

## THE NMR SPECTRA OF PORPHYRINS—19

### <sup>13</sup>C AND PROTON NMR SPECTRA OF METAL-FREE PORPHYRINS WITH THE TYPE-IX SUBSTITUENT ORIENTATION, AND OF THEIR ZINC(II) COMPLEXES<sup>1</sup>

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(Received U.K. 12 November 1981)

**Abstract**—The <sup>13</sup>C and proton NMR spectra of six porphyrins bearing the substituent orientation characteristic of the natural "Type-IX" arrangement are reported and assigned. Significant concentration effects in the spectra of the free base porphyrins, together with the broadening of the C<sub>α</sub> (and occasionally C<sub>β</sub>) carbon resonances due to NH tautomerism caused a significant loss of data in these spectra. However, the spectra of the corresponding zinc(II) porphyrins (with addition of excess pyrrolidine) show that both these extraneous effects are completely removed to give well-resolved spectra with accurately reproducible chemical shifts. These spectra are assigned and an analysis of the chemical shifts allows the deduction of substituent chemical shift (SCS) parameters for the peripheral substituents at the beta and meso carbons. There is no global effect of these beta substituents, the beta carbon SCS being confined to the immediate pyrrole ring, and the meso carbon SCS to the two adjacent pyrrole rings. The SCS parameters are analyzed and it is shown how they can be used to predict the peripheral and meso carbon chemical shifts of any porphyrin bearing the substituents discussed.

There has recently been a great deal of interest in the <sup>13</sup>C magnetic resonance of porphyrin systems.<sup>2-5</sup> Because of the intensity of <sup>13</sup>C NMR spectroscopy (relative to protons), workers have correspondingly used as much material as available in order to obtain a spectrum. Thus, the data so far recorded are for solutions of varying concentrations, although deuteriochloroform has universally been used as solvent. It was recognized many years ago that the proton spectra of porphyrins are highly sensitive, because of intermolecular ring current effects, to concentration.<sup>6</sup> Thus, porphyrin chemists often used a standard concentration, as low as possible because of solubility considerations, for spectral comparison.<sup>7</sup> This approach was obviously unsuitable for <sup>13</sup>C spectra and, indeed, for proton spectra also. A further complication in interpretation of carbon spectra is caused, for the free bases, by NH tautomerism in the macrocycle.<sup>8</sup> This results in very broad signals for the α-carbons, which often become undetectable;<sup>9</sup> the β carbons can also be broadened by this process (*vide infra*). In this paper we present the <sup>13</sup>C spectra of several important porphyrins bearing the "Type-IX" substituent orientation characteristic of porphyrins of natural origin, and we highlight problems in assignment of these systems. More importantly, we also present a method whereby more useful spectral data may be obtained. Finally, the type of information obtained from the carbon spectra will be contrasted with that obtained from proton spectra.

#### EXPERIMENTAL

<sup>13</sup>C spectra were obtained for samples approximately 0.1 M CDCl<sub>3</sub>, which was used for the field-frequency lock. One or two drops of TMS were added to serve as reference. The spectrometer was a Varian XL100 instrument, operating at 25.2 MHz in the Fourier transform mode. The probe temp. was approximately 35°. Spectra were usually obtained over a 5 KHz spectral width, with 4096 real points in the transformed spectrum. Most spectra were obtained using 5 mm tubes because of

sample limitation. Some proton spectra were obtained also on the XL100 in the FT mode at a concentration of 10 mg/ml in CDCl<sub>3</sub> solvent; most of the proton NMR spectra were run at 300 MHz (Varian SC-300). Spectra of Zn(II) complexes were obtained without pyrrolidine initially, and then again after addition of approximately 2 mole equivs.

The porphyrins used in this study were synthesized by standard procedures.<sup>10</sup> Zn(II) was inserted into the macrocycles by treatment with Zn(II) acetate in MeOH.<sup>10</sup>

#### RESULTS AND DISCUSSION

The <sup>13</sup>C data for a series of free base "Type-IX" porphyrins are depicted in Table 1. Data for their Zn(II) complexes are similarly displayed in Table 2.

Considering first the free base porphyrins, the data for deuteroporphyrin-IX dimethyl ester (1) and coproporphyrin-III tetramethyl ester (2) have been reported previously by us<sup>11</sup> but we include the data here for completeness. The first notable feature is the complete intractability of the α-carbon resonances. In all cases the signals are broad due to NH tautomerism.<sup>8</sup> Obviously, this region is uninformative so far as structural information is concerned. While the β-carbons exhibited more fine structure, these lines still remained slightly broadened. In compound 2, for example, only two broadish peaks are visible.<sup>12</sup> It is possible to assign the β-carbons; one expects C<sub>3,8</sub> and C<sub>6,7</sub> to be similar to the shifts in the four coproporphyrin isomers, where they fell in the two ranges 135.5–136.2 and 137.4–137.9 ppm respectively.<sup>12</sup> A perusal of the data in Table 1 shows this to be true, and only in the case of protoporphyrin-IX dimethyl ester (3) and the corresponding 2,4-bisacetal (6) is there any confusion, since there are extra peaks which overlap these regions. Having assigned the β carbons C<sub>3,8</sub> and C<sub>6,7</sub>, it remains to separate C<sub>1,3</sub> and C<sub>2,4</sub>. Since it is at carbons 2 and 4 that the substitutional changes occur in our series, one would expect the biggest shift changes to occur at those sites. Thus, in mesoporphyrin-IX dimethyl ester (4), one can easily assign the peak at 141.8 ppm to the β carbons C<sub>2</sub> and C<sub>4</sub>, since this is

Table 1.  $^{13}\text{C}$  chemical shifts ( $\delta$ , ppm) for free-base porphyrins with "Type-IX" substituent orientation

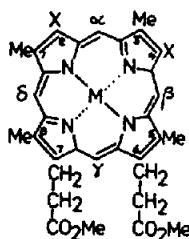
Compound	$\text{C}_\alpha^+$	$\text{C}_\beta(1,3)$	$\text{C}_\beta(2,4)$	$\text{C}_\alpha(5,8)$	$\text{C}_\beta(6,7)$	meso				$\text{CH}_2\text{-CH}_2\text{-CO-OH}^e$					
						$\alpha$	$\beta$	$\gamma$	$\delta$						
(1) Deuterioporphyrin-IX Dimethyl Ester	143.3 144.2	139.2 139.5	128.0	135.8	137.4 137.7	(99.5 98.7)	95.1	96.2	13.4	11.3	21.5	36.7	172.8	51.4	
(2) Coproporphyrin-III Tetramethyl Ester	144.0	135.8	137.8	135.8	137.8	(96.0 96.0)	96.0	96.4	11.4	11.4	21.7	36.8	172.8	51.5	
(3) Protoporphyrin-IX Dimethyl Ester	143.5	137.6	135.9	135.9	137.6	97.3	96.7	95.4	96.3	12.5	11.5	21.7	36.8	172.8	51.5
(4) Mesoporphyrin-IX Dimethyl Ester	143.8	134.6	141.8	135.7	137.7	96.0	95.8	95.8	11.7	11.5	21.8	36.9	172.9	51.8	
(5) Nematoporphyrin-IX Dimethyl Ester	142.9 134.9	134.3 134.9	140.8	135.6 136.1	137.4	(97.8 98.1)	95.2	96.0	11.3	11.3	21.5	36.6	172.8	51.5	
(6) Bis-acetal	144.0	134.3	137.1	135.9	137.4 137.7	96.8	96.8	95.8	96.4	11.7	11.7	21.8	36.8	172.9	51.5

\* All signals broad.

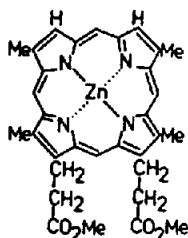
Table 2.  $^{13}\text{C}$  chemical shifts ( $\delta$ , ppm) for zinc(II) porphyrins (+ added pyrrolidine) with "Type-IX" substituent orientation

Compound	$C_\alpha$			$C_\beta(1,3)$			$C_\beta(2,4)$			$C_\beta(5,6)$			meso			$C_\beta(6,7)$			$C_\alpha$			
(7)	148.80	148.10	140.61	140.61	129.20	136.79(2)	138.67	100.42	99.23	95.89	97.15	13.68	11.74	22.16	37.37	173.55	51.51					
	148.68	147.85	140.30	140.30	129.10	138.54																
	148.55	147.45(3)																				
(8)	148.18	147.10(2)	136.63(2)	138.62(2)	136.45(2)	138.50	138.62	96.64	96.54	96.38	96.89	11.72	22.23	37.43	173.48	51.45						
	148.09(3)																					
	147.21(2)																					
(9)	148.57	147.72(3)	136.41	137.02(2)	136.86(2)	138.64(2)	138.64(2)	98.20	97.52	96.07	97.19	12.86	11.74	22.14	37.34	173.48	51.51					CH=CH <sub>2</sub>
	148.21	147.08	136.86																			CH <sub>2</sub> -CH <sub>3</sub>
	147.93	146.58																				CH(OH)CH <sub>3</sub>
(10)	148.53	147.64	135.20(2)	142.48(2)	136.23(2)	138.32(2)	138.32(2)	96.49	96.49	96.15	96.49	11.80	11.60	22.23	37.46	173.58	51.50					
	148.38	147.09																				
	147.92	146.74(3)																				
(11)	148.13	147.22	136.27	141.96	137.05	138.55(2)	138.55(2)	98.67	98.27	96.00	96.88	11.92	11.73	22.08	37.30	173.53	51.54					
	147.97	146.01	135.73	141.83	136.72																	
	147.51(3)	145.41																				
(12)	147.94(5)		135.09(2)	137.97	136.58	138.47(2)	138.47(2)	97.34	97.14	96.19	96.84	11.97	11.66	22.18	37.41	173.44	51.40					CH <sub>2</sub> -CH-(OMe) <sub>2</sub>
	147.79(1)																					
	147.70(2)																					
(13)	150.51	146.90	138.07	144.56	137.42	139.31	139.31	103.29	100.71	95.90	98.21	14.29	11.61	21.94	37.06	173.34	51.60					CH <sub>3</sub> -CO
	149.96(2)	146.10	139.10	144.47	137.27	139.20	139.20															
	148.63	145.95(2)																				
(14)	148.34	147.60(3)	137.48(2)	139.86	137.02	138.57(2)	138.57(2)	98.48	98.20	96.10	96.78	11.72	11.72	22.18	37.36	173.49	51.47					CH-(Me)-OMe
	148.04	147.50	139.71	136.94																		
	147.70	146.66																				

Numbers in parentheses represent the number of lines affording the single signal.



- (1) X = H; M = 2H
- (2) X = CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Me; M = 2H
- (3) X = CH=CH<sub>2</sub>; M = 2H
- (4) X = Et; M = 2H
- (5) X = CH(OH)Me; M = 2H
- (6) X = CH<sub>2</sub>CH(OH)Me; M = 2H
- (7) X = H; M = Zn
- (8) X = CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Me; M = Zn
- (9) X = CH=CH<sub>2</sub>; M = Zn
- (10) X = Et; M = Zn
- (11) X = CH(OH)Me; M = Zn
- (12) X = CH<sub>2</sub>CH(OH)Me; M = Zn
- (13) X = CH<sub>3</sub>CO; M = Zn
- (14) X = CH(OAc)Me; M = Zn



(15)

the peak furthest downfield in the C<sub>β</sub> region, just as one would expect for the ethyl substituent. By default, one therefore assigns C<sub>1,3</sub> to the peak at 134.6 ppm, which is reasonable because it comes close to the methyls of C<sub>5,8</sub>. Similarly, in deuteroporphyrin-IX dimethyl ester (1), the assignment of C<sub>2,4</sub> is clearly the peak at 128.0 ppm, which is the highest field peak in the region since it lacks an "α-effect" of a substituent. Also the release of steric strain causes C<sub>1,3</sub> to move downfield, so it is not surprising that of all of the isomers in the series, C<sub>1,3</sub> in 1 appear at lowest field (139.2, 139.5 ppm).

Assignment of the meso carbon regions in the spectra is of particular importance since, in the <sup>13</sup>C biosynthetic studies<sup>3</sup> the label often appears in the meso positions of the product porphyrins. However, Table 1 indicates that the meso region is difficult to assign. In the cases of coproporphyrin-III tetramethyl ester (2) and mesoporphyrin-IX dimethyl ester (4) there is a considerable loss of information due to signal degeneracy. Battersby *et al.*<sup>3</sup> obtained the carbon spectra of hematoporphyrin-IX dimethyl ester (5) and protoporphyrin-IX dimethyl ester (3); no assignments were offered in the former case, but 3 was assigned by regioselective labelling via total synthesis. Battersby *et al.* also assigned the meso carbons in 2,4-diacetyldeuteroporphyrin-IX dimethyl ester by specific synthesis, and one useful common factor to arise from this work was the fact that the γ-meso carbon occurs at highest field. Thus, in Table 1 we are able to assign the high field meso signal to the γ carbon in each instance. However, the range of values is from 95.1 (1) to 96.0 ppm (2), and this appears anomalously large for a

carbon atom so removed from the site of substituent variation. In conjunction with this point, it is interesting to note that Battersby *et al.* obtained the spectrum of protoporphyrin-IX dimethyl ester (3) on four different occasions, and obtained shift variations for a given carbon atom that were considerably outside of experimental error. We ascribe this effect to the fact that these porphyrins are aggregating and thus are suffering variable aggregation shifts. Thus, a given porphyrin measured at different concentrations will be expected to give different shifts; moreover, the extent of the aggregation shift will be variable and will be dependent upon structural features within the particular porphyrin. It is this factor, superimposed upon the inherent proximity of the meso carbon shifts, that makes the meso region so uninformative, as seen in Table 1. We will discuss a more convenient method for obtaining structural information from porphyrin spectra. Finally, assignment of the various side chain groups is trivial and has been commented upon elsewhere.<sup>11</sup>

In previous papers<sup>4,12,13</sup> we have indicated that the problem caused by tautomerism in porphyrins can be overcome by insertion of a metal atom into the porphyrin, and we have chosen Zn as a convenient case because it can be both inserted and removed with relative ease and minimal losses. The aggregation phenomena alluded to above for free base porphyrins is even more of a problem with the Zn(II) complexes because the tendency to aggregate is much greater in most cases. However, we have demonstrated that these problems can be conveniently surmounted by addition of small amounts of the base, pyrrolidine. This compound, we presume, forms a sterically demanding apical ligand on the zinc atom which makes face-to-face aggregates of the Zn porphyrins impossible to exist.<sup>4,12,13</sup> In many cases, many of the Zn(II) porphyrins were not sufficiently soluble for their spectra to be measured in the absence of pyrrolidine. Accordingly, in Table 2, data are presented for various Zn(II) porphyrins in the presence of about 2 mole equivalents of pyrrolidine.

The most gratifyingly improved region of the spectra proved to be the crucial meso carbon region. Only in the case of Zn(II) mesoporphyrin-IX dimethyl ester (10) was any information lost due to signal degeneracy. Otherwise, complete signal assignments can be made, apart from Zn(II) coproporphyrin-III tetramethyl ester (8) where it is difficult to differentiate between the meso α- and β-carbons since their environments are almost identical. The γ-carbon, flanked by two propionic esters, is invariably at highest field as in the free base porphyrins; however, the total range of shifts here is only about 0.4 ppm, with the average being 96.09 (±0.12) ppm, which compares with a mean deviation of 0.3 ppm in the free bases. Although the shift of the γ-carbons in the metalloporphyrins here are considerably downfield from the free base porphyrins (Table 1), we feel that the assignment is sound since we have proved the assignment of the γ-carbon in Zn(II) coproporphyrin-II tetramethyl ester by regiospecific deuteration.<sup>12</sup> Also, we can unambiguously assign the γ-carbon in Zn(II) deuteroporphyrin-III dimethyl ester because of the symmetry properties of the molecule.<sup>4</sup>

The δ meso carbon, flanked by two methyl groups, also shows a consistent value through the series, as expected, since its environment is similar in all the compounds, although it should be more susceptible to substitutional changes (at 2) than the γ-carbon. The veracity of this assignment is also beyond dispute since the δ-carbons in

Zn(II) coproporphyrin-II tetramethyl ester and Zn(II) deuteroporphyrin-III dimethyl ester have been unambiguously assigned.<sup>4,12</sup> The only  $\delta$ -meso carbon that is out of line is in Zn(II) diacetyldeuteroporphyrin-IX dimethyl ester (13), where it appears at 98.21 ppm. This undoubtedly arises because of the exceptionally strong electron-withdrawing acetyl group at position 2.

The  $\alpha$ - and  $\beta$ -meso carbons vary most through the series since they are close to the variable 2 and 4 positions. Assignments were made on the expected effects of the substituents. Thus, in Zn(II) deuteroporphyrin-IX dimethyl ester (7) the release of steric compression compared with other groups causes both  $\alpha$ - and  $\beta$ -meso carbons to resonate at much lower fields; this release of steric compression is expected to be most significant in the case of the  $\alpha$ -carbon, hence this is assigned to the lower field value. In the Zn(II) diacetyldeuteroporphyrin-IX dimethyl ester (14), the low field resonance position is ascribed to the strong electron-withdrawing effect of the 2 and 4 substituents, this again being greater in the case of the  $\alpha$ -carbon.

Assignment of the side chain resonances is again trivial. The propionate side chain and the 5 and 8 methyl resonances exhibit values within 0.1 ppm of those found in the four Zn(II) coproporphyrin isomers.<sup>13</sup> Methyl

resonances at 1 and 3, both adjacent to the variable substituents, are the only peaks which alter through the series. It should be noted that only one resonance is seen for each side chain carbon [except for 14], although the molecules only possess  $\sigma$ , symmetry. All these cases of signals being anisochronous indicate that the 5,8 propionate side chains, for example, are too distant from the 2 and 4 substituents to sense their disposition. While this may be expected for the side chains at 5, 6, 7 and 8, it is a little surprising for the 1 and 3 methyl groups. It is only in the case of the Zn(II) diacetyl compound (14) that separate signals are observed for the 1, 3 and 5, 8 methyls.

The  $\beta$ -carbons can be assigned as four pairs in each case, although these pairs often only give a single resonance. This very small signal separation means that we can never distinguish between carbons 1 and 3, 2 and 4, 5 and 8, or 6 and 7, though we can always distinguish between each pair. The first basis for assigning these carbons is to compare the shifts with those obtained for the four coproporphyrin isomers. Here it was found that the  $\beta$ -carbons attached to methyl resonated at 136.5 ( $\pm 0.1$ ) ppm, while the  $\beta$ -carbons attached to propionate resonated at 138.5 ( $\pm 0.1$ ) ppm. In virtually all cases the resonances for the 5, 8 and 6, 7 carbons fall close to these values, so making assignment here simple. To assign the 1-4 carbons

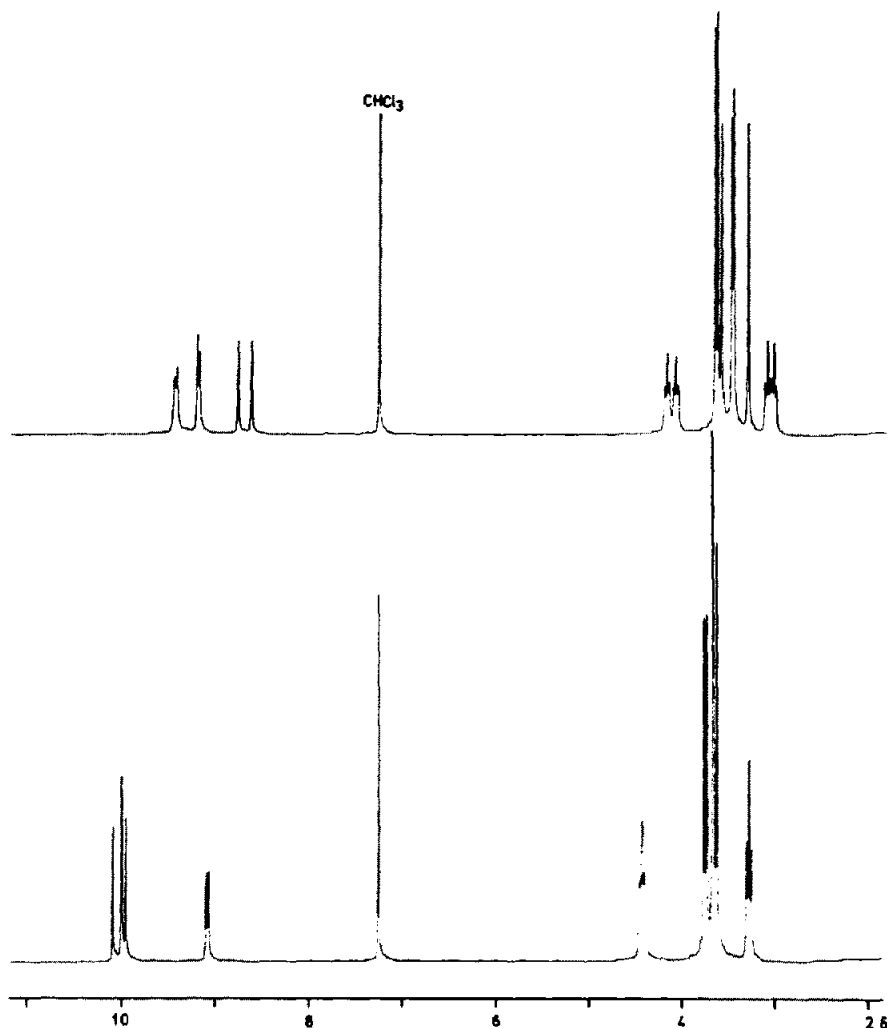


Fig. 1. 300 MHz Proton NMR spectra, in  $\text{CDCl}_3$ , of (above) zinc(II) deuteroporphyrin-IX dimethyl ester (7), and (below) the same sample after addition of approx. 2 mole equiv of pyrrolidine.

the same approach was adopted as in the free bases. Only in the case of Zn(II) protoporphyrin-IX dimethyl ester (9) and Zn(II) coproporphyrin-III tetramethyl ester (8) is there any ambiguity. The acetyl group in 13 again causes some anomalous shifts insofar as 5, 8 and 6, 7 fall downfield of their usual ranges.

In three cases, the Zn(II) bis-acetal (12), Zn(II) protoporphyrin (9), and Zn(II) mesoporphyrin (10), it was possible to run spectra without pyrrolidine added. Addition of pyrrolidine, in all cases, caused downfield shifts and significant changes in the fine structure appearance of the spectra. We have carried out a detailed study of the aggregation in Zn(II) protoporphyrin-IX dimethyl ester.<sup>14</sup>

The proton spectra of these Zn(II) porphyrins also show fine structure and upfield shifts due to aggregation. Figure 1 shows the spectrum of Zn(II) deuteroporphyrin-IX dimethyl ester (7) with and without pyrrolidine. Table 3 gives proton data at 300 MHz for all the subject por-

phyrins at constant concentration in presence of pyrrolidine, while Table 4 gives proton data for those compounds without pyrrolidine. Because of a combination of poor solubility and broad lined spectra, no useful data for Zn(II) diacetyldeuteroporphyrin-IX dimethyl ester (13), Zn(II) hematoporphyrin-IX dimethyl ester (11), and Zn(II) diacetoxyhematoporphyrin-IX dimethyl ester (14) are reported. A detailed study of the proton spectra of 9 has been carried out<sup>14</sup> and we have already commented in detail upon the proton spectrum of Zn(II) coproporphyrin-III tetramethyl ester (8), and also pointed out the salient factors affecting aggregation in Zn(II) porphyrins.<sup>15, 16</sup>

The assignment of the meso protons in the Zn(II) coproporphyrin isomers became trivial once it was shown that the shifts were only a function of the adjacent peripheral substituents.<sup>13</sup> Following this pattern allows the assignments of the meso protons of the compounds studied to be made easily, except for the  $\alpha$ - and

Table 3. Proton chemical shifts ( $\delta$ , ppm) for zinc(II) porphyrins with added pyrrolidine<sup>a</sup>

Compound	meso	CH <sub>2</sub>	CH <sub>2</sub>	Me	Me	OMe	2,4-Side Chain	
(7)	10.102( $\delta$ ) 10.012 10.007( $\alpha, \beta$ ) 9.965( $\gamma$ )	4.445	3.294	3.777	3.638	3.677	9.110 (2,4-H) 9.086	
(8)	10.044( $\delta$ ) 10.003( $\alpha, \beta$ ) 9.989( $\gamma$ )	4.433	3.283	3.657	3.654	3.714 3.698 3.684 3.673		
(9)	10.232( $\delta$ ) 10.150( $\alpha, \beta$ ) 10.075( $\delta$ ) 9.947( $\gamma$ )	4.419	3.282	3.766 3.761	3.653 3.636	3.680	8.41 (CH)	6.39 (CH <sub>2</sub> ) 6.14
(10)	10.030( $\delta$ ) 10.018( $\alpha, \beta$ ) 9.971( $\gamma$ )	4.440	3.289	3.683 3.673	3.639 3.633	3.661	4.095 (CH <sub>2</sub> )	1.860 (CH <sub>3</sub> )
(11)	10.446( $\delta$ ) 10.403( $\alpha, \beta$ ) 10.050( $\delta$ ) 9.966( $\gamma$ )	4.425	3.285	3.751 3.713	3.678 3.672	3.648 3.607	6.693 (CH) 6.135	2.317 (CH <sub>3</sub> )
(12)	10.107( $\alpha, \beta$ ) 10.088 10.062( $\delta$ ) 9.978( $\gamma$ )	-4.4	3.292	3.672	3.656	3.688	-4.4 (CH <sub>2</sub> )	5.210 (CH) 3.474 (OMe) <sub>2</sub> 3.455

<sup>a</sup> Concentration 6.5 mM in CDCl<sub>3</sub>

Table 4. Proton chemical shifts ( $\delta$ , ppm) for zinc(II) porphyrins in the absence of pyrrolidine<sup>a</sup>

Compound	meso	CH <sub>2</sub>	CH <sub>2</sub>	Me	Me	OMe	2,4-Side Chain	
(7)	9.46 9.43 9.21 9.19	4.18	3.10	3.59	3.46	3.66	8.78 (2,4-H) 8.64	
(8)	9.38 9.46 9.57	4.24	3.14	3.52 3.45	3.43 3.40	3.71 3.68 3.67 3.65		
(9)	9.16 8.90 8.87 8.84	4.03	2.98 2.95	3.32 3.28	3.23	3.65 3.63	-6.08 (=CH <sub>2</sub> )	
(10)	9.61 9.51 9.47 9.45	4.24 4.18	3.14 3.12	3.51 3.45	3.43 3.93	3.68 3.65	3.93 (CH <sub>2</sub> ) 3.84	1.77 (CH <sub>3</sub> ) 1.73
(12)	9.58 9.56 9.45 9.36	-4.26	3.18 3.15	3.49 3.45	3.37 3.35	3.69 3.65	3.39 (OMe) 3.32	4.94 (CH) 4.84 3.97 (CH <sub>2</sub> ) 4.11

<sup>a</sup> Concentration 6.5 mM in CDCl<sub>3</sub>.

$\beta$ -meso protons, which in all cases either coalesce or are very close together. These assignments are given in Table 3 and confirm the original premise found for the coproporphyrins.<sup>13</sup> For example, the  $\gamma$ -meso proton remains constant at 9.97 ( $\pm 0.2$ ) ppm. The  $\delta$ -meso proton shows a slightly larger range of variation (10.03 to 10.10 ppm) and this supports the predictive scheme of Clezy and Fookes,<sup>17</sup> who noted that the next but one peripheral substituent (to the meso proton considered) needed to be taken into account to give a precise explanation of the meso proton shifts in the Zn(II) protoporphyrin dimethyl ester isomers.

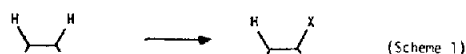
#### Carbon-13 substituent chemical shifts (SCS) in porphyrins

We have previously shown how the <sup>13</sup>C SCS can be calculated in the porphyrin ring and that they provide useful chemical information on the partial bond orders in the macrocycle.<sup>13</sup> These studies were limited to the peripheral methyl and propionate groups of the coproporphyrin esters.

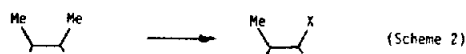
The accurate data and detailed assignments of Table 2 allow the deduction of the SCS in the porphyrin ring of a more extensive range of substituents. Any substituent can be considered to have two separate effects on the porphyrin ring, a specific effect on a particular nucleus, and a global effect on the macrocycle. The results in Table 2 show immediately that the peripheral substituents considered here do not have an appreciable global effect on the macrocycle, at least with regard to the beta and meso carbon chemical shifts. This is clearly seen by the constancy of the C<sub>5,8</sub>, C<sub>6,7</sub>, and  $\gamma$ -meso carbon chemical shifts. The ranges of the observed shifts are 1.2 ppm (C<sub>5,8</sub>), 1.0 ppm (C<sub>6,7</sub>), and 0.5 ppm ( $\gamma$ -meso), and these ranges should be considered along with the experimental error of measurement of ca. 0.1 ppm. In both the beta carbon sets, the 2,4-diacetyldeuteroporphyrin-IX comes at the limit of the range, and thus the strongly electron-withdrawing acetyl groups at positions 2 and 4 may be exerting a small global effect. This result is of interest as it demonstrates the resistance of the

porphyrin macrocycle to beta, as opposed to meso, substitution. It also allows the analysis of the SCS to be performed easily, as only the localized effects need to be considered. Table 5 gives the shift differences ( $\Delta\delta$ ) of the separate meso carbons and the grouped beta carbons C<sub>1,3</sub> and C<sub>2,4</sub> from the corresponding shifts of Zn(II) octamethylporphyrin. The comparison with Zn(II) octamethylporphyrin rather than with Zn(II) porphyrin itself is made for practical reasons, as the great majority of all naturally occurring porphyrins have one Me substituent on each pyrrole subunit. The above procedure allows the prediction of the carbon chemical shifts in these molecules by the use of only one substituent parameter for each carbon, instead of two if porphyrin were used (*vide infra*).

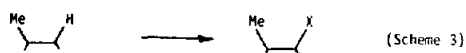
The beta carbon SCS of Table 5 show the expected large direct substituent effect at C<sub>2,4</sub> and the smaller *ortho* substituent effect at C<sub>1,3</sub>. Note that the use of octamethylporphyrin as the base molecule means that the SCS of Table 5 are from Scheme 2 in which the substituent X replaces a methyl group, and cannot be compared directly with the more usual SCS from the parent hydrocarbon, as in Scheme 1.



(Scheme 1)



(Scheme 2)



(Scheme 3)

Although the SCS of Scheme 2 can be converted to the corresponding ones for Scheme 3 simply by altering the origin so that the values for Zn(II) deuteroporphyrin-IX dimethyl ester in Table 5 are 0.00, the process occurring in Schemes 2 and 3 differs from that in Scheme 1 in that a steric Me-X interaction is present in the former. This is clearly apparent from the observed values. For X=Me, the direct and *ortho* SCS in the porphyrin ring are, for Scheme 1, 8.7 and -2.6 ppm,<sup>†</sup> and for Scheme 3, 6.6 and

<sup>†</sup>From the values for Zn(II) deuteroporphyrin-IX dimethyl ester (Table 3) and Zn(II) porphyrin (131.7 ppm).<sup>4</sup>

Table 5. <sup>13</sup>C substituent chemical shifts (SCS) in porphyrins

Compound	2,4-Substit.	C <sub>5</sub> (1,3) <sup>b</sup>	C <sub>6</sub> (2,4) <sup>b</sup>	meso carbons <sup>c</sup>				
				$\alpha$ meso	$\beta$ meso	$\delta$ meso	Syn-X	Anti-X
7	H	4.74	-6.57	4.14	2.95	0.87	2.80	0.72
8	CH <sub>2</sub> CH <sub>2</sub> CO <sub>2</sub> Me	0.91	2.90	0.36	0.26	0.61	-0.10	0.15
9	CH=CH <sub>2</sub>	0.92	1.30	1.92	1.24	0.91	1.09	0.76
10	CH <sub>2</sub> CH <sub>3</sub>	-0.52	6.76	0.21	0.21	0.21	0.06	0.06
11	CH(OH)CH <sub>3</sub>	0.28	6.18	2.39	1.99	0.59	1.84	0.44
12	CH <sub>2</sub> CH(OMe) <sub>2</sub>	-0.63	2.15	1.06	0.86	0.56	0.71	0.41
13	COCH <sub>3</sub>	2.67	8.79	7.01	4.43	1.93	4.28	1.78
14	CH(OAc)CH <sub>3</sub>	1.76	4.07	2.20	1.92	0.50	1.77	0.35

<sup>a</sup> In ppm, using zinc(II) octamethylporphyrin as a base:  $\alpha$  148.16,  $\beta$  135.72, meso 96.28, -Me 11.86 ppm.

<sup>b</sup> Average shifts from Table 2, average of C<sub>5</sub>(5,8) 136.63, C<sub>6</sub>(6,7) 138.52 ppm.

<sup>c</sup>  $\gamma$ -meso shift 96.10 ppm (average).

-4.7 ppm. The increased steric repulsion from two *ortho* methyl groups decreases the direct effect and increases the *ortho* effect. Precisely analogous effects are observed in simpler molecules, e.g. in methyl substituted benzenes the corresponding figures are, for Scheme 1, 8.9 and 0.7 ppm<sup>18</sup>, and for Scheme 3, 7.1 and -1.4.<sup>19</sup> The trend is the same, although the initial *ortho* effect is positive in benzene and negative in porphyrins due to the increased  $\pi$  bond order of the C $_{\beta}$ -C $_{\beta}$  bond in the porphyrin ring.<sup>13</sup>

The beta SCS of Table 5 for the different groups show also some expected effects, though again the actual values will differ (from the benzene series) because of the different hybridization and geometry of the porphyrin ring. Increasing the side chain by one carbon unit (Me  $\rightarrow$  Et) has the expected effect of a further downfield shift of C $_{2,4}$ , analogous to the beta Me effect in saturated systems, and an upfield shift of C $_{1,3}$ , corresponding to the upfield  $\gamma$ -Me shifts in saturated systems.<sup>16</sup> Also, the acetyl group, as expected, has a strong deshielding effect on both C $_{2,4}$  and C $_{1,3}$ . However, there are some unpredicted features; the various  $\beta'$ -substituents (compounds 11, 12, 14) produce pronounced changes in the SCS which could not have been anticipated, and which probably arise from the different steric requirements and thus conformations of these groups, together with the strong electric fields of the polar OR substituents.<sup>20</sup>

The SCS of the substituents on the  $\alpha$ -,  $\beta$ -, and  $\delta$ -meso carbons are also given in Table 5, and these can be analyzed as follows. The constancy of the  $\gamma$ -meso chemical shift to the variation of the substituents on C $_{2,4}$  suggests that changing the substituent on C $_4$  should not affect the  $\delta$ -meso carbon shift, as the spatial relationship of the  $\gamma$ -meso to C $_2$  and the  $\delta$  meso to C $_4$  are identical. Thus, the variations of the  $\delta$ -meso carbon are due entirely to the substituent at C $_2$ . If also the C $_2$  substituent does not affect the  $\beta$ -meso carbon then the meso SCS of Table 5 can be separated into two additive effects, a *syn* effect of the substituent on the adjacent meso carbon (given by the  $\beta$  meso SCS) and an *anti* effect (given by the  $\delta$  meso SCS). The  $\alpha$  meso SCS should then be simply the sum of the  $\beta$ - and  $\delta$ -SCS, as both these effects operate on the  $\alpha$ -carbon. This postulate can be tested by evaluating the linearity of goodness of fit of eqn (1), using the data in Table 5.

$$\Delta\delta_{\alpha} = m(\Delta\delta_{\beta} + \Delta\delta_{\delta}) + c \quad (1)$$

At least mean squares analysis of the data shows that there is indeed an excellent correlation ( $m = 1.188$ ,  $c = -0.561$ , rms error 0.134, correlation coefficient 0.998). In particular, the rms error is essentially within the experimental error of the measurements, when it is remembered that these  $\Delta\delta$  values are less accurate (by *ca.*  $\sqrt{2}$  than the  $\delta$ -values).

The non-zero value of the intercept of eqn (1) is an artifact resulting from the origin of the  $\Delta\delta$  values being taken for convenience as octamethylporphyrin, rather than the "true" origin, which would be 6,7-di(2-methoxycarbonyl)ethyl-1, 2, 3, 4, 5, 8-hexamethylporphyrin (*vide infra*).

The above analysis allows the deduction of the SCS of the substituents at the meso carbons. These are given simply by the  $\Delta\delta$  values for the  $\beta$ -meso and  $\delta$ -meso carbons in Table 5, and can now be considered together with the corresponding SCS for the beta carbons. Noteworthy is the large upfield *syn* effect on the  $\beta$ -meso carbon due to the release of steric strain on going from

Me to H, and this release of steric strain is probably also transmitted to the  $\delta$ -meso carbon and accounts for the upfield shift of this carbon. This steric effect of the beta Me groups is so large that all the meso carbon chemical shifts of Table 2 fall within those of Zn(II) porphyrin (104.3  $\delta$ ) and Zn(II) octamethylporphyrin (96.3  $\delta$ ). The vinyl group also produces an appreciable *syn* effect, and again this could be due to release of steric strain, particularly as the vinyl group is known to be at an angle to the porphyrin plane.<sup>21</sup> Of the other groups, the large SCS of the acetyl is to be expected, the  $\delta$  meso shift is now probably due to conjugation effects across the *trans* coplanar pathway, and the hemato-group [CH(OR)Me] SCS again suggests steric effects leading to a preferred orientation of this group with the OH function close to the porphyrin.

The SCS of Table 5 are of practical utility in that they provide a simple and ready means of predicting the meso and beta carbon chemical shifts for a variety of porphyrins. The beta carbon SCS values of columns 3 and 4 may be used directly, together with eqn (2) to give the resulting beta carbon chemical shifts. However, for the meso carbons, the SCS cannot be used directly as they include the effects of the C $_{6,7}$  propionate groups which have not been isolated, but merged with the  $\beta$ -meso and  $\delta$ -meso SCS. Using the constant  $\gamma$ -meso carbon shift, together with the above analysis of additive contributions of the *syn* and *anti* substituents, allows the values for the C $_{6,7}$  propionate groups to be removed to give the parameters in columns 8 and 9 of Table 5. These can be used with eqn (3) to predict the meso carbon shifts.

$$\delta(\text{beta-C}) = 135.7 + \delta_x(\text{beta}) \quad (2)$$

$$\delta(\text{meso-C}) = 96.3 + \sum_i (\text{syn}_i + \text{anti}_i) \quad (3)$$

The operation of the above rules is best illustrated by an actual example. In deuteroporphyrin-III dimethyl ester (15), these rules would predict the following: C $_{1,4} = 135.7 + 4.7 = 140.4$  ppm,  $\beta$ ,  $\delta$  meso =  $96.3 + \text{Anti}_H + \text{Anti}_P = 97.2$  ppm.

The calculated and observed<sup>4</sup> (in parentheses) values for Zn(II) deuteroporphyrin-III are, for the beta carbons, C $_{1,4}$  140.4 (140.4) C $_{2,3}$  129.1 (129.2), C $_{5,6}$  136.3 (136.7) and C $_{6,7}$  138.6 (138.7 ppm), and for the meso carbons,  $\alpha$  101.9 (103.0),  $\beta$ ,  $\delta$  97.2 (96.9), and  $\gamma$  96.1 (96.2 ppm). The generally good agreement, which is almost within experimental error, apart from the  $\alpha$  meso carbon (in which the two large *syn* effects are probably not quite additive), is very pleasing considering the conceptual simplicity of the scheme. It will be of some interest both to extend this scheme to other common beta substituent groups and also to apply it to the complex spectra produced by less symmetric porphyrins which are at present extremely difficult to assign and interpret. It must however be noted that this scheme is for *disaggregated* Zn(II) porphyrin spectra; its application to spectra of either metalloporphyrins without disaggregating ligands attached, or to the spectra of free base porphyrins is not encouraged.

*Acknowledgements*—We thank the Science Research Council for a grant to purchase the XL-100 spectrometer, and an I.C.I. Fellowship (to H.P.). We are also grateful to Dr. F. Heatley and (the late) R. Warren (University of Manchester) for assistance and access to the Varian SC-300 spectrometer. This research



was supported by grants from the National Science Foundation, the National Institutes of Health (HL 22252), and the Scientific Affairs Division of N.A.T.O. (RG 256.80).

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