Metalation Shifts in the Nuclear Magnetic Resonance Spectra of ' Capped ' Porphyrins

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The ' capped ' porphyrins CP2, CP3, and their zinc derivatives were studied by ^{1}H n.m.r. spectroscopy. An examination of the changes in the chemical shifts of the capped porphyrin resonances on binding zinc in various solvents indicates that for CP2 the structure of the free-base and zinc porphyrins are similar to one another with a cavity size similar to that observed in the crystal. The spin–spin coupling constants of the aliphatic chain resonances together with the observation of only four resonances shows that dynamic processes are present for both CP2 and CP3. The metalation shifts observed for CP3 demonstrate the greater flexibility of the molecule and in particular the variable cavity size. Additionally the zinc in ZnCP3 is shown to co-ordinate DMSO with the DMSO binding from the cavity side. A consequence of the difference in behaviour of CP2 and CP3 with respect to solvents and metalation is that the interpretation of the differences in dioxygen binding of the iron(II) capped porphyrins is made complex.

Metal ' capped ' porphyrins (MCP) have been prepared by Baldwin and his co-workers [1,2] to act as synthetic oxygen carriers. Two of the capped porphyrins, CP2 and CP3, both of which are *ortho*-substituted tetraphenylporphyrins, are shown in Figure 1. A crystal structure has been reported for CP2 at −150 °C.[3] The base ligation and oxygenation equilibria of the iron(II)- and cobalt(II)-substituted capped porphyrins have been studied [4–6] with a view to investigate the factors which influence the binding of dioxygen in myoglobin and haemoglobin. It was found that the capped porphyrins had a rather low O_2 affinity and that Fe^{II}CP3 had a lower affinity that Fe^{II}CP2. In view of the latter result, which appears to rule out steric interactions between the bound dioxygen and the porphyrin cap, the lower O_2 affinity was attributed to an enhancement of conformational strain energy in MCP(B) upon oxygenation to MCP(B)(O_2). However, on studying the capped porphyrins by n.m.r. we have observed a considerable solvent dependence in the spectra of the free-base and metal-substituted porphyrins. This suggested that solvation may play an important part in determining the O_2 affinities of Fe^{II}CP2 and Fe^{II}CP3. Furthermore, as we show below any simple interpretation of the solution behaviour of the capped porphyrins in terms of the low temperature crystal structure is not justified.

As both Fe^{III}CP2 and Fe^{III}CP3 are paramagnetic and the presence of a paramagnetic shift would greatly complicate an interpretation of a metalation shift we studied the zinc complexes. We thus report the effect of the binding of zinc on the n.m.r. spectra of the capped porphyrins CP2 and CP3 in different solvents and as a function of temperature.

Experimental

The free-base and zinc-substituted porphyrins were prepared following the procedures published by Baldwin and his co-workers.[1]

The deuteriated solvents were obtained from Merck, Sharp and Dohme Ltd. and used directly. Neat non-deuteriated DMSO was used in the titration of ZnCP3 in [^{2}H]chloroform obtained from B.D.H. Ltd.

Ca. 0.005M solutions of the porphyrin were prepared in the appropriate fully deuteriated solvent, [^{2}H]chloroform, [$^2H_6$]-DMSO, [$^2H_6$]benzene, and [$^2H_8$]toluene. Tetramethylsilane and 1,4-dioxan were used as internal n.m.r. standards. A concentration dependence of CP2 in [^{2}H]chloroform was carried out by preparing six solutions covering the concentration range 0.0025—0.08M. ^{1}H N.m.r. spectra were measured at 270, 300, and 470 MHz. 270 and 300 MHz spectra were obtained with Bruker spectrometers with Oxford Instruments Company superconducting magnets. The 270 MHz spectrometer was interfaced with a Nicolet 1180 computer and a 293B pulse controller and the 300 MHz spectrometer used an Aspect 2000 computer system. The 470 MHz spectra were acquired on a spectrometer developed in the Department of Biochemistry, Oxford University, using an Oxford Instruments Company superconducting magnet with a Nicolet 1180 computer and a 293A pulse controller.

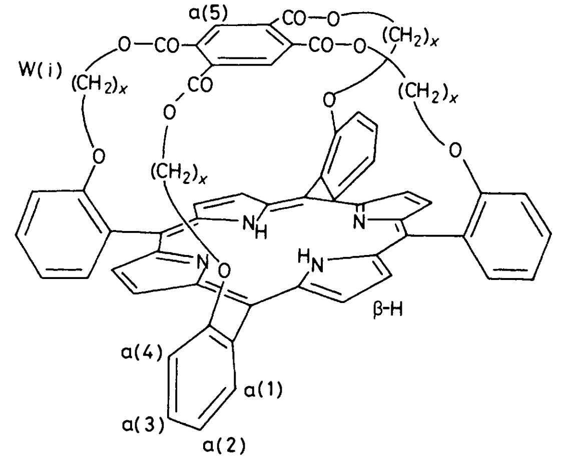

Figure 1. Capped porphyrin molecules and labelling scheme: (a) CP2, $x = 2$; (b) CP3, $x = 3$. In refs. 1—6 the abbreviations H_2Cap and H_2HmCap were used for CP2 and CP3, respectively

Most spectra were accumulated using 8 K data points over a spectral width of 14 p.p.m. collecting 100 transients. The coupling constants were measured from spectra using 32 K data points giving a digital resolution of 0.26 Hz/point.

Results

The ^{1}H n.m.r. spectra of the free-base porphyrins CP2 and CP3 in [^{2}H]chloroform at 300 K are shown in Figures 2 and 3,

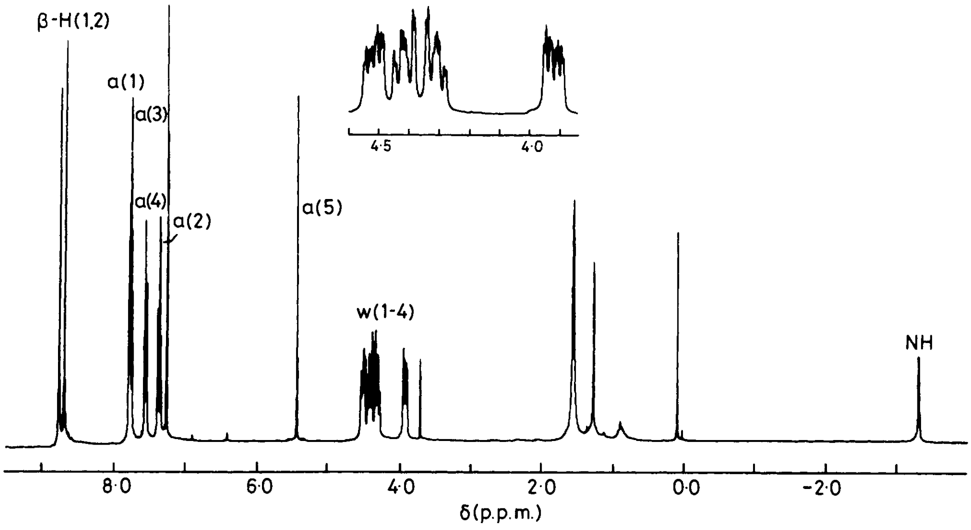

Figure 2. 300 MHz ^1H N.m.r. spectrum of CP2 (0.005M in $CDCl_3$) at 27 °C indicating the resonance assignments

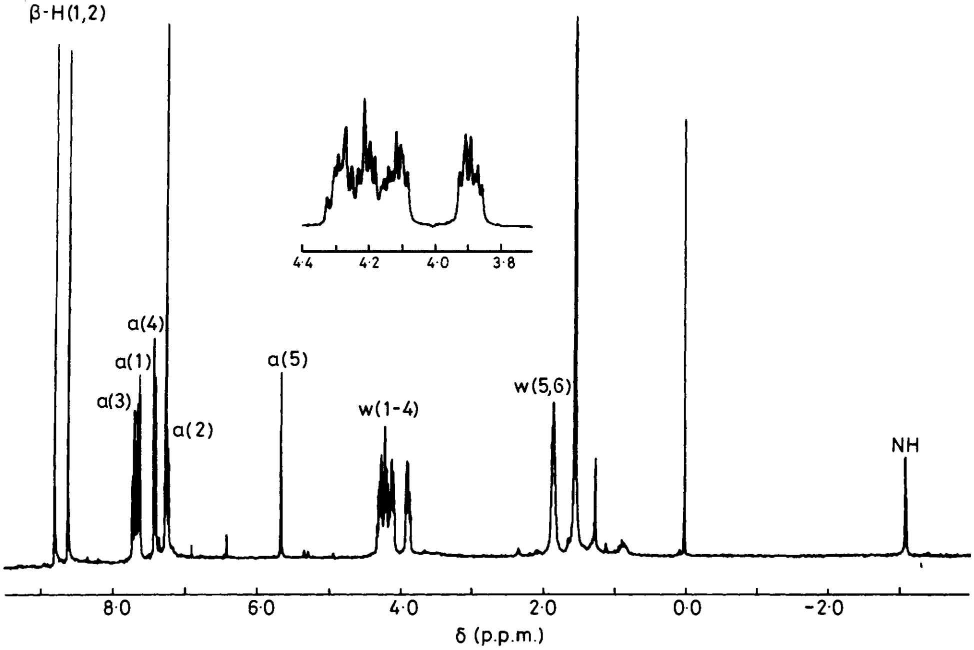

Figure 3. 300 MHz ^1H N.m.r. spectrum of CP3 (0.005M in $CDCl_3$) at 27 °C indicating the resonance assignments

respectively. The resonance assignments shown in the spectra refer to the labelling of the protons in Figure 1 and will be outlined below. The solvent dependence of the chemical shifts of the resonances in the spectra of CP2 and ZnCP2 is shown in Table 1, and those of CP3 and ZnCP3 in Table 2. The aliphatic coupling constants for CP2 and ZnCP2 in the different solvents are listed in Table 3. The shifts found in the titration of ZnCP3 in [^{2}H]chloroform with DMSO are shown in Table 4.

Discussion

Assignment of Spectra.—A necessary preliminary is the assignment of the observed resonances to particular protons in the capped porphyrins. This will only be given in detail for CP2. To a large extent the assignments are based on a comparison with tetraphenylporphyrin (H_2TPP). Thus we can assign the two furthest downfield resonances to the eight pyrrolic β-H and the most upfield resonance to the two NH protons. The latter assignment is confirmed by the absence of this resonance in the zinc-substituted porphyrin. The observation of two β-H resonances indicate that the lowering of the porphyrin symmetry from D_{4h} to C_{2v} brought about by the capping benzenoid ring is reflected in the porphyrin plane. We could not assign β-H(1) and β-H(2) to specific sets of protons. The spin connectivity in the aromatic region was deduced from J decoupling experiments and so to complete the aromatic assignment it is only necessary to assign one of the doublets to either a(1) or a(4). This was done by comparison with H_2TPP. The proton a(1) is *meta* to the ether substituent and its chemical shift will consequently be only slightly perturbed from that observed in H_2TPP while a(4) as it is *ortho* will experience a large upfield shift. In H_2TPP the phenyl proton *ortho* to the porphyrin lies at δ 8.30 while the *meta* proton lies at δ 7.80; [7]

Table 1. Observed chemical shifts for CP2 and ZnCP2

	$CDCl_3$			C_6D_6			$C_6D_5CD_3$			[$^2H_6$]DMSO		
Proton	CP2	ZnCP2	Δ	CP2	ZnCP2	Δ	CP2	ZnCP2	Δ	CP2	ZnCP2	Δ
β-H(1)	8.78	8.88	0.10	8.89	9.03	0.14	8.77	8.92	0.15	8.67	8.59	−0.08
β-H(2)	8.71	8.84	0.13	8.85	9.00	0.15	8.76	8.91	0.15	8.61	8.55	−0 06
a(1)	7.80	7.80	0.00	7.77	7.92	0.15	7.73	7.89	0.16	7.77	7.71	−0 06
a(2)	7.38	7.38	0.00	7.13	7.20	0.07	7.14	7.21	0.07	7.42	7.36	−0 06
a(3)	7.77	7.80	0.03	7.47	7.51	0.04	7.49	7.53	0.04	7.85	7.79	−0.06
a(4)	7.55	7.56	0.01	7.04	7.08	0.04		7.11		7.74	7.68	−0.06
a(5)	5.46	5.42	−0.04	5.82	5.73	−0.09	5.72	5.70	−0.02	5.55	5.52	−0.03
w(1)	4.52	4.52	0.00	3.97	3.99	0.02	3.98	3.99	0.01	4.46	4.42	−0.04
w(2)	4.44	4.42	−0.02	4.15	4.15	0.00	4.11	4.10	−0.01	4.17	4.13	−0.04
w(3)	4.31	4.31	0.00	3.62	3.64	0.02	3.68	3.70	0.02	4.31	4.27	−0.04
w(4)	3.92	3.91	−0.01	3.42	3.39	−0.03	3.43	3.45	0.02	3.91	3.90	−0.01
NH	−3.32			−2.73			−2.89			−3.38		

Table 2. Observed chemical shifts for CP3 and ZnCP3

	$CDCl_3$			C_6D_6			$C_6D_5CD_3$			[$^2H_6$]DMSO		
Proton	CP3	ZnCP3	Δ	CP3	ZnCP3	Δ	CP3	ZnCP3	Δ	CP3	ZnCP3	Δ
β-H(1)	8.80	8.93	0.13	8.87	8.98	0.11	8.89	8.89	0.00	8.68	8.57	−0.11
β-H(2)	8.61	8.74	0.13	8.75	8.93	0.18	8.58	8.81	0.23	8.55	8.50	−0.05
a(1)	7.63	7.61	−0.02	7.88	8.22	0.34	7.47	8.07	0.60	7.67	8.20	0.53
a(2)	7.25	7.23	−0.02	7.12	7.22	0.10				7.30	7.42	0 12
a(3)	7.69	7.70	0.01	7.50	7.53	0.03	7.48	7.56	0.08	7.76	7.75	−0.01
a(4)	7.41	7.44	0.03	6.91	6.83	−0.08				7.55	7.38	−0.17
a(5)	5.67	5.49	−0.18	6.22	6.43	0.21	5.64	6.13	0.49	5.61	7.12	1.51
w(1)	4.29	4.32	0.03	3.70			3.95	3.69	−0.26	4.24	3.83	−0.14
w(2)	4.12	4.11	−0.01	3.68			3.83		−0.14	4.00	3.70	−0.30
w(3)	4.20	4.27	0.07	3.69					−0.14	4.14		−0.44
w(4)	3.89	3.83	−0.06	3.60				3.55	−0.28	3.81	3.48	−0.33
w(5)	1.84	1.92	0.08	1.48	1.42	−0.06	1.62	1.54	−0.08	1.66	1.57	−0.09
w(6)		1.84	0.00	1.31	1.21	−0.10	1.43	1.36	−0.07		1.06	−0.60
NH	−3.11			−3.15			−2.80			−3.23		

Table 3. Coupling constants for CP2 and ZnCP2 [a]

Coupling constant [b]	$CDCl_3$		C_6D_6		$C_6D_5CD_3$		[$^2H_6$]DMSO	
	CP2	ZnCP2	CP2	ZnCP2	CP2	ZnCP2	CP2	ZnCP2
J_{12}	2.2	2.2	2.5	2.5	2.6	2.5	11.8	11.5
J_{13}	11.1	11.1	7.4	7.4	7.3	7.4	2.6	2.4
J_{14}	5.6	5.6	12.0	11.8	11.7	11.7	5.1	5.2
J_{23}	7.2	7.2	11.5	11.3	11.3	11.3	7.6	7.6
J_{24}	11.7	11.7	5.6	5.6	5.6	5.6	2.3	2.4
J_{34}	2.1	2.1	2.3	2.6	2.3	2.2	11.9	11.9

[a] Coupling constants in Hz, ±0.26 Hz. [b] J_{ij} where i and j are the sequential number of the resonance.

Table 4. ZnCP3–DMSO Titration shifts

10^3 [DMSO]/	Resonance shifts δ_{obs} [a]					
	a(1)	a(5)	w(3)	w(4)	w(5)	w(6)
58.3	0.165	0.57			0.065	0.145
116.6	0.230	0.73	0.260	0.135	0.065	0.225
174.9	0.255	0.81	0.310	0.170	0.085	0.260
250.0	0.295	0.92	0.355	0.220	0.095	0.315
437.5	0.325	1.03	0.375	0.265	0.105	0.390

[a] Shifts in p.p.m.

consequently we can unambiguously assign the low-field doublet to a(1). The rest of the aromatic assignments then follow from the spin connectivity.

A complete assignment of the aliphatic protons was not possible. The geminal protons could be identified on the basis of their strong positive NOE and large coupling constant, *J* 11 Hz. The NOE experiments also indicate that w(1) and w(3) are at the end of the chain adjacent to the ether bond since we observed a positive NOE between w(3) and a(4). Furthermore, the assignment of w(2) and w(4) to the methylene group close to the ester group is supported by the NOE between w(4) and a(5). It should be noted that the ordering of the aliphatic resonances is solvent dependent so that the above assignment is only valid in [^{2}H]chloroform. In the other solvents we assumed that the most upfield resonance is always from the proton w(4) (thereby minimising solvent shifts, a point which does not affect the discussion on metalation shifts) and then used the coupling constants to obtain the geminal pairs. The resonance labelled a(5) is assigned to the cap-proton on the basis of its chemical shift and integrated intensity. A similar procedure was used to assign the spectra of the other free-base and zinc-substituted porphyrins. For CP3 and ZnCP3 the geminal aliphatic protons could be clearly identified from the multiplet structure seen on decoupling the central methylene protons w(5) and w(6). The complex multiplet structure associated with the aliphatic region in CP3 prevented the measurement of the vicinal coupling constants except in [^{2}H]chloroform.

Concentration Dependence.—A major problem when studying porphyrins by n.m.r. is their tendency to aggregate and thus give intermolecular ring-current shifts. Consequently it is necessary to obtain the concentration dependence of the spectrum and it is often necessary to derive the chemical shifts at infinite dilution.[7] Aggregation is less likely to be important in the capped porphyrin solutions because of the steric restrictions to π–π interactions. Nevertheless it was shown that there was only a very small concentration dependence of the spectrum of CP2 in [^{2}H]chloroform over the range 0.0025—0.08M. Thus the largest shift observed was on the cap proton, a(5), which moved downfield by 0.04 p.p.m. In view of the small concentration dependence we shall compare the chemical shifts without recourse to extrapolation to infinite dilution.

Marker Resonances.—Certain of the resonances provide a useful monitor of the porphyrin structure. A particularly sensitive marker of the conformation is the upfield shifted capping benzenoid proton, a(5). Its ring-current shift from the porphyrin, as estimated using Abrahams 16-dipole method [8] with dipole magnitudes μ_P 20.0 and μ_H 23.0 Å^3, will vary in magnitude by ± 0.1 p.p.m. for a ∓ 0.1 Å change in the cap–porphyrin plane distance. It would be useful to interpret the absolute magnitude of the secondary shift on this proton. We define the secondary shift on a(5) as the difference in the chemical shift of this proton in the tetra-aldehyde precursor (δ 8.03 [1]) and in the capped porphyrin, giving a secondary shift of 2.57 p.p.m. for CP2 in [^{2}H]chloroform. However, such an analysis is complicated by the presence of two carbonyl groups *ortho* to a(5) in the cap ring the orientations of which with respect to the cap proton are unknown. Using the crystal structure we can make an approximate calculation to establish whether the observed upfield shift in a(5) is consistent with the cap–porphyrin separation of *ca.* 4.0 Å observed in the crystal. The phenyl substituents give a maximum ring-current shift of -0.25 p.p.m. estimated using Haigh and Mallion's shielding tables.[9] The magnetic anisotropy [10] and electric-field shifts [10] from the carbonyl groups tend to cancel one another when the carbonyl groups are in the crystal conformation of one perpendicular to the cap plane and the other coplanar but pointing away from the proton. A significant downfield shift due to the carbonyl groups could only arise if they were rotated towards coplanarity pointing towards the proton. Taking the carbonyl and phenyl shifts into account the secondary shift due to the porphyrin ring-current is 2.82 p.p.m. corresponding to a cap–porphyrin separation of *ca.* 4.3 Å. The quantitative effect of deviations form planarity of the porphyrin plane on its ring-current are not known [7] though the decrease in symmetry will reduce its magnitude. A 10% reduction in the ring-current would reduce the cap–porphyrin separation to *ca.* 4.1 Å. Therefore the observed secondary shift on a(5) does appear consistent with the cap–porphyrin separation observed in the crystal.

Another useful marker is the proton a(1) the chemical shift of which is sensitive to the rotation of the phenyl substituent as this alters the ring-current it receives from the porphyrin. In CP2 in [^{2}H]chloroform a(1) lies at δ 7.80 which is significantly upfield of the shift found for the *ortho* proton in H_2TPP. Three factors contribute to this: (i) the small *meta*-substituent effect of the ether substituent, (ii) a reduction in the porphyrin ring current, and (iii) the reduced freedom of the phenyl groups' torsional oscillations. The last factor arises because rotation of the phenyl group towards co-planarity with the porphyrin increases the downfield shift.

The β-H non-equivalence, although of potential use because of its variation from system to system, was not found to be amenable to a consistent interpretation.

Metalation Shifts in CP2.—A comparison of the chemical shifts observed in CP2 and ZnCP2 shown in Table 1 indicates that in [^{2}H]chloroform and [^{2}H$_6$]DMSO only minor perturbations occur in the spectrum on binding the zinc, suggesting very similar structures. Somewhat larger changes in chemical shifts are observed in the aromatic solvents for the pyrrolic and aromatic hydrogens though the aliphatic protons again show only small shifts. We shall not attempt a comparison between the spectra in the aromatic and non-aromatic solvents in view of the significant shifts caused by aromatic solvents. However, it is of note that large changes in shifts are observed on almost all the resonances, the least affected being a(1), β-H(1), β-H(2), and a(2) where the shifts are less than 0.2 p.p.m.

The general trend of the metalation shifts, except in [^{2}H$_6$]-DMSO, is in the direction of increasing porphyrin ring-current. On binding a metal the porphyrin ring-current will be affected by (i) a change in the porphyrin π-electron density depending on the electronic characteristics of the metal and (ii) the enhancement of the porphyrin symmetry.[7] The symmetry enhancement increases the ring-current while the zinc, as it is a σ-acceptor, will lead to a decrease in the ring-current by indirectly reducing the π electron density. Normally zinc-substituted porphyrins have a reduced ring-current shift.[7] Thus, relative to a ' flat ' porphyrin such as porphin where the β-Hs shift upfield by 0.2 p.p.m.,[11] on binding zinc CP2 undergoes a greater symmetry enhancement leading to a β-H downfield shift of *ca.* 0.1 p.p.m.

On the other hand the shifts in [^{2}H$_6$]DMSO are inconsistent with this simple view. Thus if we attribute changes only to a change in the ring-current then the β-H shift indicates a decrease in the ring-current and the shift on a(5) an increase. This shows that additional affects are present namely a possible conformation change or change in solvation on binding zinc. The similarity in chemical shifts for CP2 and ZnCP2 in [^{2}H]chloroform and [^{2}H$_8$]toluene suggests that conformational changes are not important. Hence the reason ZnCP2 in [^{2}H$_6$]DMSO is anomalous is because of co-ordination between the zinc and [^{2}H$_6$]DMSO. This illustrates the problem of studying the capped porphyrins, namely the dependence of their behaviour on the solvent. The larger shifts noted above on the aromatic protons in the aromatic solvents could thus arise from a differential aromatic solvent induced shift, ASIS. Though whether this is caused by the binding of the zinc altering the conformation and thus the solvation or by the nature of the solvation changing the way in which the zinc binds it is not possible to say. Yet, in spite of the problems of interpreting the small metalation shifts which is due partly to the very fact they are small, the general impression to be gained from the metalation shifts in CP2 is that little conformational change occurs on binding zinc.

Metalation Changes in Coupling Constants.—The four aliphatic protons of CP2 and ZnCP2 form an AMPX spin system. The coupling constants in each solvent are shown in Table 2. Within experimental error, principally the digital resolution, the geminal and vicinal coupling constants are the same in the free-base and zinc substituted porphyrin. An analysis of the vicinal coupling constants using the Karplus

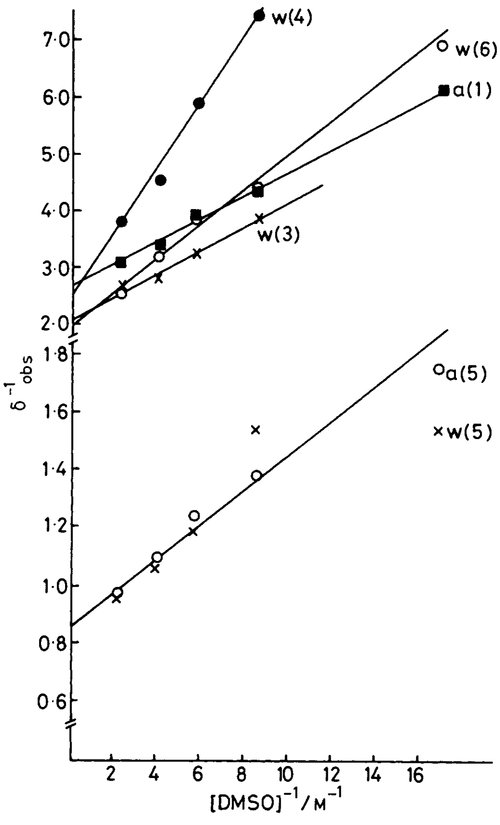

Figure 4. Titration shift plot assuming 1 : 1 complex formation between ZnCP3 and DMSO. δ^{-1} scale times 0.1 for w(5)

equation [12] with J^0, J^{180} 10, and C -0.3 Hz did not give consistent torsional angles. However, as these parameters are appropriate for an unsubstituted ethane fragment and as J^0 and J^{180} are known to be decreased by electronegative substituents [13] smaller values of these constants would be expected for the $-CO_2-CH_2-CH_2-O-$ fragment. In spite of allowing for a reduction in J^0 and J^{180} a consistent conformation still could not be derived. The observed vicinal coupling constants can only represent a single conformation if the constant C is more negative, *e.g.* -1.5 Hz, when J^0 8 and J^{180} 10 Hz. Therefore, although the vicinal coupling constants could be consistent with just one conformation it is unlikely to be the case. The presence of more than one conformer is suggested by the temperature dependence. As the temperature is lowered to -60 °C in [$^2H_8$]toluene broadening of the aliphatic resonances occur while the β-H stay sharp and split. The most likely reason for this is the slowing of the exchange of the aliphatic chain between different conformers. Furthermore even at 93° in [$^2H_6$]DMSO only small shifts are seen in the aliphatic region and it seems unlikely that over such an extended temperature range only one conformer is present. Therefore the vicinal coupling constants represent averaged values precluding the derivation of quantitative conformational information though qualitatively they indicate mobility in the aliphatic chains. The close similarity between the coupling constants in CP2 and ZnCP2 indicates that only small conformational changes can occur on binding zinc. In terms of the crystal structure this is surprising if we consider the zinc to bind from the side opposite the cap since in CP2 doming of the porphyrin towards the cap occurs while in the zinc complex as the zinc will lie *ca.* 0.3 Å out of the porphyrin plane [14] doming in the opposite sense is required. On the other hand if the zinc binds from the cap side then the lack of structural changes is understandable.

Table 5. Fully bound shifts, Δ_b, and equilibrium constants, K, for the ZnCP3–DMSO complex

	Resonance					
	a(1)	a(5)	w(3)	w(4)	w(5)	w(6)
K/mol l^{-1}	13.1	13.2	10.5	3.4	13.1	6.7
Δ_b (p.p.m.)	0.38	1.19	0.48	0.43	0.12	0.50

Solvent Dependence of CP3. Analysis of the Titration Shifts.—The titration of ZnCP3 with DMSO in [^{2}H]chloroform solution was analysed in terms of a 1 : 1 complex for which relationship (1) holds. In this expression Δ_b is the fully bound

$$\delta_{obs}^{-1} = \Delta_b^{-1} + (\Delta_b K[\mathrm{DMSO}])^{-1} \qquad (1)$$

shift and K is the equilibrium constant for the association represented by equation (2). δ_{obs} is the observed shift which

$$\mathrm{ZnCP3} + \mathrm{DMSO} \overset{K}{\rightleftharpoons} \mathrm{ZnCP3(DMSO)} \qquad (2)$$

requires the chemical shift of ZnCP3 in DMSO in the absence of complex formation. This was taken to be the chemical shift of the resonance in CP3 in [$^2H_6$]DMSO, δ_{CP3}^{DMSO}. δ_{obs} is then defined by equation (3). A plot of δ_{obs}^{-1} *versus* [DMSO]$^{-1}$ is

$$\delta_{obs} = \delta_{ZnP3}^{CDCl_3}(\mathrm{DMSO}) - \delta_{CP3}^{DMSO} \qquad (3)$$

shown in Figure 4. The linear nature of the plot supports the assumption of a 1 : 1 complex as do the similar equilibrium constants obtained from the plot. The fully bound shifts, Δ_b, and equilibrium constants, K, obtained are set out in Table 5. It is obvious that some considerable conformation change occurs on binding DMSO.

Metalation Shifts in CP3.—In contrast to CP2 the binding of zinc to CP3 causes significant shifts. The magnitude of these shifts is highly solvent dependent, for example the shift on a(5) is only -0.18 p.p.m. in [^{2}H]chloroform but $+1.51$ p.p.m. in [$^2H_6$]DMSO. A comparison of the metalation shifts in [^{2}H]chloroform for CP3 and CP2 reveals very similar changes so that the behaviour of CP3 seems to resemble that of CP2 in this solvent. On the other hand in [$^2H_6$]benzene, [$^2H_8$]toluene, and [$^2H_6$]DMSO we observe a downfield shift on a(5) in CP3 as opposed to an upfield shift in CP2. In addition, CP3 appears to be more sensitive to solvent shifts than CP2; thus a(1) has a shift of δ 7.88 in [$^2H_6$]benzene but δ 7.47 in [$^2H_8$]toluene. The resonance a(1), corresponding to the *ortho*-proton of the meso-phenyl substituent, has a chemical shift of δ 8.30 in H_2TPP in [^{2}H]chloroform solution. This resonance should be an indicator of the degree to which the phenyl substituent can undergo torsional oscillations since the greater the amplitude of the oscillation the more downfield the resonance will be found. For example, in CP2 in [^{2}H]chloroform a(1) lies at δ 7.80. However, the chemical shift of the resonance a(1) in [$^2H_8$]toluene is abnormally upfield compared with its shift in [$^2H_6$]benzene in which its chemical shift is more normal. The differences in the chemical shifts of the resonances in CP3 in [$^2H_8$]toluene and [$^2H_6$]benzene solutions are quite general ranging from a larger β-H non-equivalence in [$^2H_8$]toluene (0.31 *versus* 0.12 p.p.m.) to 0.58 p.p.m. difference in the chemical shift of a(5). Whatever the cause of these shifts either a different ASIS or a change in structure it is clear that very specific solvation interactions are present in order for the presence of the [$^2H_8$]toluene methyl group to alter the nature of the solution.

Although in general vicinal coupling constants could not be obtained it was possible to derive them from the spectrum of CP3 and ZnCP3 in [^{2}H]chloroform. For CP3 we get J_{35} 7.2, J_{36} 3.8, J_{45} 3.8, and J_{46} 6.2 Hz. These coupling constants are not consistent with a single conformation. Furthermore in ZnCP3 we find J_{35} 7.2, J_{36} 3.0, J_{45} 3.8, and J_{46} 7.2 Hz indicating some change in the average conformation. The supposition that the chemical shifts are an average due to fast exchange between different conformers as implied by the coupling constants is supported by the broadening of the resonances at low temperature (*ca.* −60 °C in [$^2H_8$]toluene) and the absence of a high temperature dependence up to 127 °C in [$^2H_6$]DMSO.

Both the chemical shifts of the resonances and the coupling constants indicate CP3 undergoes a structural change on binding zinc. However, the interpretation of these shifts in terms of different structures is not clear. The shift on a(5) is a sensitive indicator of changes in the cap–porphyrin distance and the striking downfield shift of 1.51 p.p.m. observed in [$^2H_6$]DMSO suggests an increase in the cap–porphyrin distance from *ca.* 4.5 to *ca.* 8 Å. Two points are clear (i) in the free-base the additional methylene unit in CP3 does not lead to a very large increase in the cap–porphyrin distance, 4.1—4.5 Å, and (ii) CP3 exhibits a great deal of flexibility in the cavity size.

In view of the changes observed for ZnCP3 in [$^2H_6$]DMSO we considered that complex formation between metal and DMSO occurs. The results of the titration of ZnCP3 in [^{2}H]-chloroform with DMSO are consistent with the formation of a 1 : 1 complex with K 10 l mol^{-1}. The fully bound shifts do not account for all the metalation shifts in pure DMSO, the residual difference arising from differences in solvation. An inference from the titration results and the downfield shift on a(5) is that a DMSO molecule can enter the cavity between the cap and porphyrin in CP3 and thence bind to the zinc. The solvent accessibility of the metal from the cap side indicated here will necessarily complicate the studies of dioxygen binding as there will be competition between the solvent and dioxygen for entry into the cavity. This observation provides an explanation for the reduced affinity of the iron-substituted capped porphyrins for dioxygen. If the equilibrium represented by equation (4) is present then provided that K_{sol} is not

$$\mathrm{FeCP} + \mathrm{Sol} \xrightleftharpoons{K_{sol}} \mathrm{FeCP(Sol)} \quad (4)$$

entirely negligible the high solvent concentration will cause the removal of FeCP and require a higher partial pressure of oxygen to achieve significant dioxygen binding. Furthermore, the greater flexibility in the cavity size of CP3 allows K_{sol} to be higher for FeCP3 than FeCP2 with a consequent further decrease in oxygen affinity. The entry or partial entry of small molecules into the cavity is supported by the formation of a six-co-ordinate complex FeCP3(1-MeIm)$_2$.[5]

Conclusions.—The free-base and zinc-substituted capped porphyrins were studied in various solvents by n.m.r. Specific solvent effects influence the absolute value of the chemical shift so that comparisons of the chemical shifts between solvents is complicated. However, given this caveat surprising differences were seen for CP3 on changing the solvent from [$^2H_6$]benzene to [$^2H_8$]toluene with the shifts in [$^2H_8$]toluene appearing anomalous. This points to subtle changes in the solvation of the capped porphyrin. The metalation shifts for CP2 were on the whole small and together with the coupling constants and the temperature dependence suggest that binding zinc does not significantly perturb the structure which appears at variance with the doming observed in the crystal structure. On the other hand CP3 shows larger metalation shifts particularly in [$^2H_6$]DMSO in which a specific association between the porphyrin and a DMSO molecule occurs. This association we believe involves the DMSO molecule entering the cavity of the capped porphyrin. The importance of the solvent in determining the magnitude of the metalation shift implies that we must consider the nature of the solvent–porphyrin interaction when interpreting ligation and oxygenation equilibria. The presence of greater conformation strain in the five co-ordinate Fe^{II}CP3 than in Fe^{II}CP2, suggested to explain the lower O$_2$ affinity of Fe^{II}CP3,[6] is not supported by our results since the cap and the connecting aliphatic chain show a considerable flexibility. This flexibility we believe would allow a relaxation in the structure and thus a reduction in conformational strain.

For CP2 and CP3 we have equilibria (5)—(7). The lower

$$\mathrm{Fe^{II}CP2} + \mathrm{B} \xrightleftharpoons{K_B} \mathrm{Fe^{II}CP2(B)} \quad (5)$$

$$\mathrm{Fe^{II}CP3} + \mathrm{B} \xrightleftharpoons{K_B} \mathrm{Fe^{II}CP3(B)} \quad (6)$$

$$\mathrm{Fe^{II}CP3(B)} + \mathrm{B} \xrightleftharpoons{K_B^B} \mathrm{Fe^{II}CP3(B)_2} \quad (7)$$

oxygen affinity of Fe^{II}CP3 relative to Fe^{II}CP2 we attribute to a lowering of the effective concentration of the pentaco-ordinate species by competitive binding of the solvent or ligand.

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