Tetrahedron Vol. 33, pp. 2277 to 2285 Pergamon Press 1977 Printed in Great Britain

THE NMR SPECTRA OF PORPHYRINS—12[1]

^{13}C AND PROTON NMR SPECTRA OF THE ZINC(II) COPROPORPHYRIN ISOMERS[2]

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(*Received in the UK 20 January 1977; Accepted for publication 21 March 1977*)

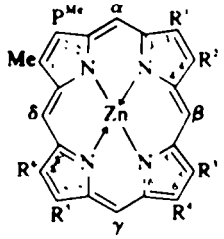
Abstract—The ^{13}C and proton NMR spectra of the zinc(II) complexes of the tetramethyl esters of the four coproporphyrin type isomers are reported and assigned. Effects of aggregation phenomena on these shifts are discussed and a method involving addition of a slight excess of pyrrolidine is proposed for measurement of the spectra of the "monomeric" species; spectra obtained under these conditions are capable of simple, straightforward interpretation and assignment in terms of molecular symmetry. Thus, a facile distinction between the type isomers is obtained.

The "monomer" chemical shifts so derived allow consistent SCS parameters to be derived. The C_β-Me SCS are shown to be related to the bond order of the C_β-C_β bond in the porphyrin ring, and are thus quite different from the corresponding SCS in pyrroles.

Aggregation shifts in the ^{13}C and proton spectra are shown to be consistent with the presence of "stacked" aggregates with the ring current of one molecule affecting the other, together with an additional effect on the chemical shifts of the *meso* carbons, which is probably steric in origin.

The use of ^{13}C NMR for the characterisation of porphyrins and in elucidation of the biosynthetic pathways to the pyrrole pigments is now well established.[3] Previous publications in this Series have dealt with the detailed assignments of the ^{13}C spectra of free base peripherally substituted porphyrins,[4] of important chlorophyll degradation products,[5] and of some *meso*-tetra-arylporphyrins.[6] In all of these compounds, however, the NH tautomerism process produced exchange-broadened ^{13}C signals for all of the "α-pyrrole" carbons (which were often broadened beyond detection) and to a lesser extent the "β-pyrrole" and *meso* carbons. Thus, our initial aim of obtaining the complete assignment of all ring carbons in unsymmetrical porphyrins was thwarted because many of these lines were not resolved. Our solution[4] to the problem of ill-resolved spectra provided the means for circumvention of the problem by protonation or metal insertion. We chose the latter alternative and thus began a systematic study of zinc(II) porphyrins. In the present paper we report the ^{13}C spectra of the type isomers of zinc coproporphyrin esters. However, in the event, these spectra like those of other zinc porphyrins examined by us, e.g. Refs 7 and 8 showed concentration dependence and it was therefore necessary to investigate both this concentration dependence and conditions required to give reproducible spectra. Similar problems have already been encountered in the now classical case of chlorophyll NMR[9] in which donor ligands were used to dissociate the chlorophyll aggregates. Although the mechanism of aggregation in these zinc(II) porphyrins is totally different to that in the chlorophylls, a similar method can be used to dissociate the aggregates.

We present here the ^{13}C and proton NMR spectra of the tetramethyl esters (**1–4**) of the zinc(II) complexes of the coproporphyrin type isomers in $CDCl_3$, delineate the problems of aggregation, and show how these are overcome to produce spectra capable of simple and specific assignment and interpretation. From these spectra we derive the substituent chemical shifts (SCS) in this series, and show how these SCS in the porphyrin differ fundamentally from those in the pyrrole ring,[10] as indeed is to be expected on simple valency arguments. Some of these results were reported in our preliminary communication.[2]



$P^{Me} = CH_2CH_2CO_2Me$

Zinc(II) Copro-I, (**1**):
$R^1 = R^3 = R^5 = Me$; $R^2 = R^4 = R^6 = P^{Me}$

Zinc(II) Copro-II, (**2**):
$R^2 = R^3 = R^4 = Me$; $R^1 = R^4 = R^5 = P^{Me}$

Zinc(II) Copro-III, (**3**):
$R^1 = R^3 = R^4 = Me$; $R^2 = R^4 = R^5 = P^{Me}$

Zinc(II) Copro-IV, (**4**):
$R^2 = R^4 = R^5 = Me$; $R^1 = R^3 = R^4 = P^{Me}$

RESULTS

^{13}C *Spectra and assignments*

The ^{13}C data are given in Tables 1 and 2. In Table 1 the data is that obtained by measurement of the spectra of (**1–4**) in chloroform solution alone; in Table 2 the data obtained from the same solutions after addition of *ca.* 2

Table 1. ^{13}C chemical shifts (δ_C) of zinc(II) coproporphyrin tetramethyl esters[a]

	C_α	C_β	meso	CH_2	CH_2	CO_2	Me	β-Me
(1)	147.10 146.13	138.19 136.33	96.6	31.78	32.—	173.59	51.59	11.—
(2)	147.5— 146.5—	138.—5 136.43	[b]	31.7—	46.9—	173.78	51.95	11.50
(3)	146.5— 146.2— 146.05 145.45 145.95	139.81 137.50 137.39 137.19 135.78 135.61 135.50	95.95 95.78 95.—9(β)	31.—9 31.53 31.14	36.8— 36.7—	173.— 173.06	51.—6	11.51 11.—3(2) 10.91
(4)	146.59 146.1— 145.85 145.40	139.9— 137.57 136.1— 135.59	96.1	31.62 31.33	46.86	173.33 173.1—	51.5—	11.46 11.95

[a]In $CDCl_3$ solns of conc.: (1) *ca.* 13 mg/ml; (2) *ca.* 3 mg/ml; (3) *ca.* 70 mg/ml; (4) *ca.* 50 mg/ml.
[b]Not observed, see text.

Table 2. ^{13}C chemical shifts (δ_C) of zinc(II) coproporphyrin tetramethyl esters in $CDCl_3$/pyrrolidine soln[a]

	C_α[b]	C_β	meso	CH_2	CO_2	CH_2	Me	β-Me
(1)	148.18(1,4,5,8) 147.99(2,3,6,7)	139.62(1,4,5,8) 138.—8(2,3,6,7)	96.5—	31.——	173.58	51.—5	51.55	11.81
(2)	148.14(1,4,5,8) 147.97(2,3,6,7)	139.84(1,4,5,8) 139.61(2,3,6,7)	96.84(β,δ) 96.—4(α,γ)	31.—7	173.—9	51.—4	51.—5	11.—1
(1)	148.18(1,4,5,8) 148.09 147.—7(2,3,6,7) 147.—1	139.63(4,5) 139.49(1,8) 138.61(6,7) 138.5 (2,3)	96.89(δ) 96.6—(α,β) 96.5— 96.28(γ)	31.—7	173.—8	51.—4	51.—5	11.70
(4)	148.09 148.—3(1,4,5,8) 147.—5 147.11(2,3,6,7)	139.—3(1,4) 138.91(5,8) 138.58(2,3) 138.—4(6,7)	96.9—(γ) 96.55(β,δ) 96.—7(α)	31.18	173.—5	51.—1	51.56	11.7—

[a]Using the same solutions as in Table 1, but with approx. 2 equiv of added pyrrolidine
[b]Numbers and Greek letters in parentheses are assignments; nomenclature as indicated on structural formula.

equiv of pyrrolidine† are reported. Before evaluating the latter data it is worthwhile to consider the differential aggregation shifts implied in Table 1 which stem directly from the very different concentrations of the individual solutions. The order of solubility is $3 > 4 \gg 1 > 2$ [(3) 75 mg/ml; (1) 13 mg/ml; (2) ~3 mg/ml]. The ^{13}C shifts in Table 1 were obtained with saturated solutions for the isomers 1 and 2; in contrast, the data for the isomers 3 and 4 were obtained with solutions containing *ca.* 70 and 50 mg/ml respectively. This qualitative order of solubility is merely a manifestation of the degree of symmetry present in each of the molecules (1–4), the least symmetrical being the most soluble. The choice of zinc as the chelating metal was based upon the ease of insertion and removal of this metal,[12] though the zinc complexes were usually rather less soluble than the metal-free porphyrins (in the absence of pyrrolidine).

Bearing these solubilities in mind it is interesting to compare the shifts in Table 1. The type-I and type-II isomers 1 and 2 respectively compare satisfactorily, as do compounds 3 and 4, but there is poor correspondence between the pairs 1, 2 and 3, 4. For example, δ (β-Me) for 1 and 2 is 11.4 and 11.5, but for 3 and 4 the shifts are 10.9–11.3δ. Similar considerations apply to the propionate methylene adjacent to the macrocycle which are to higher field in 3 and 4 by as much as 0.6 ppm. In contrast, the other side-chain resonances show similar shifts for all isomers. Clearly, the high field shifts in 3 and 4 are associated with greater aggregation in these isomers owing to the higher concentrations of their solutions.

The shift differences observed for the ring carbons are larger than observed for the side-chains, although the trend is the same. That is, 1 and 2 show similar shifts, but

†The choice of base for disaggregation was a difficult one. We eventually decided upon pyrrolidine (rather than, for example pyridine) because of its relatively simple ^{13}C and proton spectra. In particular, the proton resonances are to high field and do not interfere with the resonances of the porphyrin substrates. Coordination with the metal atom in the metalloporphyrin also introduces a further upfield shift.[11]

different from 3 and 4 which are themselves similar. For example, the "α-pyrrole" resonances in 1 at 147.1 and 146.1 δ are very close to the corresponding resonances for 2 at 147.3 and 146.3 δ, although the lower field shifts for the more dilute solution of 2 are undoubtedly significant. The "β-pyrrole" resonances for 1 and 2 are also similar, although 2 again shows lower field shifts. The "α-pyrrole" resonances for isomers 3 and 4 each fall into two ranges which clearly correspond to the $C_\alpha P$ and $C_\alpha M$ resonances, and these shifts agree closely for the two isomers. Comparison of all of the peaks for 3 and 4 shows them to be considerably to higher field than in 1 and 2, with some as far as 1.3 ppm upfield. In the case of the *meso* carbons comparison is made difficult by the fact that for 2 and 4 the peaks are severely broadened, so much so that the resonance is not observable at all for 2. However, the *meso* carbon lines for 3 and 4 are again to high field of that for 1.

Thus the data in Table 1 are capable of rationalisation in terms of dimer or aggregate formation which introduces upfield shifts, but this circumstance is unsatisfactory for making structural interpretations for the monomeric species because extrapolation is difficult.

In Table 2 the ^{13}C data obtained for the isomers (1–4) in the presence of pyrrolidine are presented. A visual representation of the effect of addition of pyrrolidine is given in Fig. 1, which shows the aforementioned broad resonances (α, β and *meso* carbons only) in metal-free coproporphyrin-III tetramethyl ester (Fig. 1A). Below that is shown (Fig. 1B) the spectrum of the zinc(II) complex (3) in $CDCl_3$ alone which possesses multiple resolved resonances due to aggregation effects. Finally, in Fig. 1C is shown the situation after addition of a slight excess of pyrrolidine; considerable simplification is apparent owing to formation of the disaggregated monomer in which the shifts are dependent only upon structural features and are independent of intermolecular interactions. Table 2 also indicates the simplification occurring for all of the isomers (1–4). For example, only singlets are observed for the nuclear methyl groups, though simple molecular symmetry arguments might lead one to expect four lines for 3 and two lines for 4. This shows clearly that the fine structure observed in the pyrrolidine-free samples is due to aggregation. Moreover, the methyl resonances all fall at virtually identical positions which are downfield from those in the aggregated species;

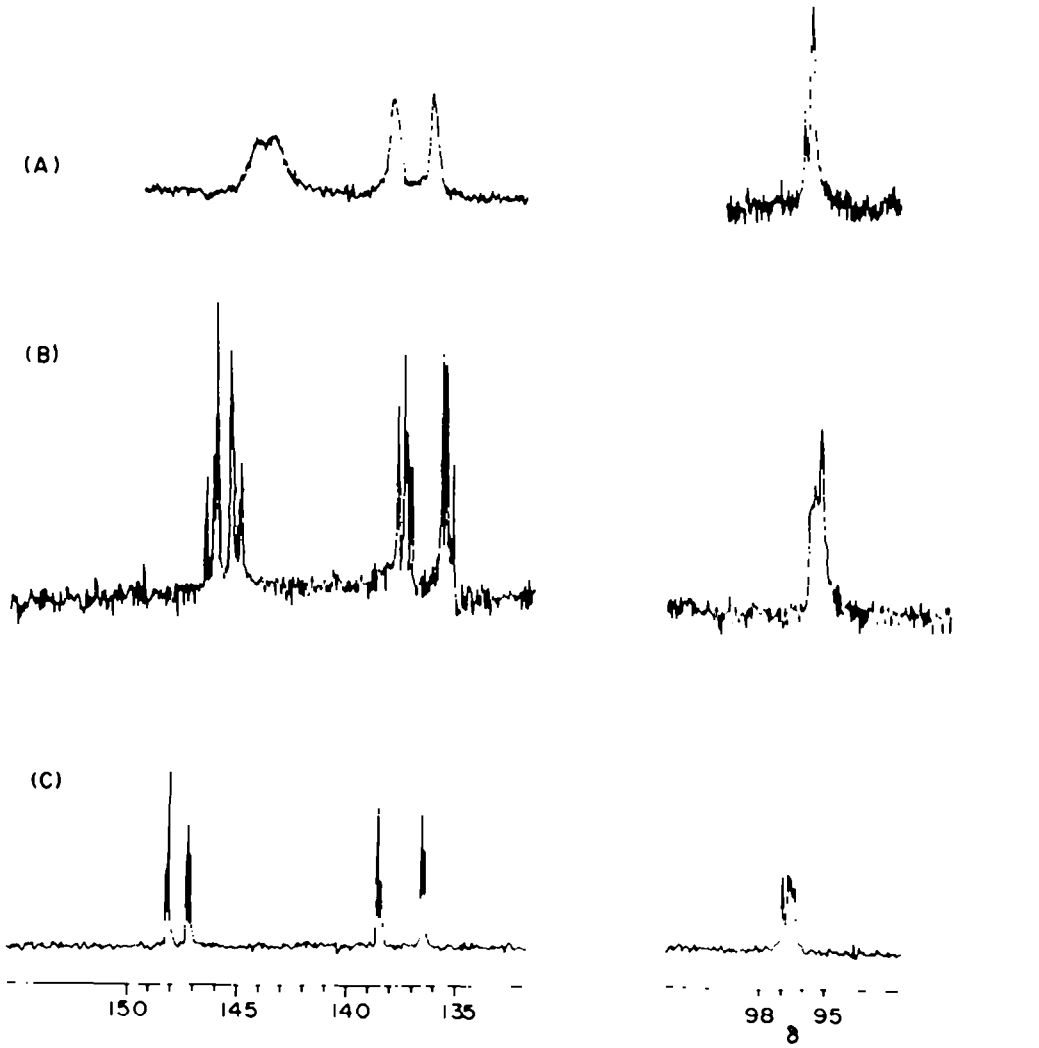


Fig. 1. ^{13}C NMR spectra (Varian XL-100) of skeletal carbons in (A) Coproporphyrin-III tetramethyl ester ($CDCl_3$ soln). (B) Zinc(II) coproporphyrin-III tetramethyl ester 3 ($CDCl_3$). (C) Zinc(II) coproporphyrin-III tetramethyl ester ($CDCl_3$ plus *ca.* 2 equiv pyrrolidine).

indeed, all side-chain carbons show remarkably consistent shift values. The actual assignment of the propionate side-chain follows previous work.[13]

Whereas the side-chains are of little use in determining the nature of the "type-isomer", the *meso* carbons faithfully reflect molecular symmetry. It is possible to assign all *meso* carbon lines simply on the basis of neighbouring β-carbon substituents, (i.e. M-P (1); M-M and P-P (2); etc.). One ambiguity in this scheme, namely the choice between M-M and P-P, was removed by regiospecific synthesis of the $\alpha\gamma$-dideuterio derivative[14] of (2), from which it was deduced that *meso* carbons between neighbouring β-propionate residues (P-P) are to higher field (by *ca.* 0.4 ppm) of those between β-methyls (M-M). The only remaining ambiguity are the α and β *meso* carbons in 3 (both M-P) at 95.6 and 96.4, which cannot be uniquely assigned.

For the remaining nuclear (quaternary) carbons, molecular symmetry is reflected in all isomers except 3, where there is signal degeneracy leading to only half of the expected number of lines. Again, all signals show consistency, with all β-carbons bearing a Me group falling at 136.5 ± 0.1 δ, while those bearing a propionate side-chain fall at 138.5 ± 0.1 δ following previous assignments.[13] Similarly, the "α-pyrrole" resonances at 148.1 δ are assigned to carbons two-bonds removed from a methyl group, while those near to 147.1 ppm are due to "α-pyrrole" carbons two bonds removed from propionate side-chains. Thus for isomers 1 and 2 the assignment of the skeletal carbons as given in Table 2 is complete. In the isomers 3 and 4 a total assignment is difficult. Thus, for example in 4, it is difficult to assign the two lines at 136.63 and 136.52 to each of the pairs 1, 4 and 6, 7; a similar situation pertains in isomer 3. However, for the "β-pyrrole" carbons we have indicated (Table 2) tentative assignments which were made by considering a fragment in 3 and 4 and relating it to a similar fragment in 1 or 2 where the shifts are known with certainty. In the case of isomer 4 for example, one expects carbons 6 and 7 to be very similar to the 1 and 8 carbons in isomer 2; since the shift of the latter is 136.5 δ we assign the 136.5 δ peak in isomer 4 to the 6 and 7 carbons. Thus, the 1 and 4 carbons in 4 appear by elimination at 136.6 δ which is as expected by comparison with isomer 1. A similar approach could be used for the "α-pyrrole" shifts in 3 and 4, but we consider this to be unwarranted because of the smaller shift differences.

Proton spectra

Considering our findings with regard to the ^{13}C spectra of isomers (1–4) we felt it worthwhile to study the corresponding proton spectra, particularly since outside of the chlorophylls there appears to be a dearth of systematic information on metalloporphyrins.[15] The spectra were obtained on the Varian SC 300 (300 MHz) instrument at concentrations† of 5 mg/ml (6.5×10^{-3} M) in $CDCl_3$ alone, and then with *ca.* 2 equiv of added pyrrolidine. The data are collected in Table 3.

Similar comments to those made in the ^{13}C series can be made about the proton spectra, isomer 2 having shifts to lower field by a small, but significant, amount. The lines in the aggregated species are broader than in the disaggregated species as a result of the longer correlation times. Fine structure present in the aggregates disappears upon going to the monomer. Figure 2 shows the two relevant spectra for the isomer 4; in the aggregated species one can clearly discern two pairs of broad multiplets corresponding to the propionate methylenes. In the monomer these multiplets move downfield and are almost completely overlapped. Similarly, the two nuclear Me resonances which are separated by 0.12 ppm in the aggregate are separated by only 0.01 ppm in the monomer, the peaks having moved downfield by 0.24 and 0.13 ppm. The *meso* protons are exceptionally broad ($\Delta\nu_{1/2} \sim 14$ Hz) in this aggregated isomer and one can just discern some fine structure; however, the peaks sharpen up considerably on going to the monomer.

The fact that these data (with the exception of isomer 2) have been recorded at constant concentration show up

†Owing to solubility problems, isomer 2 was run using a saturated solution of only *ca.* 3 mg/ml.

Table 3. Proton chemical shifts (δ) of zinc(II) coproporphyrin tetramethyl esters[a]

	meso-H	β-Me	CH_2 —— CH_2 —— CO_2Me		
(1)	9.41 (10.00)	3.43 (3.66)	4.20 (4.43)	3.09 (3.28)	3.70 (3.71)
(2)[b]	9.72 (10.04) β,δ 9.64 (9.99) α,γ	3.53 (3.65)	4.27 (4.44)	3.18 (3.29)	3.66 (3.67)
(3)	9.38[c] (10.04) δ 9.46 (10.00) α,β 9.57 (9.99) γ	3.52 3.45 (3.66) 3.43 (3.65) 3.40	4.24[d] (4.43)	3.14[d] (3.29)	3.71 (3.71) 3.68 (3.70) 3.67 (3.68) 3.65 (3.67)
(4)	9.49[c] (10.05) γ 9.58 (10.00) β,δ 9.72 (9.99) α	3.53 (3.66) 3.41 (3.65)	4.32 (4.43) 4.20	3.20 (3.29) 3.11	3.68 (3.70) (3.69)

[a]Solutions in $CDCl_3$, concentration 5 mg/ml (6.5×10^{-3} M). Data in parentheses are shifts after addition of approx 2 equiv pyrrolidine to the same solution.

[b]Saturated solution (*ca.* 3 mg/ml).

[c]Broad peaks.

[d]Centre of gravity of broad unresolved multiplets.

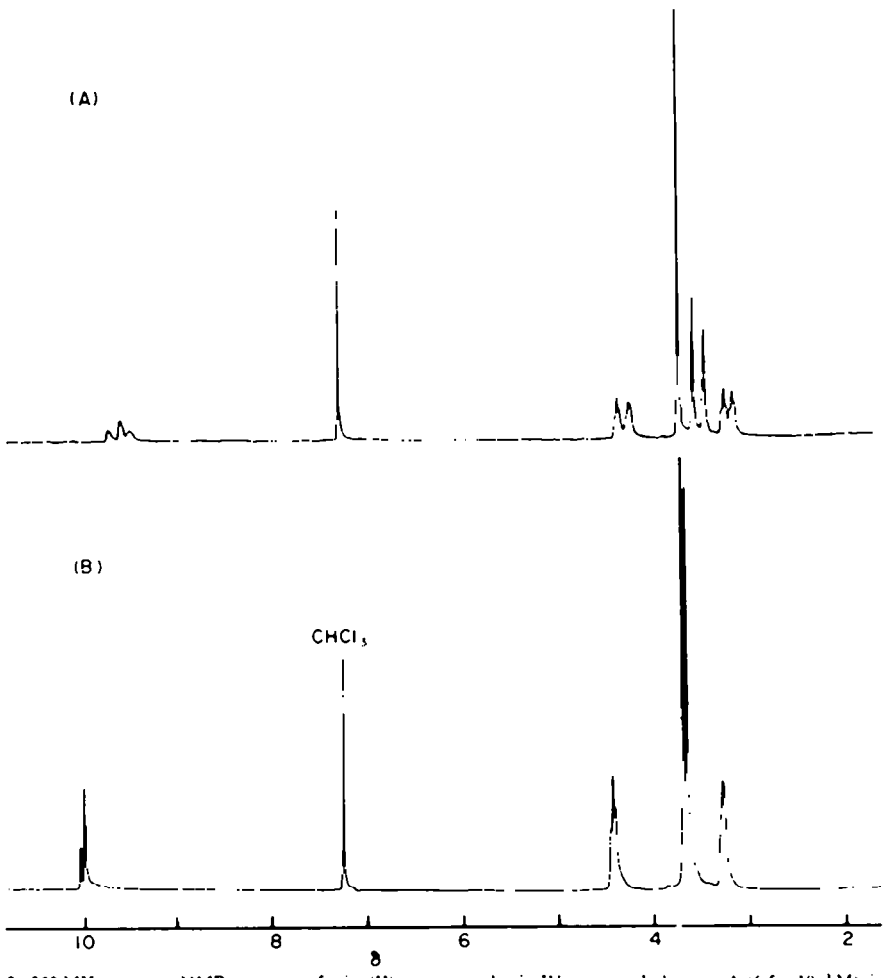


Fig. 2. 300 MHz proton NMR spectra of zinc(II) coproporphyrin-IV tetramethyl ester 4 (6.5×10^{-3} M) in (A) $CDCl_3$, and (B) $CDCl_3$ plus *ca.* 2 equiv pyrrolidine.

in the similar shifts for the various types of proton. In this respect, all of the α-methylenes lie within the range 4.20–4.32 δ, while the β-methylenes fall in the narrow range 3.09–3.20 δ. However, the remarkable data for the side-chains in the $CDCl_3$/pyrrolidine solutions makes these ranges look large; thus, for the α-methylenes every shift is 4.43 δ except for isomer 2† which is 4.44 δ. The "spread" in the ring methyls and the β-methylenes is similarly only 0.01 ppm in each case, while the ester Me varies over 0.04 ppm. The side-chain shifts indicate one advantage of proton over ^{13}C NMR in that molecular symmetry differences are more easily observed. For example, in isomer 4 we can pick out two lines for both the methyoxyl and methyl moieties. Similarly, in the isomer 3 more lines are resolved than in the carbon spectrum.

Addition of pyrrolidine to the porphyrins again renders the *meso* shifts interpretable in terms of neighbouring groups. For isomer 2 the upfield peak at 9.99 δ is assigned to the α, γ protons since this peak is the one which disappears in the spectrum of the dideuterio derivative mentioned earlier. We immediately conclude that the shifts for a *meso* proton between a Me and a propionate (M–P), or two propionates (P–P), or two Me's (M–M) are 10.00 (from isomer 1), 9.99 and 10.04 δ respectively. Assignment of the *meso* protons in isomers 3 and 4 is a trivial sequel. However, even at a 69 kilogauss field one is unable to resolve the α and β protons in isomer 3. Although these shift differences appear small (in ppm) it should be noted that at 300 MHz, 0.01 ppm corresponds to 3 Hz, a significant shift.

The aggregation shifts

Since aggregation shifts are a function of the concentration of the solute, the ^{13}C spectrum of 1 has been measured at the same concentration (5 mg/ml; with and without pyrrolidine) as the proton spectra in Table 3; this facilitates direct comparison of the proton and ^{13}C shifts. These data and the resultant aggregation shifts, Δδ, (defined as the difference between the shifts with and without pyrrolidine) for both protons and ^{13}C are given in Table 4.‡ Also given are the corresponding Δδ, value for the zinc(II) copro-I (1) data in Tables 1 and 2 of a more concentrated solution.

These aggregation shifts are of some interest. Within each nucleus the shifts follow a similar pattern, generally

†Owing to solubility problems, isomer 2 was run using a saturated solution of only *ca.* 3 mg/ml.

‡We assume, in deriving these values that none of the "α- or β-pyrrole" assignments cross-over due to addition of pyrrolidine. This is actually of no consequence because we could also have taken the shift of the centre of gravity of the resonances, which gives the same answer.

Table 4. ^{13}C chemical shifts (δ_c) and ^{13}C and ^1H aggregation shifts ($\Delta\delta$) for zinc(II) coproporphyrin-I tetramethyl ester (I) in $CDCl_3$

		C_α	C_β	meso	β-Me	CH_2	CH_2	CO_2	Me
δ_c	a	147.16 146.04	138.21 136.42	96.56	11.51	21.85	37.01	173.3	51.61
	b	148.06 147.04	138.41 136.63	96.54	11.87	22.19	37.40	173.5	51.59
$\Delta\delta_c$	c	0.90 0.80	0.20 0.21	-0.02	0.36	0.38	0.39	0.20	-0.02
	d	0.96 0.96	0.29 0.29	-0.06	0.36	0.38	0.45	0.19	-0.04
$\Delta\delta_H$	e	-	-	0.59	0.23	0.23	0.19	-	0.01

[a] 5 mg/ml in $CDCl_3$.
[b] 5 mg/ml in $CDCl_3$ + 2 equiv pyrrolidine.
[c] $\Delta\delta = \delta_b - \delta_a$.
[d] Data from Tables 1 and 2, conc. *ca.* 13 mg/ml.
[e] Data from Table 3.

decreasing steadily on going away from the porphyrin ring, suggesting that there is no pronounced lateral movement of the ring planes in the aggregate, and thus as expected on the basis of ring current effects and a vertical aggregation. The $\Delta\delta_H$ values in particular decrease monotonically from the porphyrin centre; *meso*-H (0.59), β-CH_2 and Me (0.23), β-CH_2CH_2 (0.19), β-$CH_2CH_2CO_2Me$ (0.01 ppm). Furthermore, the side-chain shifts of both the carbons and the protons are similar, as they should be because the attached nuclei are in similar positions in space; a ring current shift is independent of the nucleus experiencing the shift and only a function of the position of the nucleus in space. For example, the positions of a nuclear methyl carbon and the methyl hydrogens are not identical, the hydrogens always being further removed from the porphyrin centre than are the attached carbons, and this is clearly seen in the generally smaller $\Delta\delta$ values of the protons compared with their neighbouring carbons, e.g. β-Me 0.30(C), 0.23(H); $CH_2CH_2CO_2Me$ $\Delta\delta_c$, 0.38, 0.39, −0.02 (excluding C=O); $\Delta\delta_H$ 0.23, 0.19, 0.01 ppm.

However, this straightforward pattern is not followed in the ^{13}C shifts of the ring C atoms. Although the "α-pyrrole" carbons experience the largest shifts (as expected), the "β-pyrrole" carbons and particularly the *meso* carbons experience much smaller shifts than the side-chain carbons; indeed, the *meso*-carbons experience no shift at all upon disaggregation. These results are confirmed by the $\Delta\delta_c$ values of the more concentrated solution which are all, as expected, slightly larger but in which the pattern is identical. Similar but less extreme values are shown by the other type-isomers, but here (because the assignments in the aggregated and disaggregated species are less certain) we define the $\Delta\delta_c$ values as the shifts in the centre of gravity of the various groups. On this basis the type-IV (4) chemical shifts in Tables 1 and 2 (which are for a much more concentrated solution, *ca.* 50 mg/ml) give $\Delta\delta_c$ values of 1.61 (α-pyrrole), 0.81 (β-pyrrole), 0.48 (*meso*), 0.62 (β-Me) and 0.71, 0.55, 0.21 and −0.04 ppm for the propionate side-chains. Again, the *meso* carbon values (and possibly those of the "β-pyrrole" carbons) are less than expected on the basis of ring current effects. Although the geometry of the aggregates is not known for these porphyrins, a very detailed investigation of the aggregation behavior of zinc(II) protoporphyrin-IX dimethyl ester, leading to a defined geometry for the aggregate shows that the phenomenon of low *meso* carbon shifts is general and not dependent upon the particular porphyrin.

It is possible that there is a "complexation shift" of the *meso* carbons which is additional to that produced by the ring current of one molecule on the other. In the pyrrolidine complex the zinc(II) atom is (presumably[16]) out of the porphyrin ring plane by approximately 0.3 Å. However, we do not know whether the zinc atom is in the plane in the free zinc(II) porphyrin or whether it moves upon complexation with another zinc(II) porphyrin in solution. If this does occur then it is possible that the *meso* carbons, which have a γ relationship to the zinc atom, are also more susceptible to small changes in the porphyrin geometry than the α and β pyrrole carbons, would also experience an intrinsic shift; a direct shift from the abutting pyrrolidine atoms might also be experienced. These effects will be considered further in a quantitative study of the dilution effects in zinc(II) protoporphyrin-IX.[11]

^{13}C *substituent chemical shift parameters in porphyrins*

The accurate data obtained here for the zinc(II) porphyrins allows the determination of more precise ^{13}C SCS parameters than hitherto, and also the evaluation of the effect of introducing the zinc atom upon porphyrin chemical shifts. For convenience, data previously communicated[17] of ^{13}C shifts in zinc(II) porphin and zinc(II) deuteroporphyrins-III and -IX in $CDCl_3$/pyrrolidine solutions, as well as for the porphin and coproporphyrin-I tetramethyl ester free bases are presented in Table 5.

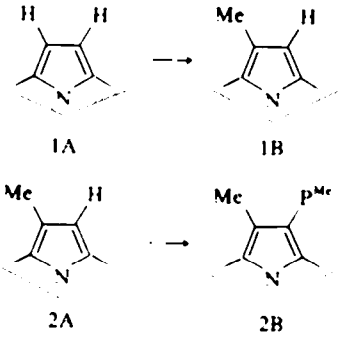
Comparison of the data for the same fragment (1B) i.e. $C_{1,3}$ and $C_{3,4}$ of deutero-III and deutero-IX shows the

Table 5. ^{13}C chemical shifts (δ) of "monomeric" porphyrins

	"α-Pyrrole"	"β-Pyrrole"	meso	β-Me	CH_2—— CH_2—— CO_2—— Me
Porphin					
Zinc(II) porphin					
Coproporphyrin-I tetramethyl ester[a]	ca.				
Zinc(II) Deutero-porphyrin-III dimethyl ester			(α) (β) (γ) (δ)		
Zinc(II) deutero-porphyrin-IX dimethyl ester			(α) (β) (γ) (δ)		

[a]Concentration 5 mg/ml.

consistency of the shifts (C_β-Me 140.4; C_β-H 129.2 δ), which are independent of the orientations of the other substituents, and lead, when taken with the zinc(II) porphin results, to the SCS of the β-methyl group (1A→1B) of 8.7 ppm (Me_α) and 2.5 ppm (Me_β).



1A 1B

2A 2B

Similarly, the further introduction of a β-propionate group (2A→2B) gives SCS of 9.4 ppm (P_α^{Me}) and −3.9 ppm (P_β^{Me}), almost identical with those in metal-free porphyrins.[4] These SCS together with the δ value for the parent zinc(II) porphin, allow the possibility of additive predictions of the "β-pyrrole" carbon shifts of the form $\delta = \delta_C + \Sigma_i S_i$.

This will be further developed for a wider range of substituents in a future paper. The β-Me SCS (1A→1B) is very different from that of the comparable SCS in the pyrrole ring (Table 6), i.e. the shifts of the C_4 carbon upon introduction of a C_3-Me, and it is of interest to examine this discrepancy more closely. Although the α-effect of a methyl group is well documented and remarkably constant for both saturated and unsaturated systems[18] the β-effect does not seem to have been considered in depth, though wide variations are observed.

We define here the β-Me effect (Me_β) as δ (Me·C·C*) − δ (H·C·C*). In saturated systems, this effect is large and positive (i.e. downfield shifts occur on introduction of a methyl group); in ethane Me_β is 9.7 ppm[19] whereas in ethylene it is −7.4 ppm.[20] In benzene, Me_β (the *ortho* shift of a methyl group) is 0.7 ppm[21] and this monotonic relationship is roughly proportional to the square of the π-bond order of the intervening bond, which has some theoretical support from the Karplus–Pople theory of ^{13}C chemical shifts.[22]

It is therefore of interest to obtain the Me_β shifts in the 5-membered heterocycles to see how these compare with the porphyrin, and these are given in Table 6. The same basic pattern is seen in that the β-Me effect

Table 6. SCS of methyl groups in heterocycles in ppm

	Furan	Pyrrole	Thiophen
α-Me /C_2	[a] [b]	[a] [c]	[a] [b]
β-Me /C_3	[d]	[c]	[b]
α-Me /C_4	[d]	[c]	[b]

[a]G. C. Levy and G. L. Nelson, *Carbon-13 NMR for Organic Chemists*, p. 97. Wiley, New York (1972).
[b]E. Breitmaier and W. Voelter, *^{13}C NMR Spectroscopy*, p. 184. Verlag Chemie, Weinheim (1974).
[c]R. J. Abraham, R. D. Lapper, K. M. Smith and J. F. Unsworth, *J. Chem. Soc.*, Perkin Trans. 2, 1004 (1974).
[d]R. T. LaLonde, T. N. Donvito and A. I.-M. Tsai, *Can. J. Chem.* 53, 1714 (1975).

becomes more negative as the double bond character of the intervening bond increases. This is clearly seen in the sequence furan, pyrrole, thiophen for the 2-Me/C_3 shifts and again in comparison of the 3-Me shift of C_4, i.e. via the "single bond" and on C_2 via the "double bond".

The general pattern is clear and has an important implication for the porphyrin ring. The β-Me effect in the porphyrin is identical with the 2-Me/C_3 shift in the pyrrole ring and very different from the apparently analogous 3-Me/C_4 shift. This is immediately explicable in terms of the aromatic structure of the porphyrin ring, as for example evidenced by the bond lengths. The length of the C_β–C_β bond in the porphyrin ring (1.36 Å)[23] is comparable with that of the C_2–C_3 bond in pyrrole, whereas the C_α–C_β bond is the longer bond (1.44 Å) and this compares with the C_3–C_4 bond length in pyrrole. Thus, the β-Me effect in the porphyrins is a striking illustration of the very different bond orders in the porphyrin as compared with the isolated pyrrole ring. It will be of interest to determine whether this is reflected in other SCS in the porphyrin series.

The comparison between porphin and zinc(II) porphin allows an estimation of the effect of introduction of a zinc atom into the macrocycle. Owing to low solubility, the spectrum of porphin was obtained at remarkably low concentration,[17] and effects of aggregation will be small under these circumstances. The "α-pyrrole" carbons were not visible, but the other shifts are fascinating in that they are almost identical with the shifts observed for zinc(II) porphin. Thus, the net effect of replacement of the two inner hydrogens with a pyrrolidine-coordinated zinc atom appears to be zero as far as the "β-pyrrole" and *meso* carbons are concerned. It is equally interesting to compare the shifts of the skeletal carbons in monomeric zinc(II) copro-I (**1**) (Table 2) with those obtained in the free base under dilute conditions (Table 5). Again, the "β-pyrrole" and *meso* carbons are very similar, with the free base being slightly to higher field. The dilution (5 mg/ml; 0.0065 M) at which this spectrum was obtained was not as great as that for the porphin spectrum and it is probably shifted to high field by a slight aggregation effect. Thus, for the "β-pyrrole" and *meso* carbons the conclusion is that zinc-pyrrolidine insertion has no net effect on their shifts.

In contrast, the "α-pyrrole" carbons move 4.5 ppm downfield upon zinc coordination. These more accurate results confirm our earlier results[4] where the effect of zinc(II) [and thallium(III)] on the ring carbon shifts were contrasted with the effect of protonation which produces upfield shifts (*ca.* 3 ppm) at C_α and downfield shifts (*ca.* 3 ppm) at C_β. We note that the α carbons in pyrrole shift 8.6 ppm downfield on forming the pyrrolate anion, and this has been ascribed to the decrease in the average excitation energy. A similar effect may be occurring here in the metalloporphyrins.

In conclusion it can be stated that a clear indication of structure in porphyrins is best obtained from ^{13}C spectra measured using the zinc(II) complexes in $CDCl_3$ solution containing a slight excess of pyrrolidine. Under such disaggregated conditions the *meso* carbon region alone provides unequivocal identification of the type isomers in the zinc(II) coproporphyrin esters. Complementary information, although less unequivocal, may also be gleaned under similar conditions from the proton spectra. The information so far reported should help to unravel more complex porphyrin spectra. Aggregation shifts can be larger than 1 ppm for skeletal carbons, thereby highlighting the necessity for measurement of spectra under disaggregated conditions.

EXPERIMENTAL

^{13}C NMR spectra were obtained for saturated solns of zinc(II) copro-I (**1**) and zinc(II) copro-II (**2**) using 12 mm tubes. For the more soluble type-III and -IV isomers (**3** and **4**), a 5 mm insert was used. Solns were in $CDCl_3$ which was also used for the field frequency lock. One or two drops of TMS were added to serve as an internal reference. The spectrometer was the Varian XL-100, fitted with a crystal filter to increase the signal to noise ratio. Spectra were obtained over a 5 kHz spectral width using an 8 K transform. Proton spectra were obtained at 300 MHz using the Varian SC 300 spectrometer. Spectra were obtained over a 3600 kHz spectral width using a 32 K transform. Proton spectra were obtained in 5 mm tubes at a concentration of 5 mg/ml (6.5×10^{-3} M) except for zinc(II) copro-II (**2**) where a saturated solution (corresponding to only *ca.* 3 mg/ml) was used. Solutions were in $CDCl_3$ and the instrument was locked to the deuterium resonance. When pyrrolidine was added, approx 2 equiv was used.

Synthetic routes to the four coproporphyrin ester type isomers have been reported earlier.[15b] Zinc was inserted by treatment of the free base in methylene chloride with an excess of zinc(II) acetate in methanol. After slight warming, spectrophotometry indicated complete metallation, so the solution was poured into methylene chloride and water, washed with more water, dried (Na_2SO_4), and then evaporated to dryness. The products were then crystallised from methylene chloride–n-hexane and dried thoroughly (1 mm Hg, 100°, 12 hr).

Acknowledgements—We thank the SRC for a grant to purchase the XL-100 spectrometer. An ICI Fellowship (to H.P.) and financially supported leave (to F.E.) from Azarabadegan University (Tabriz, Iran) are gratefully acknowledged. We are also grateful to Drs. F. Heatley and R. Warren (Manchester) for assistance and access to a Varian SC-300 spectrometer.

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