Tetrahedron Vol. 40, No. 17, pp. 3263 to 3272, 1984
Printed in the U.S.A.

0040–4020/84 $3.00 + .00

THE NMR SPECTRA OF PORPHYRINS—25[1]

MESO-SUBSTITUENT EFFECTS IN NEUTRAL AND PROTONATED PORPHYRINS

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(*Received in U.S.A.* 3 *October* 1983)

Abstract—The meso (methine) substituent chemical shifts (SCS) of a range of common functional groups have been obtained both for the neutral porphyrin molecule, and for the corresponding dications, in substituted octaethylporphyrin (OEP), etioporphyrin-I, and pyrroetioporphyrin-XV derivatives. The SCS are discussed in terms of both ring current variations and specific effects at the neighboring beta-substituents and the meso-proton opposite the perturbing substituent, using a ring current model to quantify the former. In the neutral molecules, meso substitution in OEP (Me, NO_2, CN, CHO) causes a 10% decrease in the macrocyclic ring current, and marked anisotropic shifts at the beta-positions flanking the meso function. The meso-NH_2 group introduces a much larger decrease (*ca* 35%) in the main ring current, due to conjugation of the amino group with the porphyrin π-system. In the porphyrin dications, SCS are much larger and there is some evidence of a concomitant decrease in the ring current of the adjacent pyrrole subunits. The meso-NMe_2 substituent at the γ-meso-position in pyrro-etioporphyrin-XV has only small SCS in the neutral molecule, but a large shift (similar to that of NH_2) in the dication, due to the different orientation of the substituent with respect to the porphyrin plane in each case. The meso-OH substituent in the oxophlorin from etioporphyrin-I behaves as a conjugated OH group in the dication. The anomalous position of the meso-proton opposite to the perturbing substituent is noteworthy, and this could be due to electronic (resonance) effects, or to some protonation at this position.

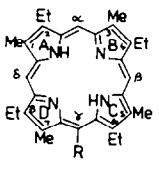
The large π-electron ring current of the porphyrin macrocycle dominates the proton NMR spectra of the porphyrins,[2] and thus provides a sensitive probe of any perturbations of the macrocycle by extraneous influences. Using an accurate model of the ring curent,[3-5] we have shown in previous parts of this series how the effects of chlorin formation[5] and protonation[6] can be explained quantitatively, and these studies have provided a ring current model for the chlorin (7,8-dihydroporphyrin) system of the chlorophylls.[5] In this paper we utilize the same approach to quantitatively evaluate the effects of some meso-substituents on the porphyrin ring current.

Scheer and Katz[2] have defined three consequences of the effects of meso substitution on porphyrin proton chemical shifts. These are: (a) the ring current is reduced; (b) the methine proton "opposite" the meso substituent is more strongly shifted to higher field than the "adjacent" methines; and (c) protons in the vicinity of the substituent experience direct magnetic anisotropic effects. These conclusions stem from a variety of investigations with different meso substituents. Most of the early studies used trifluoroacetic acid (TFA) as the solvent,[2] mainly for solubility reasons, in which solvent the porphyrin exists as the dication. Inhoffen *et al.*[7] examined the effects of some magnetically anisotropic meso substituents in neutral solution. However, there has been no comparative study of the effects of meso-substituents in both acid and neutral solution. This is of relevance for those substituents which may either protonate or conjugate with the macrocycle, because the substituent may have very different effects in the porphyrin dication than in the neutral molecule. The exceptional behavior of meso-NH_2 and meso-OH groups noted by Scheer and Katz[2] are particularly relevant to this question.

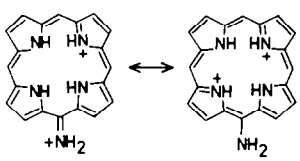
In meso-NH_2-OEP (**1**)† in TFA solution, the methine proton resonances are considerably shielded to high field (by *ca* 1 ppm) compared with other substituents, and it has been suggested[2] that the presence of imino-phlorin structures (e.g. **1A**) in which the ring current is interrupted, could be responsible for these effects. The conventional formula (**1B**) and the phlorin-like structure (**1A**) are, in this situation, resonance contributors, as distinct from the equivalent structures for the neutral molecule, which are tautomers.

Although the imino-tautomer of the neutral meso-NH_2-porphyrin (**1**) has not been described, the meso-OH-porphyrin analogues in neutral solution are present as the keto-tautomers, the oxophlorins (e.g. **2A**).[8] Because of severe line broadening, the NMR spectra of oxophlorins are difficult to observe in neutral solution;[8] this is a consequence of their low

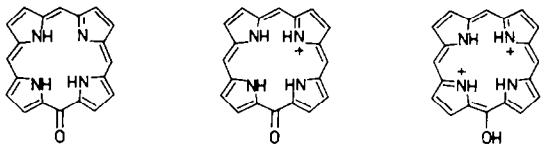
†Note that throughout this paper the meso-substituents are drawn such that they occupy the γ- rather than α-meso-position; this choice was dictated by the usual nomenclature used to depict pyrro-etioporphyrin-XV and γ-phyllo-etioporphyrin-XV, two derivatives of natural porphyrins in which the meso-substituents are located at the γ-position.



(1) R = NH_2
(12) R = H



(1A) (1B)



(2A) (2B) (2C)

oxidation potential and the presence in solution of small quantities of the corresponding π-cation radical.[9] In contrast, the oxophlorin mono- and dications give sharp, well-resolved NMR spectra. Jackson *et al.*[8] followed the acid titration of some oxophlorins, both spectrophotometrically and by proton NMR, and interpreted their results in terms of the oxophlorin structure for the neutral molecule (**2A**) and the mono-cation (**2B**), but the hydroxy form (**2C**) for the dication. They also estimated the proton chemical shifts of the neutral oxophlorin (**2A**) by extrapolation.

During the course of synthetic studies on the mechanism of the Cu(II) catalyzed cyclization of 1′,8′-dimethyl-a,c-biladiene salts,[10] we observed some unusual NMR effects of the meso-NMe_2 group in the derivative (**3**) of pyrroetioporphyrin-XV (**4**) in acid solution, as compared with neutral media; in this example the competing effects of NMe_2-group conjugation and steric hindrance of the N-Me groups with the neighboring beta substituents are well illustrated. This study was expanded to include other common meso substituents, and we present here a quantitative examination of the influence of a number of meso-substituent groups on the porphyrin ring in both the neutral and dication species. Our procedure follows that adopted previously,[6] which is to compare the chemical shifts of the meso-substituted porphyrins with those of the corresponding unsubstituted analogue under identical conditions.

EXPERIMENTAL

The meso-NMe_2 (**3**),[10] meso-Me (**5**),[10] (**6**),[11] meso-NO_2 (**7**),[12] meso-CHO (**8**),[13] meso-CN (**9**),[12] meso-NH_2 (**1**),[14] and meso-OH (oxophlorin) (**10**),[15] porphyrins were prepared according to published procedures.

Proton NMR spectra were recorded on a Nicolet NT-360 FT spectrometer; typical conditions were 16 K data points, sweep width 5 KHz, pulse width 2 μs, aquisition time 2.0 s and *ca* 60–200 accumulations. The spectra of the free bases were measured in $CDCl_3$ solution, and the protonated species were obtained by addition of *ca* 200 equivalents of TFA to these solutions. The results obtained are presented in Tables 1–3.

SPECTRAL ASSIGNMENTS

The assignments of the various peripheral substituent groups on the macrocycle are not unequivocal, apart from the symmetric parent compounds, octaethylporphyrin (OEP) (**11**) and etioporphyrin-I (**12**).

Table 1. Proton chemical shifts (δ) of some meso substituted octaethylporphyrin free bases and dications

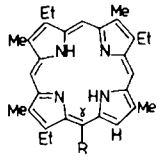
		Free Bases[a]				Dications[c]			
		Me	NO_2	CHO	CN	Me	NO_2	CHO	CN
Meso	β,δ	10.022	10.221	10.058	10.172	10.255	10.581	10.436	10.552
	α	9.819	10.061	9.952	10.062	10.088	10.498	10.391	10.540
beta-CH_2	1,4	4.056	4.067	4.038	4.034	3.987	4.063	4.019	4.019
	2,3		4.086		4.065			4.011	4.046
	5,8	4.077	4.125	4.018	4.100	3.844	3.962	3.870	4.056
	6,7	4.021	3.731	3.865	4.337	3.714	3.586	3.493	4.131
beta-CH_3	1,4	1.895	1.929	1.887	1.893	1.667	1.695	1.660	1.665
	2,3	1.884	1.919	1.880			1.668	1.639	1.684
	5,8	1.839	1.911	1.838	1.904	1.524	1.557	1.494	1.650
	6,7	1.820	1.691	1.722	1.916	1.433	1.376	1.354	1.582
N-H		-2.89[b]	-3.58[b]	-2.84[b]	-3.01	-2.62[b]	-2.67[b]	-2.28[b]	-2.45[b]
		-2.90[b]	-3.79[b]	-2.92[b]	-3.07	-3.48[b]	-3.14[b]	-2.97[b]	-2.89[b]
Meso Substit.		4.605		12.778		4.734		12.514	

Footnotes: [a] In $CDCl_3$ solution, ca. 10^{-2} M ; [b] Broad signals; [c] As in a + 100-200 equiv. TFA

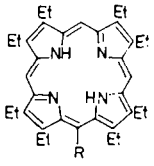
Table 2. Proton chemical shifts (δ) of meso substituted etioporphyrin-I free bases and dications

		Free Base[a]		Dications[b]		
		H	NH_2	H	NH_2	OH
Meso	β,δ	10.095	9.400 9.371	10.740	9.231	10.116 10.104
	α		9.073		8.744	9.817
β-CH_2		4.103	3.820	4.182	3.630 3.610 3.590 3.405	3.951 3.930 3.878 3.784
β-Me		3.646	3.368 3.340	3.698	3.181 3.140 3.076 2.935	3.482 3.470 3.421 3.327
β-CH_2CH_3		1.873	1.742 (2) 1.722 1.666	1.767	1.640 1.580 1.563 1.415	1.707 1.686 1.584 1.515
N-H		-3.75	[d]	-4.34[c]	-0.17[c] -0.24	-2.00[c] -2.21 -2.90 -3.14

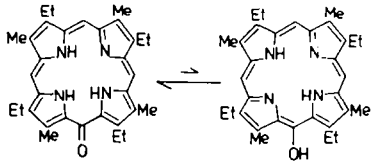
Footnotes: [a] In $CDCl_3$ solution, ca. 10^{-2} M; [b] As a + 100-200 equiv TFA; [c] Broad signals; [d] Not observed, meso-NH_2 6.42 δ.



(3) R = NMe_2
(4) R = H
(5) R = Me



(6) R = Me
(7) R = NO_2
(8) R = CHO
(9) R = CN
(11) R = H



(10)

In the meso-substituted OEPs (Table 1), the only unambiguous assignment, on symmetry grounds, is that of the meso protons. Also, by symmetry, there are four non-equivalent pairs of Et groups, 1,4; 2,3; 5,8; and 6,7. In the meso-NO_2- and meso-CHO-OEPs (**7** and **8**, respectively) the beta Et resonances at these applied fields are resolved into three almost identical resonances, with one Et appearing at higher field. This is assigned, following Ref. 7, to the 6,7-groups flanking the meso-substituents. In the meso-CN-OEP (**9**) this becomes the lowest field Et resonance, and in meso-Me-OEP (**6**) all of the resonances are very close together. In Table 1, the most constant resonances have been assigned to the 1,4 and 2,3 pairs, as any perturbation of the macrocycle should decrease with increasing distance from the meso-substituent. This is not unequivocal (*cf* the meso-protons), but the chemical shift separations are so small within these groups that the subsequent analysis is not dependent on this assignment.

In the protonated OEP derivatives, the Et groups are more separated, into a 2:1:1 pattern, and the assignment follows similarly, the least affected resonances being assigned to those on pyrrole subunits A and B.

The meso-substituted etioporphyrins (Table 2) were assigned in a similar manner. The meso-OH analogue [i.e. oxophlorin (**10**)] in neutral solution gives a broad unresolved NMR spectrum[8,9] for reasons outlined above. In the free base meso-NH_2-etioporphyrin-I (**1**), although all the resonances are considerably shifted from the parent compound **12** (see later), the separations within the individual groups of resonances are too small to make any definitive assignments, apart from the meso protons in which, by analogy with the OEP derivatives, the separate high-field resonance is assigned to the α-proton.

Both of the protonated etioporphyrin species give sharp well resolved spectra in which, as in the OEP

Table 3. Proton chemical shifts (δ) of meso substituted pyrro-etioporphyrin-XV derivative free bases and dications

		Free Base[a]			Dications[b]		
		H	Me	NMe_2	H	Me	NMe_2
Meso	β,δ	10.135(2)	10.039 10.035	10.056 10.041	10.696 10.691	10.480 10.467	9.059 (δ) 8.969 (β)
	α	10.103	9.855	9.875	10.674	10.341	8.511
β-H-6		9.091	9.325	9.139	9.414	9.228	8.062
β-CH_2	2,4	4.103	4.095	3.987 4.008	4.149	4.084 4.063	3.524 3.484
	7	4.125	3.995	4.210	4.180	3.855	3.200
β-Me	5	3.762	3.722	3.717	3.787	3.630	2.992 (5)
	1,3,8	3.668 3.653 3.625	3.634 3.607 3.572	3.646 3.620 3.559	3.688 3.672(2)	3.599 3.577 3.452	3.088 (1) 3.051 (3) 2.748 (8)
β-$CH_2\underline{CH}_3$	2,4	1.887	1.868	1.857 1.836	1.756	1.712 1.697	1.568 1.556
	7	1.871	1.842	1.688	1.735	1.689	0.805
N-H		-3.79	-3.2[c]	-3.31[c] -3.43[c]	-3.70 -3.81 -3.92 -3.97	-2.99 -3.47 -3.71 -3.97	0.84[c] 0.53[c]
Meso Substit.		10.036	4.661	3.886	10.701	4.730	4.29[c]

Footnotes: [a] In $CDCl_3$ solution, ca. 10^{-2} M; [b] As a but plus 100-200 equivalents of TFA; [c] Broad signals.

spectra, the beta resonances are more separated. It is tempting to assign as previously the least shifted signals to those on subunits A and B, but in view of the larger general substituent effects in these molecules, this can only be a provisional assignment.

The assignment of the peripheral resonances in the pyrro-etioporphyrin-XV (**4**) spectrum (Table 3) follows previous work in assigning the substituents next to the unsubstituted C-6 position (i.e. the γ-methine and C-5 beta methyl)to the low-field resonance within their respective groups.[2] The remaining resonances within the separate groups are too close together for any unambiguous assignment. The assignment of the meso-Me derivative, [γ-phyllo-etioporphyrin-XV (**5**)], follows by comparison, as the entire spectrum is very similar to that of the parent compound; in the meso-NMe_2 derivative **3** an analogous assignment can be made, except that in this case the C-7 ethyl resonance is assigned as the most shifted line (compared with the parent compound **4**).

The assignment of the spectra of the dications of the pyrro- and γ-phylloetioporphyrins **4** and **5**, respectively follow similar considerations; however, that of the -NMe_2 derivative **3** differed appreciably and was considered in greater detail. In this case much larger relative shifts occurred within the substituent group resonances, and this enabled a complete study to be performed on the beta Me signals. By irradiating each of the beta Me signals separately and observing the differential nOes of the methine and C-6 protons it was possible to arrive at an unambiguous assignment of these signals.[16] This is given in Table 3 and will be considered subsequently.

RESULTS AND DISCUSSION

The data recorded in Tables 1–3 may be compared with the less well resolved data from previous investigations using lower applied fields and more concentrated solutions in various solvents. Considering the lower concentrations used here, the data for the neutral meso CHO- (**8**), and CN- (**9**), and Me- (**10**) OEPs (Table 1) are in good agreement with those previously recorded.[2] Interestingly, in all three compounds, only one distinct NH resonance was observed, compared with the two resolved peaks observed here, and predicted by symmetry considerations. Meso NO_2-OEP (**7**) does not appear to have been previously recorded as the neutral molecule, but our data is in complete agreement with that recorded for the zinc(II) derivative (using pyrrolidine to disaggregate the metalloporphyrin).[17]

The chemical shifts for the protonated meso-NO_2- and meso-Me-OEP species (**7** and **10**, respectively) in $CDCl_3$/TFA solution given in Table 1 differ appreciably, where they have been measured, from the results of previous workers using neat TFA as sol-

vent, as we have noted previously. We have evaluated the effect of varying the TFA concentration on the chemical shifts, and within the limits used (*ca* 100–200 equiv of TFA) the solute chemical shifts are all within 0.01–0.02 ppm. However, the early investigations in neat TFA often obtained different δ-values, particularly for the NH protons (which could vary by as much as 0.5 ppm), due perhaps to concentration and possibly exchange effects. The meso-CHO (**8**) and meso-CN (**9**) OEPs have not been recorded previously as the dications.

Our data for the dication and meso-NH_2-etioporphyrin-I (Table 2) differs from that reported for the dication of meso-NH_2-OEP[18,19] in that we do not observe a NH signal at *ca* 1.0δ, but two NH signals at *ca* -0.2δ. Bonnett and Stephenson[18] and Johnson and Oldfield[19] both recorded NH signals in neat TFA at *ca* 1.0 and -0.4δ. In view of the similarity of OEP (**11**) and etioporphyrin-I (**12**) we would only expect, at most, two resolved NH resonances in the dication, and this suggests that the lower field NH signal recorded previously is extraneous.

Substituent chemical shifts (SCS) of meso substituents

Before discussing the SCS in terms of any possible ring current changes, it is convenient to consider the effect of varying the ring currents in the porphyrin on the different protons in the molecule. This may be evaluated very simply from the ring current model of the porphyrin ring presented [3] and parameterized[4-6] in previous Parts of this Series. In this model, the various ring current loops in the macrocycle are replaced by their equivalent dipoles, and the total ring current shift at any point (R) is obtained as the sum of the contributions from the equivalent dipoles, using the standard dipole–dipole equation. This gives eqn (1),

$$\delta_R = \sum_{i=1,8} \mu_{Hi} f(iR) + \sum_{j=1,8} \mu_{Pj} f(jR) \qquad (1)$$

where f(R) depends only on the coordinates of R, and μ_H and μ_P are the values of the equivalent dipoles for the hexagons and pyrrole rings, respectively. A close range approximation was included[5] to extend the calculation to points within the current loop and thus, for our purposes, to include the NH protons. The effective symmetry of the meso substituted porphyrins considered here is such that there are two different sets of pyrrole rings [i.e. (A&B) and (C&D)], and thus the effect of varying the ring current of each of these sets needs to be considered. However, the main macrocyclic ring current can only be considered as one integral path (although, for computational purposes, this is broken down into eight separate loops of current, four above and four below the ring plane), as the electron flow past any of the four meso positions must always be equal.

These factors, when considered in terms of the equivalent dipole formulation of eqn (1), mean that only variations in (a) every μ_H together, (b) pyrrole dipoles A, B and (c) pyrrole dipoles C, D, need to be evaluated, i.e. differentiating eqn (1) with respect to these separate equivalent dipoles gives the chemical shift changes $(\partial\delta/\partial\mu)$ for any given position (R). Using the standard porphyrin geometry given previously[4] these partial differentials may be immediately calculated, and these are given in Table 4 for all the protons on the porphyrin ring. Note that as the geometry of any substituent on rings C and D with respect to the pyrrole equivalent dipoles is merely transposed to that for the same substituents on rings A and B, the calculated shifts for substituents on C-5, 6, 7, 8 are given immediately from Table 4. Note also that the NH differential shifts with respect to both the inner loop (i.e. the hexagons) and the pyrrole rings are obtained from the close range approximation given previously. This has been shown to be a good approximation, even for those compounds (e.g. the chlorins) in which one pyrrole ring has zero equivalent dipole moment.[5,6]

The results in Table 1–3, together with the equiv-

Table 4. Calculated ring current shifts ($\partial\delta/\partial\mu \times 10$) at the porphyrin protons for variation in the equivalent dipoles

		Hexagons	Pyrrole Subunits	
			A,B	C,D
Meso-H	α	1.294	1.056	0.106
	β,δ		0.581	0.581
beta-H	1,4	0.670	1.290	0.153
	2,3		1.350	0.093
beta-Me	1,4	0.408	0.507	0.119
	2,3		0.559	0.067
beta-$CH_2\underline{CH}_3$	1,4	0.231	0.151	0.080
	2,3		0.172	0.052
N-H	A,B	-5.295	-0.418	0.291
	C,D		0.291	-0.418

Table 5. Substituent chemical shifts ($\delta_X - \delta_H$) of meso substituents in the neutral porphyrins

		Calc.[e]	Me[a]	NO_2[a]	CHO[a]	CN[a]	NH_2[b]	Me[c]	NMe_2[c]
Meso	α	-0.24	-0.33	-0.09	-0.20	-0.09	-1.02	-0.15	-0.06
	β,δ		-0.13	0.07	-0.09	0.02	-0.70	-0.10	-0.15
beta-CH_2[d]	1-4,5,8	-0.08	-0.07	-0.05	-0.11	-0.07	-0.28	0.00[f]	-0.10[f]
	6,7		-0.12	-0.41	-0.27	0.20	-0.31	-0.13[f]	0.08[f]
beta-CH_2CH_3	1-4,5,8	-0.05	-0.08	-0.02	-0.07	-0.04	-0.14	-0.02	-0.03
	6,7		-0.12	-0.25	-0.22	-0.02	-0.21	-0.03	-0.18
N-H		1.00	0.87	0.28	1.02	0.85		0.60	0.49
			1.04	0.07	1.06	0.79			0.37
beta-H-6		-0.13						0.24	0.06

Footnotes: [a] In OEP; [b] In etioporphyrin-I; [c] In pyrro-etioporphyrin-XV; [d] Includes β-CH_2 and CH_3; [e] Calculated for a change in μ_H of 1.9 (see text); [f] CH_2's only.

alent data for OEP (**11**),[6] allow the calculation of the SCS of the meso-substituents at the porphyrin protons in both the neutral molecule and the dication. The SCS for the neutral molecules are given in Table 5. In this table we have recorded merely the average SCS of the methyl (and methylene) substituents at positions 1, 2, 3, 4, 5, 8. The individual SCS at these positions are so small that the variations within the group are hardly significant. In contrast, the SCS on the beta-substituents at positions 6 and 7 (adjacent to the meso perturbation) are significantly different, and these are recorded separately. The methyl signals of the beta-ethyl groups have been treated similarly.

Inspection of Table 5 shows that, for the OEP derivatives (i.e. meso-Me-NO_2-, CHO-, CN-) although many of the SCS are small, they present a consistent pattern. The general effect is one of a high-field shift on all the peripheral protons, which decreases with increasing distance from the macrocycle, and a much larger low-field shift of the NH protons. The obvious explanation for this is a decrease in the main macrocyclic ring current upon meso substitution, and this explanation is supported by the fact that, apart from the exceptional substituents at positions 6 and 7, all the beta substituents behave similarly. Thus, there is no specific effect, for example, on pyrrole rings C and D as compared with A and B. Quantifying this explanation, we give also in Table 5 the calculated shifts at the various protons for a change in μ_H of 1.9 units, representing a decrease of *ca* 10% in the main ring current. It can be seen that the calculated shifts are in very good agreement with the observed SCS, especially when it is considered that ring current changes are only one possible mechanism for the SCS.

The meso-Me and meso-NMe_2 derivatives (**5** and **3**, respectively) of pyrroetioporphyrin-XV (**4**), in which the meso substituent is flanked by a beta-ethyl and a beta-proton, behave similarly, except that the SCS are much smaller than in the corresponding OEP analogues. This is clearly observed for the meso-Me derivative, δ-phyllo-etioporphyrin-XV (**5**), in which all the SCS are, to a good approximation, 50% of those for meso-Me-OEP (**6**). This offers some support for the concept of a steric origin of the ring current shifts, at least for the meso-Me group, as the replacement of one beta Et group by hydrogen would considerably reduce the steric strain in the macrocycle. Interestingly, the NMe_2 substituent also shows very small SCS in contrast to the meso-NH_2 substituent (see later). In the proton NMR spectrum of the neutral molecule, the NMe_2 substituent shows no temperature dependence,[16] in contrast to the dication (see later), and our interpretation of these facts is that the NMe_2 substituent is orthogonal to the porphyrin ring and in consequence has no conjugative effect on the macrocyclic π-system. This is clearly demonstrated by comparison of the NMe_2 and meso-NH_2 SCS (Table 5). The meso-NH_2 SCS are considerably larger than those for any other substituent recorded. Unfortunately, the NH protons could not be observed in this molecule, probably due to fast exchange with the meso-NH_2 protons. Even in this case, however, there is no evidence of any difference between rings A and B and rings C and D, and the observed shifts are in very good agreement with those calcu-

lated for a 35% decrease in the main macrocyclic ring current. The increase in the meso-NH_2 SCS would thus appear to be due entirely to conjugation of the amino group with the π-electron system of the macrocycle, which of course will hinder the free flow of the π-electron ring current. This provides quantitative support for the original postulate of Scheer and Katz[2] on the effect of the meso-NH_2 substituent, though it should be noted that it is not necessary to postulate tautomeric imino structures to account for these effects; dipolar resonance contributions are just as effective in breaking the macrocyclic conjugation pathway.

The general effects of meso substitution in the neutral porphyrins considered here are seen to be in good overall agreement with the suggestion of a decrease in the main macrocyclic ring current upon introduction of the substituent. However, there are specific effects which are clearly due to other factors. The most obvious example is the large SCS of the neighboring beta substituents on positions 6 and 7. The data in Table 5 show clearly the additional low-field shifts on the 6,7 methylene protons in the meso-NO_2 and meso-CHO-OEPs [(**7**) and (**8**), respectively], which contrasts with the high field shift of these protons in meso-CN-OEP (**9**). These specific effects have been noted previously and explained in terms of the known magnetic anisotropies of the NO_2, CHO, and CN groups.[2] (In these explanations, the meso-NO_2 and meso-CHO groups are considered to be perpendicular to the porphyrin ring plane). In accord with this explanation, the meso-Me and -NH_2 groups, which are much less anisotropic, show much smaller *specific* effects at the 6 and 7 positions. Interestingly, the introduction of the meso-Me group into pyrro-etioporphyrin-XV (**4**) (to give γ-phyllo-etioporphyrin-XV **5**) causes a *downfield* shift of the C-6 beta proton, in contrast to the upfield shifts observed at the C-6,7 methylenes in **5** and **6**. This low-field shift is in the correct direction for a steric (van der Waals) shift, which is not unexpected. However, the meso-Me/beta-Me steric interaction is far larger than the meso-Me/beta-H one, and one may therefore have expected larger low-field shifts in this case. The relative orientations of the interacting C–H bonds are very different in the two cases, and in C-13 NMR, steric shifts in both directions have been documented.[20]

The other specific effect is the high-field shift of the α-meso proton (opposite the meso substituent) compared with the β- and δ-meso protons. This was noted previously for the meso-Me group in porphyrin dications[21] and was explained in terms of a possible deformation of the macrocycle. The dication system will be considered subsequently, but the results in Table 5 show that the effect is both general for all meso substituents (except NMe_2) and also that the SCS of the α-meso proton agrees just as well with the calculated ring current shifts as those of the β, δ-protons. Thus, the reasons for the difference in the α-meso and β, δ-meso SCS may well be a combination of ring current and long-range electronic effects.

The corresponding SCS for the the meso substituents in the porphyrin dication are given in Table 6. The data here compare reasonably well with the data in pure TFA. For meso-Me-octamethylporphyrin, the α, β and NH SCS in pure TFA are -0.50, -0.36, 1.3 and 0.5 ppm,[21] all somewhat less than the data for meso-Me-OEP (**6**) in Table 6. For meso-NO_2-OEP (**7**), the corresponding values are -0.22, -0.13, 1.5, 1.0 ppm,[2] in quite good agreement with our data, considering the possible concentration shifts in these much more concentrated solutions.

More interestingly, the SCS for the OEP derivatives are seen to be much larger in general than the corresponding values for the neutral molecules. The large meso-Me SCS is particularly significant inasmuch as the Me SCS is very likely the result of steric interactions, and this suggests that steric effects are more important in the dication than in the neutral molecule. This is entirely reasonable in that protonation already causes a considerable increase in steric strain in the macrocycle. Furthermore, in the dications, in direct contrast to the neutral molecules, there is now a pronounced asymmetry of the SCS at the pyrrole subunits. The SCS on the beta substituents on pyrrole rings A and B differ markedly from those on rings C and D, even when the anisotropic effects of the meso substituents on the nearest neighbors is removed. A rough measure of the direct anisotropic shift is the difference in the SCS at positions 6, 7 and 5, 8. Inspection of Table 5 and 6 shows that this difference is almost identical for the neutral molecules and dications for the meso-Me- and meso-NO_2-OEP [(**6**) and (**7**), respectively], whilst for the CHO group the anisotropy is much more pronounced in the dication and for the CN group it is considerably decreased. These specific effects will be considered subsequently. The differential shifts between the substituents on rings A and B and those on C and D are most simply explained in terms of a decreased mobility of the π-electron ring current of pyrrole rings C and D, leading to a decrease in the effective equivalent dipole. In the light of the probable occurrence of steric strain in the macrocycle, some deformation of the porphyrin around rings C and D may well be expected, and on this basis it would be anticipated that pyrrole rings A and B would be essentially unperturbed by the meso substituent. Following this criterion, we give in Table 6 the calculated ring current shifts for a change in the equivalent dipoles of both the hexagons and pyrrole rings C and D representing a *ca* 16% decrease in the main macrocyclic ring current and a *ca* 12% decrease in the ring current of rings C and D. Comparison of these calculated shifts with those observed for the meso substituted OEPs shows at least the correct pattern of SCS. It would hardly be expected that merely one mechanism would explain these SCS, as not only specific anisotropic shifts, but also charge differences, solvation, and direct steric effects could all be contributing to the observed SCS.

The results for the meso-NH_2 and meso-OH substituents in the etioporphyrins are particularly striking, as the SCS clearly reflect, as in the neutral meso-NH_2-etioporphyrin-I (**1**), the restraints on the macrocyclic ring current due to conjugation with the meso substituent. In the case of the meso-NH_2 dication, the SCS are twice those of the neutral molecule and they are in reasonable overall agreement with those calculated for a decrease of 40% in the macrocyclic ring current. The calculated shifts are -1.04, -0.32, -0.18, and 4.2 ppm for the meso, beta-Me, beta-Et, and NH protons, respectively.

Table 6. Substituent chemical shifts ($\delta_X - \delta_H$) of meso substituents in porphyrin dications

		Calc.[e]	Me[a]	NO_2[a]	CHO[a]	CN[a]	NH_2[b]	OH[b]	Me[c]	NMe_2[c]
Meso	α	-0.41	-0.70	-0.29	-0.40	-0.25	-2.00	-0.93	-0.33	-2.16
	β,δ	-0.50	-0.56	-0.21	-0.35	-0.24	-1.51	-0.63	-0.21	-1.69
β-CH_2	1-4	-0.15	-0.23	-0.16	-0.20	-0.19	-0.56(-0.53)[d]	-0.24(-0.22)[d]	-0.08(-0.10)[d]	-0.65(-0.61)[d]
	5,8	-0.22	-0.38	-0.26	-0.35	-0.16	-0.59(-0.62)	-0.31(-0.28)	(-0.21)	(-0.88)
	6,7	-0.23	-0.41	-0.63	-0.73	-0.09	-0.78(-0.76)	-0.40(-0.36)	-0.32	-0.98
β-$CH_2\underline{CH}_3$	1-4	-0.08	-0.11	-0.11	-0.14	-0.12	-0.16	-0.07	-0.05	-0.20
	5,8	-0.10	-0.27	-0.23	-0.30	-0.14	-0.20	-0.19		
	6,7	-0.11	-0.36	-0.41	-0.44	-0.21	-0.35	-0.25	-0.15	-0.93
N-H	C,D	1.7	1.7	1.6	2.1	1.8	4.2	2.3, 2.1	0.7, 0.3	3.0
	A,B	1.5	0.8	1.2	1.3	1.4	4.1	1.4, 1.2	0.2, 0.0	3.4
β-H-6		-0.47							-0.19	-1.35

Footnotes: [a] In OEP; [b] In etioporphyrin-I; [c] In pyrroetioporphyrin-XV; [d] beta-CH_3 in parentheses;

[e] For $\Delta\mu_H$ 3.0, $\Delta\mu_p$(C,D) 2.0, $\Delta\mu_p$(A,B) 0.0

There are, as expected, some significant deviations (e.g. the meso-proton), which will be considered subsequently.

In the meso-OH-etioporphyrin-I (**10**), the results demonstrate very clearly the lower propensity of the meso-OH compared with the meso-NH_2 group to conjugate with the porphyrin ring. The observed SCS are essentially identical with those of the meso-NH_2 group in the neutral porphyrin (Table 5), and a precisely analogous explanation follows. It is further support for the ring current explanation that in this case the NH protons can be observed clearly in acid solution and their SCS agree very well with those predicted. The meso-OH group in the porphyrin dication is thus very clearly demonstrated to be a conjugated OH group and not a keto (oxophlorin) type of system, as was likewise concluded by Jackson *et al.*[8] in their early studies on these molecules. This study reinforces all of their structural conclusions, as well as quantifying the influence of the meso-OH group.

The pyrro-etioporphyrins studied are also of some interest. The meso-Me group in the dication has much less effect than in the OEP series, exactly as was found for the neutral porphyrins and presumably for precisely similar reasons. Note however that the beta-C-6 proton SCS is now negative, in agreement with the prediction for a decrease in the ring current, rather than positive as in the neutral molecule. The observed SCS are clearly a combination of ring current and steric effects which alter relative to each other in the two cases.

The NMe_2 substituent in this series is of particular interest. Inspection of Table 6 shows immediately that the NMe_2 group in the dication, in complete contrast to the neutral molecule, has very large SCS, comparable in all respects with those of the meso-NH_2 group. Clearly, therefore, the NMe_2 group is now conjugating efficiently with the porphyrin, and this can only occur if the NMe_2 group is planar, or nearly so, with the porphyrin maçrocycle. This conclusion has considerable support from the results of variable temperature measurements on the proton NMR spectrum, which will be detailed in full elsewhere.[16] To summarize, the signals of the NMe_2 group, which are a broad band at room temperature, resolve into two sharp signals (T_c approx. 15°, $\Delta G \neq 13.6$ kcal/mole). The observation of two non-equivalent Me groups can only be consistent with a planar (or nearly so) system, and the observed barrier to rotation is entirely consistent with that for a partial C:N double bond (e.g. dimethylacetamide, $\Delta G \neq$ 17.5 kcal/mole[22]), especially when one considers that the planar (ground) state has greater steric interactions and will therefore be raised in energy compared with the transition state, hence lowering the observed barrier height.

There is some evidence for this additional steric interaction in the NMe_2 case, compared with meso-NH_2-etioporphyrin-I (**1**) in that the SCS of the beta substituents (excluding C-7) are more asymmetric than those for the meso-NH_2 case. In view of the presence of other possible shift mechanisms in this very crowded system, further calculations were not deemed necessary. However, the very large SCS of the C-7 beta Me (-0.93 ppm) is strong support for the existence of extra steric interactions. Such a large SCS is unlikely to arise from electronic effects or the anisotropy of the NMe_2 substituent, and any positive charge on the NMe_2 group would produce a low-field shift, contrary to that observed. The observed SCS has an obvious explanation as steric interactions with the "effectively planar" NMe_2 group may well force the C-7 Et group to be orthogonal to the porphyrin plane. In this orientation the Me protons could experience an upfield ring current shift, as is observed.

Thus, the general trends of the meso SCS in porphyrin dications as well as the neutral molecules are consistent with changes in the various current loops. There are, however, a number of specific factors which do not fit into this generalization and are worthy of note. The obvious one is the high-field shift of the α-meso-proton compared with the β,δ-meso protons. On a ring current basis, decreasing the macrocyclic ring currents affects all the meso protons equally, and any decrease in the ring current of pyrrole subunits C and D will only serve to move the β,δ-protons to high field of the α-proton, the reverse of the observed shifts. It has been suggested previously[21] that in the case of the meso-Me substituent, deformations of the macrocycle could cause this high field shift, i.e. buckling along the α, δ-axis, and certainly this is one possible method for relieving the steric interactions at the meso substituent. In the absence of a definitive crystal study of the dication, such an hypothesis cannot be confirmed or disproved.

The results in Table 6 do suggest an alternative possibility. The shift difference between the α- and β,δ-meso protons is very dependent upon the nature of the meso substituent. The shift difference is in the order $CN \approx NO_2 \approx CHO < Me < OH < NH_2 \approx NMe_2$. This is precisely the order expected for an electronic resonance effect at the α- (i.e. "para") position, and there is a rough correlation between this shift difference and the Hammett σ_p value of the substituent. One would not expect any more than a rough correlation in this complex system, but this is suggestive of a direct electronic effect of the substituent at the α-meso position. Certainly, the increased nucleophilicity at the α-position compared with β,δ is well documented in these systems. In both the meso-NH_2 and meso-OH (oxophlorin) compounds, ^1H–^2H exchange occurs rapidly in acid solution at the position opposite the meso-substituent,[2] but this might also be related to the stability of the intermediate phlorin dication.[8] Indeed, this raised an alternative description of both the observed reduction in ring current in these molecules and the high field shift of the α-proton. Any protonation at the α-position would block the macrocyclic ring current and shift the α-proton upfield. If the resulting phlorin dication was in fast exchange with the porphyrin dication, the observed spectrum could result. However, the meso-NH_2-etioporphyrin-I (**1**) in neutral solution shows this decrease in the macrocyclic ring current, and a considerably shifted α-meso proton, and it is not likely that any significant protonation is occurring in this case.

Acknowledgements—We thank the National Science Foundation (CHE-81-20891), the National Institutes of Health (HL 22252), and the Scientific Affairs Division of N.A.T.O. (RG 256.80) for generous support of this research.

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