complex with the magnesium of the other molecule. The calculated interplane separation of 3.65–3.90 Å implies a direct coordination which need not be through a hydrogen bonding network involving a water molecule. Since both geometries are very similar, they exhibit similar errors. In both cases the shift of the α, 3-Me and 5-Me protons are in error. These errors could be accounted for by a slightly skew sandwich dimer [Fig. 8(*b*)] in which the region of complexation is about 3.6–3.90 Å above the plane, whereas the 3-Me and α protons are much higher, giving a much reduced complexation shift. There is no reason why this dimer molecule, which aggregates *via* this flexible functional group should be a sandwich type dimer with parallel macrocycle planes.

(c) **DODPC 6**.—In this molecule the C-9 keto function and the 7-propionate are both removed. It was found that upon titration of the molecule with [$^2H_4$]-methanol, no complexation shifts were observed. The spectrum of this chlorin is unaffected by the addition of methanol, implying no aggre-

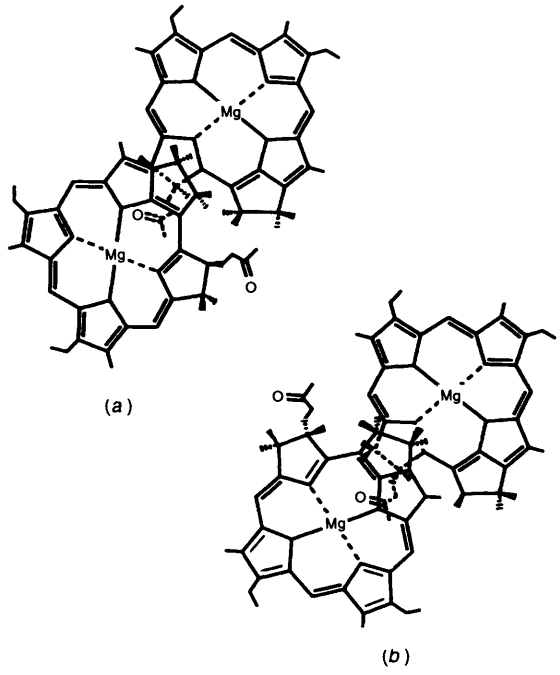


Fig. 7 Calculated dimer geometry: (*a*) back-to-face; (*b*) back-to-back

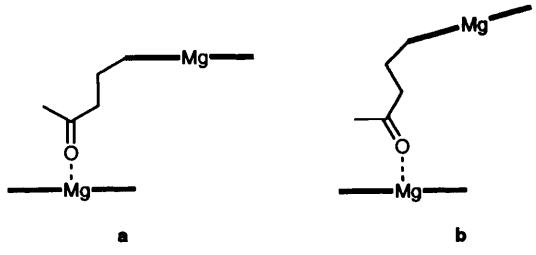


Fig. 8 (*a*) Sandwich dimer; (*b*) skewed sandwich dimer

gation in solution. The observed chemical shifts (Table 7) are identical with those of the DOC except for 7-H which no longer experiences the presence of the 7-ester function.

Conclusions

Our aggregation studies clearly indicate the influence of both the C-9 and C-7 propionate carbonyl in the aggregation behaviour of the Chl a dimer. The dimer geometries obtained are based upon several assumptions. One of the most important is that the observed chemical shift changes upon going from the dimer to the monomer are solely due to the ring current shifts, not geometry changes. The actual geometries calculated in most cases reflect the observed shifts, however the calculations are limited to sandwich type dimers (except specific fixed orthogonal geometries). In the case of DPC **4** where coordination is *via* a ketone which is in the plane of the chlorin, sandwich type dimers appear to account exactly for the observed shifts.

In the case of DOC **5** the flexibility of the 7-ester group practically, means that any type of dimer geometry could be adopted. The lack of aggregation in the nonfunctional chlorin DODPC **6** implies no significant π–π attractive interactions, which would favour the sandwich dimer structure in the DOC aggregate. This is probably the reason for the lack of agreement seen between calculated and observed shifts for this molecule. However the calculated geometries do reflect the monofunctional nature of this dimer, with the C-7 propionate ideally placed for coordination. This implies that the calculated solution is not significantly in error.

Table 7 Observed ^{1}H NMR chemical shifts for DODPC **6**[a]

	δ
Meso β	9.57
α	9.51
δ	8.58
10-CH a, 10-CH b	4.76–4.58
9-CH a, 9-CH b	3.94–3.84
8-H	4.76–4.58
7-H	4.33
2a-CH, 4a-CH	3.94–3.84
5-Me, 3-Me	3.44
1-Me	3.44
7a-H, 7b-H	2.38–2.22
7a'-H, 7b'-H	2.06–1.92
2b-Me	1.74
4b-Me	1.76
8-Me	1.79

[a] Concentration 0.037 mol dm^{-3} in $CDCl_3$ and excess [$^2H_4$]-methanol.

Experimental

(a) *NMR Studies.*—In DPC, some residual 2,4,6-tri-*tert*-butyl-1-methoxybenzene was retained in the product, even after purification. This did not appear to affect the chlorin aggregation/dissociation in any way. To minimise the formation of large aggregates the compounds were dissolved at low concentrations (*ca.* 35 × 10^{-2} mol dm^{-3}) in $CDCl_3$ which had been filtered through activated alumina to remove traces of acid and water, directly into the NMR tube. The solutions were then titrated with aliquots of a [$^2H_4$]-methanol solution in $CDCl_3$ from 0.4 to > 100 mol equiv. of [$^2H_4$]-methanol. All these operations were carried out in a dry box. The spectra were obtained on a Bruker WM 250 fitted with an Aspect 2000 computer. Typical operating conditions were: probe temperature 20 °C, sweep width 2.5 KHz, in 8K data points, zero filling to 16K, giving a digital accuracy of 0.32 Hz per point (< 0.0013 ppm). The pulse width was 7 μsec (60° flip), with an acquisition time of 1.5 s. The NOE experiments were carried out on a Bruker AM 200 spectrometer, fitted with an Aspect 3000 computer. The automated NOEDIFF.AU program was used (see Bruker manual part number Z30345), assuming a t_1 relaxation of 0.5 s for the β-methyls (C1, C3, C5 and C8 methyls).

(b) *Synthetic Studies.*—M.p.s are uncorrected and were measured on a Thomas Bristoline hot stage apparatus. Electronic absorption spectra were measured on a Hewlett-Packard 8450A spectrophotometer using solutions in dichloromethane. Proton NMR spectra were obtained in $CDCl_3$ either at 90 MHz (Varian EM-390) or at 300 MHz (General Electric QE300) using internal TMS (EM-390) or chloroform (7.258 ppm, 300 MHz) as internal standards. Reactions were usually carried out in the dark (aluminium foil) under nitrogen and were monitored using thin layer chromatography (TLC) on commercially available Eastman-Kodak 13181 (100 mm thick) silica gel sheets. Preparative TLC was carried out on 20 × 20 cm glass plates coated with Merck GF 254 silica gel (1 mm thick). Gravity and flash column chromatography employed either Merck neutral alumina (70–230 mesh) or Merck Silica Gel 60.

Elemental analyses were performed at the Mid-West Microchemical Analysis Laboratory (Indianapolis, IN). Mass spectral analyses were performed at the mass spectrometry facility, School of Pharmacy, University of California, San Francisco.

Methyl 9-Desoxo-mesopyropheophorbide a **5A**.—Methyl mesopyropheophorbide a **3** (98.5 mg) was dissolved in 10 cm^3 of TFA and stirred at room temperature. One 5/16 inch pellet of $NaBH_4$ (Aldrich) (172.9 mg) was added and the reaction mixture was stirred for 3 h at which time the UV–VIS spectrum indicated no more starting material. The reaction mixture was poured into water and the chlorin was extracted with CH_2Cl_2. The organic layer was carefully washed once with saturated $NaHCO_3$, three times with water, and then dried (Na_2SO_4) and evaporated. The residue was chromatographed on a flash silica gel column eluting with 1% MeOH–99% CH_2Cl_2. The main band was collected and, after evaporation, was crystallised from CH_2Cl_2–methanol to give 67.3 mg (70% yield) of the required compound; m.p. 179–180 °C; λ_{max}/nm (ε) 395 (160 300), 498 (1200), 526 (3400), 584 (4100) and 638 (38 100); δ_H 9.80, 9.62 (each s, 2 × 1 H, α and β meso H), 8.90 (s, 1 H, δ meso H), 4.88 (m, 2 H, 10-CH_2), 4.65 (m, 1 H, 8-H), 4.50 (m, 1 H, 7-H), 4.09 (m, 2 H, 9-CH_2), 4.06, 3.89 (each q, 2 × 2 H, 2a-CH_2 and 4a-CH_2), 3.57, 3.52, 3.48, 3.46 (each s, 4 × 3 H, 1-Me, 3-Me, 5-Me and 7-OMe), 2.77, 2.58, 2.38, 2.18 (each m, total 4 H, 7-CH_2CH_2), 1.85 (d, 3 H, 8-Me), 1.79, 1.77 (each t, 2 × 3 H, 2b-CH_3 and 4b-CH_3) and −1.68, −3.51 (each br s, 2 × 1 H, NH); *m/z* 536 (100%), 535 (38%) and 449 (17%) [Calc. for $C_{34}H_{40}N_4O_2$: C, 76.09; H, 7.51; N, 10.44%; *M*, 536.3151. Found: C, 75.9; H, 7.4; N, 10.35%; M (FAB), 536.3158].

Methyl 9-Desoxo-mesopyrochlorophyllide a **5**.—A pH = 6.8 phosphate buffer (to be used for reaction workup) was prepared by combining 6.80 g of KH_2PO_4 dissolved in 500 cm^3 of H_2O and 0.6 g of KOH in 100 cm^3 H_2O. 2,6-Di-*tert*-butyl-4-methylphenol (BHT) (339 mg, 1.5 mmol) was dissolved in 8 cm^3 freshly distilled $CHCl_3$ and stirred under argon at room temperature. Ethyl magnesium bromide (0.7 cm^3 of a 2 mol dm^{-3} solution: 1.4 mmol) was added carefully and the mixture was stirred for 10 min still under argon. An aliquot (0.7 cm^3) of this clear, colourless solution was added to a solution of methyl 9-deoxo-mesopyropheophorbide a **5A** (22.2 mg) in 3 cm^3 of $CHCl_3$ which was being stirred under argon at 55 °C. After 5 min, UV–VIS spectrophotometry indicated complete magnesium insertion, so the reaction mixture was poured into 20 cm^3 of 1 : 1 ether–phosphate buffer. After separation of the layers, the organic layer was washed once more with phosphate buffer and then 5 times with water. The ether layer was filtered through Na_2SO_4 and evaporated. Because methanol was to be avoided and the residue was soluble in hexane and heptane, crystallisation was not possible. The compound was dissolved in a minimum of CH_2Cl_2 and transferred to a small vial. The solvent was evaporated to dryness by blowing a gentle stream of N_2 onto the solution while the vial was heated in a warm water bath. The vial was then heated to 110 °C under high vacuum overnight to remove excess BHT by sublimation. 32.6 mg of product were obtained; m.p. ~60 °C (broad range); λ_{max}/nm (relative intensities) 406 (1.00), 514 (0.061), 572 (0.060) and 656 (0.197); δ_H($CDCl_3$ + [$^2H_5$]-pyridine) 9.56, 9.54 (each s, 2 × 1 H, α and β meso H), 8.54 (s, 1 H, δ meso H), 4.62 (m, 2 H, 10-CH_2), 4.52 m, 1 H, 8 H), 4.32 (m, 1 H, 7 H), 4.04 (br m, 2 H, 9-CH_2), 3.87 (m, 4 H, 2a-CH_2 and 4a-CH_2), 3.51, 3.43, 3.40, 3.12 (each s, 4 × 3 H, 1-Me, 3-Me, 5-Me and 7-OMe) and 1.71 (m, 9 H, 8-Me, 2b-Me, 4b-Me) (7-CH_2CH_2 is obscured) [*M* for $C_{34}H_{38}MgN_4O_2$; 558.2845. M, (EI) 558.2850]; *m/z* 558 (100%), 559 (46) and 560 (33).

2,4-*Diethyl*-6,γ-*ethano*-1,3,5,8-*tetramethyl*-7-(3-*hydroxypropyl*)-7,8-*dihydroporphyrin* **7** (*9-Desoxo-7-despropionate-7-hydroxypropylmesopyropheophorbide a*).—Methyl mesopyropheophorbide a **3** (99.0 mg) was dissolved in 25 cm^3 dry diethyl ether and stirred under N_2 at 0 °C. $LiAlH_4$ (47 mg) was dissolved in 20 cm^3 of additional ether and added *via* syringe all at once and the reaction was allowed to warm to room temperature. After stirring at room temperature for 50 min, the reaction was cooled back down to 0 °C and 5 cm^3 of water was slowly added dropwise. The quenched reaction was poured into more water and extracted with CH_2Cl_2–THF. The organic layer was washed with 10% aq. HCl and with water 4 times, then dried and evaporated. The residue was chromatographed on a flash silica gel column eluting with 2% MeOH–CH_2Cl_2. The main band **7** was collected and evaporated to dryness. The residue was crystallised from CH_2Cl_2–hexane to give 57.5 mg (63%) of product.

Band 1 **7**. M.p. 222–224 °C; λ_{max}/nm (ε): 395 (151 500), 498 (12 200), 526 (3400), 584 (4000) and 638 (35 900); δ_H 9.79, 9.61 (each s, 2 × 1 H, α and β meso H), 8.91 (s, 1 H, δ meso H), 4.85 (m, 2 H, 10-CH_2), 4.70 (m, 1 H, 8-H), 4.47 (m, 1 H, 7-H), 4.09 (m, 2 H, 9-CH_2), 4.05, 3.88 (each q, 2 × 2 H, 2a-CH_2 and 4a-CH_2), 3.64 (m, 2 H, 7c-CH_2), 3.52, 3.48, 3.46 (each s, 3 × 3 H, 1-Me, 3-Me and 5-Me), 2.48, 2.12 (each m, total 4 H, 7-CH_2CH_2), 1.86 (d, 3 H, 8-Me), 1.79, 1.77 (each t, 2 × 3 H, 2b-CH_3 and 4b-CH_3) and −1.67, −3.49 (each br s, 2 × 1 H, NH)[*M* for $C_{33}H_{40}N_4O$ + H; 509.3281. M (FAB), 509.3270]; *m/z* 509 (100%), 508 (87), 493 (10) and 449 (20) [Calc. for $C_{33}H_{40}N_4O$: C, 77.92; H, 7.93; N, 11.01. Found (1): C, 77.35; H, 8.0; N, 10.6. Found (2): C, 77.3; H, 8.1; N, 10.6%].

Two additional bands **8a** and **8b** were also obtained from the reaction. These were also crystallised from CH_2Cl_2–hexane to give 8.4 mg (9%) and 13.0 mg (13%), respectively of the two diastereomers of 7-hydroxypropyl-9-hydroxy compound.

Band 2. 2,4-*Diethyl*-6-γ-*ethano*-9-*hydroxy*-1,3,5,8-*tetramethyl*-7-(3-*hydroxypropyl*)-7,8-*dihydroporphyrin* **8a**. M.p. > 300 °C; λ_{max}/nm (ε) 395 (142 600), 496 (11 230), 524 (3000), 588 (3760) and 642 (33 160); δ_H 9.70, 9.64 (each s, 2 × 1 H, α and β meso H), 8.84 (s, 1 H, δ meso H), 6.47 (d, 1 H, 9-CH, J_{vic} 6), 5.28 (dd, 1 H, 10-CH *trans* to 9-OH, J_{gem} 15, J_{vic} 6), 4.53 (d, 1 H, 10-CH *cis* to 9-OH, J_{gem} 15), 4.65 (m, 1 H, 8 H), 4.40 (m, 1 H, 7-H), 4.00, 3.86 (each q, 2 × 2 H, 2a-CH_2 and 4a-CH_2), 3.60 (m, 2 H, 7c-CH_2), 3.59, 3.44, 3.43 (each s, 3 × 3 H, 1-M3, 3-M3 and 5-Me), 2.37, 2.03 (each m, total 4 H, 7-CH_2CH_2), 1.84 (d, 3 H, 8-Me), 1.78, 1.77 (each t, 2 × 3 H, 2b-CH_3 and 4b-CH_3) and −1.36, −3.26 (each br s, 2 × 1, NH) [*M* for $C_{33}H_{40}N_4O_2$ (M + H), 525.3230. M (FAB), 525.3219]; *m/z* 525 (100%), 524 (73) and 507 (37).

Band 3 **8b** (*Epimer at* C-9 *of* **8a**). M.p. > 300 °C; λ_{max}/nm (ε): 395 (132 600), 496 (10 400), 524 (2530), 540 (1690), 588 (3490) and 642 (33 180); δ_H 9.69, 9.62 (each s, 2 × 1 H, α and β meso H), 8.75 (s, 1 H, δ meso H), 6.31 (d, 1 H, 9-CH, *J* 6), 4.83 (dd, 1 H, 10-CH *trans* to 9-OH, *J* 6, 15), 4.25 (d, 1 H, 10-CH *cis* to 9-OH, *J* 15), 4.39 (m, 1 H, 8 H), 3.99 (partially obscured, m, 1 H, 7 H), 3.99, 3.84 (each q, 2 × 2 H, 2a and 4a-CH_2), 3.57, 3.42, 3.41 (each s, 3 × 3 H, 1-Me, 3-Me and 5-Me), 3.01 (m, 2 H, 7c-CH_2), 1.82–1.69 (m, total 9 H, 8-Me, 2b-CH_3 and 4b-CH_3), 1.31–1.00 (m, 4 H, 7-CH_2CH_2) and 1.4, −3.34 (each br s, 2 × 1 H, NH) [*M* for $C_{33}H_{40}N_4O_2$ + H, 525.3230. M (FAB), 525.3239]; *m/z* 526 (100%), 525 (73) and 507 (32).

2,4-*Diethyl*-6,γ-*ethanol*-1,3,5,8-*tetramethyl*-7-(3-*tosyloxypropyl*)-7,8-*dihydroporphyrin* **9**.—Compound **7** (30.72 mg) was dissolved in pyridine (10 cm^3). Toluene-*p*-sulfonyl chloride (113.8 mg) was added and the solution was stirred at room temperature under N_2 for 2.5 h. The reaction mixture was poured into water and extracted with CH_2Cl_2. The organic layer was washed once with 5% HCl and three times with water then dried (Na_2SO_4) and evaporated. The residue was purified

on flash silica gel chromatography eluting with 2% MeOH–CH_2Cl_2. The main band was collected and evaporated to dryness. The product did not crystallise well so the yield was based on evaporation to a film in a vial. 21.1 mg of material (53%) was thus obtained; m.p. 183–186 °C; λ_{max}/nm (ε) 394 nm (173 900), 498 (13 980), 526 (3600), 584 (4360) and 638 (41 510); δ_H 9.81, 9.63 (each s, 2 × 1 H, α and β meso H), 8.88 (s, 1 H, δ meso H), 7.59 (d, 2 H, Ts–H, *J* 9), 7.02 (d, 2 H, Ts-H, *J* 9), 4.78 (m, 2 H, 10-CH_2), 4.60 (m, 1 H, 8-H), 4.45 (m, 1 H, 7-H), 4.10–3.86 (m, 8 H, 2a, 4a, 7c and 9-CH_2), 3.53, 3.48, 3.47 (each s, 3 × 3 H, 1-Me, 3-Me and 5-Me), 2.43, 2.11 (each m, total 4 H, 7-CH_2CH_2), 2.14 (s, 3 H, Ts-CH_3), 1.83–1.76 (m, 9 H, 8-Me, 2b and 4b-CH_3) and −1.67, −3.51 (each br s, 2 × 1 H, NH) [*M* for $C_{40}H_{46}N_4O_3S$ + H; 663.3363. M (FAB), 663.3371]; *m/z* (FAB) 663 (100%), 662 (33), 636 (39) and 592 (40) (Calc. for $C_{40}H_{46}N_4O_3S$: C, 72.48; H, 6.99; N, 8.45. Found: C, 72.6; H, 7.0; N, 8.57%).

2,4-*Diethyl*-6,γ-*ethano*-1,3,5,8-*tetramethyl*-7-(3-*mesyloxypropyl*)-7,8-*dihydroporphyrin* **9B**.—Compound **7** (69.3 mg) was dissolved in dry CH_2Cl_2 (30 cm^3) and stirred at 0 °C. Triethylamine (1.0 cm^3) and then methanesulfonyl chloride (30 mm^3) were added. After stirring for 15 min at 0 °C, the reaction mixture was diluted with CH_2Cl_2 and washed three times with water. The organic layer was dried (Na_2SO_4) and evaporated. The residue was purified on an alumina column (Brockmann Grade III) eluting with 100% CH_2Cl_2. The main band was collected and after removal of solvent, was crystallised from CH_2Cl_2–hexane to give 70.11 mg (88%) of the product; m.p. 110–113 °C; λ_{max}/nm (ε) 394 (158 400), 498 (12 800), 526 (3500), 584 (4200) and 638 (38 500); δ_H 9.81, 9.63 (each s, 2 × 1 H, α and β meso H), 8.91 (s, 1 H, δ meso H), 4.83 (m, 2 H, 10-CH_2), 4.67 (m, 1 H, 8-H), 4.51 (m, 1 H, 7-H), 4.13–4.02, 3.89 (m and q respectively, total 8 H, 2a, 4a, 7c and 9-CH_2), 3.53, 3.49, 3.47 (each s, 3 × 3 H, 1-Me, 3-Me and 5-Me), 2.77 (s, 3 H, OSO_2CH_3), 2.49, 2.23, 1.92 (each m, total 4 H, 7-CH_2CH_2), 1.86 (d, 3 H, 8-Me), 1.80, 1.78 (each t, 2 × 3 H, 2b and 4b-CH_3) and 1.66, −3.49 (each br s, 2 × 1 H, NH) (Calc. for $C_{34}H_{42}N_4O_3S$: C, 69.59; H, 7.21; N, 9.55. Found: C, 69.55; H, 7.3; N, 9.3%).

2,4-*Diethyl*-6,γ-*ethano*-1,3,5,8-*tetramethyl*-7-*propyl*-7,8-*dihydroporphyrin* **6A**.—Chlorin **9B** (49.3 mg) was dissolved in dry diethyl ether (10 cm^3) and cooled to 0 °C. Lithium aluminium hydride (40 mg) was suspended in dry diethyl ether (5 cm^3) and added to the chlorin under N_2. The mixture was allowed to warm to room temperature and stirred for 2.5 h. The solution was cooled back to 0 °C and water (10 cm^3) was carefully added. The quenched reaction was poured into more water and extracted with CH_2Cl_2. The organic layer was washed twice with water then dried (Na_2SO_4) and evaporated. The residue was purified on flash silica gel chromatography eluting with 100% CH_2Cl_2. The main band (most mobile) was collected and evaporated to dryness. The residue was crystallised from CH_2Cl_2–MeOH to give 24.5 mg (59%) of the desired product; m.p. 249–254 °C; λ_{max}/nm (ε): 395 (165 700), 498 (13 400), 526 (3700), 584 (4400) and 638 (41 200); δ_H 9.80, 9.61 (each s, 2 × 1 H, α and β meso H), 8.91 (s, 1 H, δ meso H), 4.89–4.81 (m, 2 H, 10-CH_2), 4.72 (m, 1 H, 8-H), 4.43 (m, 1 H, 7-H), 4.05, 3.90 (m and q respectively, total 6 H, 2a, 4a and 9-CH_2), 3.52, 3.48, 3.47 (each s, 3 × 3 H, 1-Me, 3-Me and 5-Me), 2.42, 2.00 (m, 4 H, 7-CH_2CH_2), 1.86 (d, 3 H, 8-Me), 1.80, 1.76 (each t, 2 × 3 H, 2b and 4b-CH_3), 1.02 (t, 3 H, 7c-CH_3) and −1.63, −3.44 (each br s, 2 × 1 H, NH) (*M* for $C_{33}H_{40}N_4$ + H, 493.3332. M, 493.3315); *m/z* 493 (55%), 492 (56), 491 (55) and 449 (100) (Calc. for $C_{33}H_{40}N_4$: C, 80.45; H, 8.18; N, 11.37. Found: C, 80.5; H, 8.2; N, 11.4%).

Mg^{II} 2,4-*Diethyl*-6,γ-*ethano*-1,3,5,8-*tetramethyl*-7-*propyl*-7,8-*dihydroporphyrin* **6**.—Free base compound **6A** (47.8 mg) was complexed with magnesium according to the same procedure described above for compound **5** except it was necessary to add 1.7 cm^3 of the magnesiating reagent and the time necessary to complete the reaction was 2 h. Workup with phosphate buffer and washing with water proceeded as above. After heating in a high vacuum pistol at 110 °C overnight, 56.8 mg of product was obtained; m.p. > 300 °C; λ_{max}/nm (relative intensities) 388 (0.304), 406 (1.00), 514 (0.060), 572 (0.059) and 618 (0.201); δ_H($CDCl_3$ + [$^2H_5$]-pyridine) 9.54, 9.51 (each s, 2 × 1 H, α and β meso H), 8.51 (s, 1 H, δ meso H), 4.56 (m, 3 H, 10-CH_2 and 8-H, overlapped), 4.26 (m, 1 H, 7-H), 3.85, 3.69 (m, 3 × 2 H, 2a, 4a, 9-CH_2), 3.41, 3.40, 3.30 (each s, 3 × 3 H, 1-Me, 3-Me and 5-Me), 2.20–1.40 (m, 4H, 7-CH_2CH_2), 1.70 (m, 9 H, 8-Me, 2b-CH_3 and 4b-CH_3), 0.85 (t, 3 H, 7c-CH_3) (*M* for $C_{33}H_{38}N_4Mg$, 514.2942. M, 514.2939); *m/z* 514 (100%), 515 (33), 516 (24) and 492 (7).

9-*Ketal of Methyl Mesopyropheophorbide a* **10**.—Methyl mesopyropheophorbide a **3** (198.7 mg) was dissolved in 40 cm^3 of dry CH_2Cl_2 and stirred at room temperature under N_2. Ethylene glycol (2.0 cm^3) and then trimethylsilyl chloride (1.0 cm^3) were added and the reaction mixture was stirred for 2 h. The mixture was then transferred rapidly but dropwise into a vigorously stirring ice-cold 3 mol dm^{-3} ammonium hydroxide solution (200 cm^3). The quenched reaction mixture/excess NH_4OH solution were separated in a separatory funnel and the organic layer was diluted with CH_2Cl_2. The organic layer was washed four times with water, then dried (Na_2SO_4) and evaporated. The residue was purified by alumina column (Brockmann Grade III) chromatography eluting with 100% CH_2Cl_2. The main band (most mobile) was collected and evaporated to dryness. The product, 187.5 mg (87%), was obtained as a solid from methanol; m.p. 215–217 °C; λ_{max}/nm (ε) 395 (173 700), 494 (13 100), 522 (3900), 542 (2100), 588 (5000) and 642 (46 500); δ_H 9.66, 9.63 (each s, 2 × 1 H, α and β meso H), 8.77 (s, 1 H, δ meso H), 5.09 (ABq, 2 H, 10-CH_2, *J* 27, 15), 4.68–4.52 (m, 5 H, OCH_2CH_2O, and 8-H), 4.40 (m, 1 H, 7-H), 3.99, 3.83 (each q, 2 × 2 H, 2a-CH_2 and 4a-CH_2), 3.62, 3.58, 3.42, 3.40 (each s, 4 × 3 H, 1-Me, 3-Me, 5-Me and 7-OMe), 2.80–2.18 (m, 4 H, 7-CH_2CH_2), 1.81 (d, 3 H, 8-Me), 1.77, 1.74 (each t, 2 × 3 H, 2b-CH_3 and 4b-CH_3), −1.21, −3.12 (each br s, 2 × 1 H, NH) (Calc. for $C_{36}H_{42}N_4O_4$: C, 72.70; H, 7.12; N, 9.42. Found: C, 72.6; H, 7.1; N, 9.4%).

9-*Ketal of* 2,4-*Diethyl*-6,γ-*ethano*-1,3,5,8-*tetramethyl*-9-*oxo*-7-(3-*hydroxypropyl*)-7,8-*dihydroporphyrin* **11**.—The 9-ketal of methyl mesopyropheophorbide a **10** (367.0 mg) was dissolved in dry diethyl ether (25 cm^3) under N_2 and cooled to −78 °C. Lithium aluminium hydride (289.9 mg) was suspended in ether (20 cm^3) and added to the chlorin solution. The reaction temperature was maintained at −78 °C for 1.5 h, and then 1:1 methanol–water (20 cm^3) was added. The quenched reaction was poured into water and extracted with CH_2Cl_2 and a small amount of THF to help disperse emulsions. The organic layer was washed 4 times with water, then dried (Na_2SO_4) and evaporated. The residue was purified by alumina column (Brockmann Grade III) chromatography, eluting with 0.5% MeOH–CH_2Cl_2. The appropriate eluates were combined and evaporated to dryness. Crystallisation from CH_2Cl_2–heptane gave 315.6 mg (90%) of the desired product; m.p. 215–217 °C; λ_{max}/nm (ε) 395 (168 700), 494 (12 800), 522 (3600), 542 (2000), 588 (4900) and 642 (45 500); δ_H 9.65, 9.63 (each s, 2 × 1 H, α and β meso H), 8.78 (s, 1 H, δ meso-H), 5.07 (ABq, 2 H, 10-CH_2, *J* 24, 15), 4.71–4.52 (m, 5 H, OCH_2CH_2O and 8-H), 4.38 (m, 1 H, 7-H), 3.99, 3.83 (each q, 2 × 2 H, 2a-CH_2 and 4a-CH_2), 3.64 (m, 2 H, 7c-CH_2), 3.62, 3.42, 3.40 (each s, 3 × 3 H, 1-Me, 3-Me, 5-Me), 2.50–2.00 (m, 4 H, 7-CH_2CH_2), 1.83 (d, 3 H, 8-Me), 1.77, 1.74 (each t, 2 × 3 H, 2b-CH_3 and 4b-CH_3) and −1.20, −3.10

(each br s, 2 × 1 H, NH) (Calc. for $C_{35}H_{42}N_4O_3$: C, 74.18; H, 7.47; N, 9.89. Found: C, 74.48; H, 7.48; N, 9.74%).

9-*Ketal of* 2,4-*Diethyl*-6,γ-*ethano*-1,3,5,8-*tetramethyl*-9-*oxo*-7-(3-*mesyloxypropyl*)-7,8-*dihydroporphyrin* **12**.—Compound **11** (184.3 mg) was dissolved in dry CH_2Cl_2 (40 cm^3) and triethylamine (2 cm^3). After cooling to 0 °C, methanesulfonyl chloride (75 mm^3) was added and the reaction mixture was stirred under N_2 for 15 min. The cold solution was poured into a dilute aq. solution of $NaHCO_3$, diluted with CH_2Cl_2 and the layers were separated. The organic layer was washed twice with water, then dried (Na_2SO_4) and evaporated. TLC and ^1H NMR of this material showed a very clean sample; the residue was simply crystallised from CH_2Cl_2–heptane to give 214.5 mg (99%) of desired product; m.p. 203–204 °C; λ_{max}/nm (ε) 395 (180 300), 494 (13 450), 522 (3800), 588 (5100), 642 (48 100); δ_H 9.67, 9.64 (each s, 2 × 1 H, α and β meso H), 8.79 (s, 1 H, δ meso H), 5.06 (ABq, 2 H, 10-CH_2, *J* 12, 15), 4.67–4.55 (m, 5 H, OCH_2CH_2O and 8-H), 4.42 (m, 1 H, 7-H), 4.13 (5, 2 H, 7c-CH_2), 3.99, 3.83 (each q, 2 × 2 H, 2a-CH_2 and 4a-CH_2), 3.63, 3.43, 3.41 (each s, 3 × 3 H, 1-Me, 3-Me and 5-Me), 2.82 (s, 3 H, OSO_2CH_3), 2.52–1.85 (m, 4 H, 7-CH_2CH_2), 1.83 (d, 3 H, 8-Me), 1.78, 1.75 (each t, 2 × 3 H, 2b-CH_3 and 4b-CH_3) and −1.19, −3.11 (each br s, 2 × 1 H, NH) (Calc. for $C_{36}H_{44}N_4O_5S$: C, 67.06; H, 6.88; N, 8.69. Found: C, 66.95; H, 6.9; N, 8.7%).

9-*Ketal of* 2,4-*Diethyl*-6,γ-*ethano*-1,3,5,8-*tetramethyl*-9-*oxo*-7-*propyl*-7,8-*dihydroporphyrin* **13**.—Compound **12** (58.4 mg) was dissolved in dry diethyl ether (20 cm^3) and cooled to −7 °C using an ice–salt–H_2O bath. Lithium aluminium hydride (32.0 mg) was suspended in additional ether (10 cm^3) and added to the chlorin solution. The reaction mixture was stirred under N_2 at −7 °C. Careful monitoring by TLC indicated maximum product formation had occurred after 20 min, so water (20 cm^3) was carefully added to the still-cold reaction mixture. The quenched reaction mixture was diluted with CH_2Cl_2 and washed with water 4 times. The organic layer was dried (Na_2SO_4) and evaporated to dryness. The residue was chromatographed on an alumina column (Brockmann Grade III) eluting with 100% CH_2Cl_2. The appropriate eluates were combined and evaporated to dryness. The residue obtained as a film in a vial was determined to weigh 25.3 mg (52%); m.p. 237–240 °C; λ_{max}/nm (ε) 3.95 (173 500), 492 (13 400), 522 (3800), 542 (2100), 588 (5100), 642 (47 000); δ_H 9.65, 9.63 (each s, 2 × 1 H, α and β meso H), 8.79 (s, 1 H, δ meso H), 5.07 (ABq, 2 H, 10-CH_2, *J* 15, 24), 4.75–4.52 (m, 5 H, OCH_2CH_2O and 8-H), 4.35 (m, 1 H, 7-H), 3.99, 3.83 (each q, 2 × 2 H, 2a-CH_2 and 4a-CH_2), 3.63, 3.42, 3.40 (each s, 3 × 3 H, 1-Me, 3-Me and 5-Me), 2.38–1.42 (m, 4 H, 7-CH_2CH_2), 1.81 (d, 3 H, 8-Me), 1.77, 1.75 (each t, 2 × 3 H, 2b-CH_3 and 4b-CH_3), 1.01 (t, 3 H, 7c-CH_3) and −1.21, −3.10 (each br s, 2 × 1 H, NH) (Calc. for $C_{35}H_{42}N_4O_2$: C, 76.33; H, 7.69; N, 10.17. Found: C, 76.2; H, 7.6; N, 10.1%).

2,4-*Diethyl*-6,γ-*ethano*-1,3,5,8-*tetramethyl*-9-*oxo*-7-*propyl*-7,8-*dihydroporphyrin* **4A**.—Chlorin **13** (12.2 mg) was dissolved in acetone (10 cm^3) and treated with 2 cm^3 of 5% aq. HCl. After stirring at room temperature for 15 min, with monitoring by UV–VIS spectroscopy, the reaction was judged to be complete, so it was poured into water and extracted with CH_2Cl_2. The organic layer was washed with water three times, dried (Na_2SO_4) and evaporated. The residue was purified on an alumina column (Brockmann Grade III) eluting with 100% CH_2Cl_2. The main band was collected and evaporated to dryness. The residue was crystallised from CH_2Cl_2–MeOH to give 9.28 mg (83%) of desired product; m.p. 207–210 °C; λ_{max}/nm (ε) 395 (97 200), 408 (119 500), 474 (9800), 502 (16 000), 534 (15 200), 602 (14 600) and 656 (54 900); δ_H 9.46, 9.18 (each s, 2 × 1 H, α and β meso H), 8.45 (s, 1 H, δ meso H), 5.14 (ABq, 2 H, 10-CH_2, *J* 24, 21), 4.47 (m, 1 H, 8-H), 4.20 (m, 1 H, 7-H), 3.83, 3.68 (each q, 2 × 2 H, 2a-CH_2 and 4a-CH_2), 3.66, 3.28, 3.24 (each s, 3 × 3 H, 1-Me, 3-Me and 5-Me), 2.35–1.20 (m, 4 H, 7-CH_2CH_2), 1.80 (d, 3 H, 8-Me), 1.72, 1.69 (each t, 2 × 3 H, 2b-CH_3 and 4b-CH_3), 1.01 (t, 3 H, 7c-CH_3), 0.65, −1.56 (each br s, 2 × 1 H, NH) (Calc. for $C_{33}H_{38}N_4O$: C, 78.23; H, 7.56; N, 11.06. Found: C, 78.0; H, 7.5; N, 11.0%).

Mg^{II} 2,4-*Diethyl*-6,γ-*ethano*-1,3,5,8-*tetramethyl*-9-*oxo*-7-*propyl*-7,8-*dihydroporphyrin* **4**.—Free base chlorin **4A** was metallated with magnesium according to the procedure described above for preparation of compound **5**. It was necessary to use 7.0 cm^3 of the magnesiating reagent and to stir under argon overnight in order for the reaction to go to completion. After that time, the reaction mixture was washed twice with 1 : 1 ether–phosphate buffer and four times with water. The organic layer was filtered through anhyd. Na_2SO_4 and evaporated. The residue was dissolved in a minimum amount of CH_2Cl_2 and transferred to a small vial and the solvent removed by a gentle stream of N_2. After heating to 110 °C overnight under high vacuum, 36 mg of the product were obtained; m.p. > 270 °C (dec.); λ_{max}/nm (relative intensities) 408 (0.806), 426 (1.00), 582 (0.145), 614 (0.219) and 652 (0.724); δ_H 9.46, 9.01, 8.16 (each s, 3 × 1 H, α, β and δ meso H), 5.02 (ABq, 2 H, 10-CH_2, *J* 21, 18), 4.34 (m, 1 H, 8 H), 4.04 (m, 1 H, 7 H), 3.70 (m, 4 H, 2a-CH_2 and 4a-CH_2), 3.60, 3.20, 3.13 (each s, 3 × 3 H, 1-Me, 3-Me and 5-Me), 1.64–1.59 (m, 9 H, 8-Me, 2b-CH_3 and 4b-CH_3) and 0.83 (t, 3 H, 7c-CH_3) (*M* for $C_{33}H_{36}MgN_4O$, 528.2734. M (FAB), 528.2739); *m/z* 529 (84%), 528 (100) and 517 (26).

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