Coordination Chemistry and Geometries of Some 4,4'-Bipyridyl-Capped Porphyrins. Proton- and Ligand-Induced Switching of Conformations

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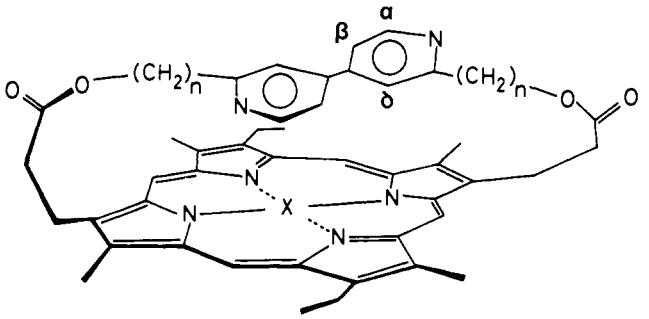
Abstract: The NMR spectra of three 4,4'-bipyridyl-capped porphyrins are analyzed in terms of a previously described ring current model to yield molecular geometries. The compound with the shortest chain connecting porphyrin and cap takes up a distorted conformation, either as a result of π-π interactions or to minimize strain. Protonation of porphyrin and cap yields a similar conformation for all three compounds, with a large separation between the two components. The NMR and UV/visible spectra of the zinc complexes of these porphyrins are strongly dependent on the presence or absence of pyridine. This is a result of competition between strained intramolecular binding and the entropically less favorable, but unstrained, intermolecular binding of the zinc. Detailed geometries are obtained for both states of each molecule, and the strain involved in intramolecular binding is estimated. The criteria to be satisfied for effective molecular switching of conformations are discussed.

Porphyrins which have been "strapped" or "bridged" or "capped" have been the focus of much recent attention as synthetic models of natural processes such as oxygen transport, oxygen activation, and photosynthesis.[1] In principle, one of the attractions of such systems is the enforced proximity of reactive groups in well-defined geometries in solution; in practice, geometries derived from X-ray crystallographic studies are much more common than those derived from solution spectroscopy. For diamagnetic systems this is slightly surprising given the opportunities which are presented by the built-in porphyrin ring current. We present here results which demonstrate the power, and limitations, of the NMR approach in defining solution geometries in this type of molecule.

The Cambridge group has been concerned with optimizing the efficiency of light-induced electron transfer from porphyrin donor to an electron-accepting cap,[2,3] and they wished to develop a means of controlling the relative orientation of the two chromophores within such a molecule. As we have already reported in a preliminary communication,[4] intramolecular coordination between the cap and central metal ion is one possibility for achieving such control. This paper presents more detailed evidence for the nature and geometry of the various species involved. We discuss in some detail the free-base bipyridyl-capped porphyrins, BP*n*, and their zinc complexes, ZnBP*n*, with emphasis on the switchable conformations of the latter. We also briefly describe the corresponding magnesium complexes, MgBP*n*.



BPn : X = H_2 n = 2,3,4

ZnBPn : X = Zn n = 2,3,4

MgBPn : X = Mg n = 3,4

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The solution chemistry of metalloporphyrins is often dominated by the coordination demands of the metal ion. In the absence of basic ligands which can bind axially to the ion, aggregation occurs.[5,6] Traditionally, ligand has been added separately to a porphyrin solution, but it can be covalently attached to the macrocycle and bind intramolecularly.[7,8] For our purpose zinc seemed an attractive possibility because it is, in porphyrins, strictly five coordinate in the presence of excess ligand;[6,9] it follows that if intramolecular binding of the cap to zinc is accompanied by conformational strain, then added external ligand should compete effectively for the metal and release the bound, and strained, cap. By contrast, magnesium can become partly six-coordinated in the presence of excess ligand,[7,8,10] and it is unlikely to provide such a good "switch".

The NMR spectra of the free base and diamagnetic metalloporphyrins are dominated by the large ring current shifts produced by the circulating π-electrons of the porphyrin macrocycle.[5,11] One of us has presented[12-14] and refined a model of the porphyrin ring current which is sufficiently accurate to be capable of providing geometric information on porphyrin–ligand[15] and porphyrin–

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Table I. Observed[a] and Calculated[b] Ring Current Shifts ($\Delta\delta$) of Pyridyl Cap Nuclei in Bipyridyl-Capped Porphyrins

nucleus	BP2	ZnBP2 + pyridine	BP3	ZnBP3	ZnBP3 + pyridine	BP4	ZnBP4	ZnBP4 + pyridine
H_α	2.0 (1.87)	1.6 (1.61)	0.75 (0.84)	2.5 (2.47)	0.6 (0.69)	0.85 (0.78)	3.7 (3.61)	0.8 (0.57)
H_β	4.0 (3.99)	3.1 (3.15)	1.30 (1.28)	1.9 (1.85)	1.1 (1.01)	1.10 (1.17)	1.4 (1.52)	0.7 (0.80)
H_δ	3.0 (2.83)	3.1 (3.16)	2.2 (2.18)	1.7 (1.83)	2.1 (2.11)	1.55 (1.51)	1.3 (1.51)	1.1 (1.12)
C_2	6.2 (2.4)		1.75 (1.54)			1.41 (1.19)		
C_3	2.1 (3.3)		1.80 (2.06)			1.37 (1.53)		
C_4	2.8 (3.8)		2.18 (1.98)			1.32 (1.59)		
C_5	2.2 (4.0)		1.13 (1.53)			1.12 (1.33)		
C_6	2.2 (2.7)		0.76 (1.20)			1.00 (1.05)		

[a] Upfield shifts relative to those in the analogous 4,4'-bipyridyl alcohols, which are for H_α, H_β, H_δ, C_{2-6}, respectively. 2-Carbon chain: 8.65, 7.43, 7.45. 3-Carbon chain: 8.65, 7.42, 7.45, 163.12, 121.12, 146.65, 119.23, 149.85. 4-Carbon chain: 8.65, 7.43, 7.44, 163.65, 120.86, 146.66, 119.18, 150.22. [b] In parentheses.

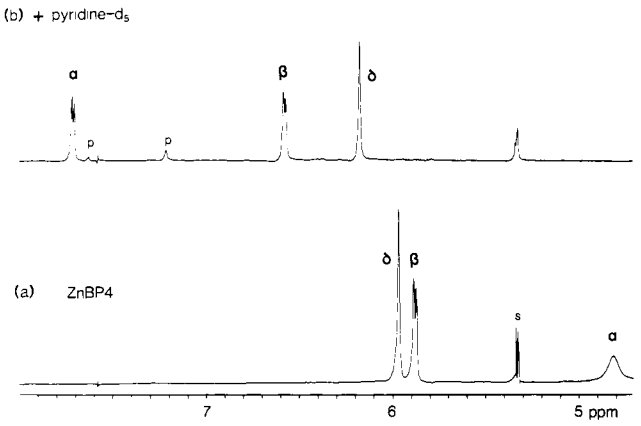

Figure 1. Aromatic region of the 400-MHz ^1H spectrum of ZnBP4 in the presence and absence of pyridine-d_5. S and P mark residual protons in dichloromethane and pyridine.

porphyrin[6] complexes. Recently a similar model for the chlorophyll ring system has been given[16] in which the perturbing effects of both the C-9 keto group and the reduction of ring D were included; this has been applied with some success to the long-standing problem of chlorophyll aggregation.[17] Thus, it is of some interest to attempt to apply this ring current model to the observed shifts of the bipyridyl cap nuclei in the compounds investigated here.

We shall show that within the constraints of the data available to us, application of the ring current model to the observed shifts does both support the conformational hypotheses previously proposed[4] and provide geometrical parameters for the molecular conformations.

Results and Discussion

Spectroscopy and Methodology. The synthesis of the bridged porphyrins has been summarized previously[4] and will be described in detail elsewhere. Proton NMR spectra of these chiral compounds are very complex, containing a large number of signals. In the case of the metalloporphyrins they are also extremely dependent on the presence or absence of external ligands. Figure 1, for example, shows the aromatic bipyridyl region of ZnBP4 in the absence and presence of pyridine-d_5; the shift of H_α changes by 2.9 ppm. The shifts in the *absence* of pyridine are, of course, those which are highly abnormal. The corresponding region (not shown) for ZnBP3 shows similar, but less dramatic, shifts and changes.

Unambiguous assignments were made for most protons by a combination of NOE difference and two-dimensional COSY experiments. In most of these compounds, NOE's are seen within both the porphyrin and bipyridyl moieties, but not between one and the other. This is the normal situation for such systems.[8] However, NOE's were seen between the two halves in BP2 (Figure 2), an observation which in itself is indicative of a different conformation. The COSY spectra were particularly useful in revealing unresolved couplings between the bipyridyl protons and the protons on the first methylene carbon of the chain, providing a good entree into the latter. A two-dimensional ^{13}C–^1H chemical shift correlation experiment was used to assign the carbon signals of the bipyridyl moiety of BP2.

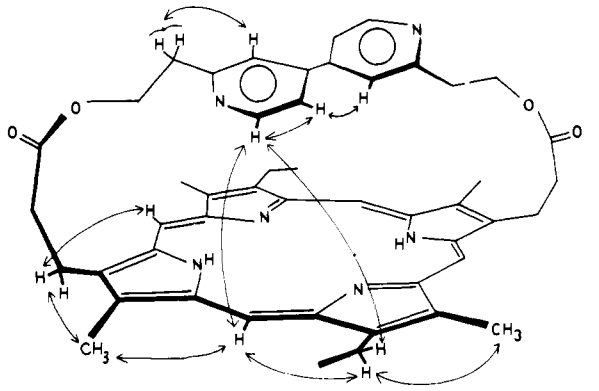

Figure 2. NOE's observed in BP2.

The ^1H and (where measured) ^{13}C shifts of the pyridyl cap nuclei are given in Table I, together with the corresponding data for the analogous bipyridyl alcohols which were taken as the reference compounds. The difference ($\Delta\delta$) may be regarded as due to the porphyrin ring current, and these ring current shifts may therefore be used to obtain the geometry of the bipyridyl cap.

However, it is important to realize the essential limitations of such geometry determinations, which arise more from the unavoidable experimental limitations in terms of data than from the approximations in the ring current model. Note in particular that the pyridyl ring nuclei in the two bipyridyl rings are equivalent in the NMR spectrum.

This could be due to the molecular symmetry, but it could also be (and undoubtedly is in the zinc complexes) due to time-averaging processes. An equilibrium between two identical conformations can be easily handled computationally, as this is equivalent to averaging the pyridine α, β, and δ protons of each ring. An equilibrium between two non-identical conformations cannot be so easily considered, nor could a dynamic model in which the cap has considerable freedom of motion. We consider, therefore, static models of the cap geometry remembering the above caveat.

Due to this averaging there are only three $\Delta\delta$ values, in most cases, to provide the required geometrical information. Thus, in order to obtain an over-determined solution, we assume a standard geometry for the bipyridyl ring and consider only the position of this entity with respect to the porphyrin. The geometry used was obtained from the accurately known geometry of the pyridine nucleus[18] combined with the crystal structure data of 2,2'-bipyridyl[19] to give the central C–C bond length of 1.50 Å.

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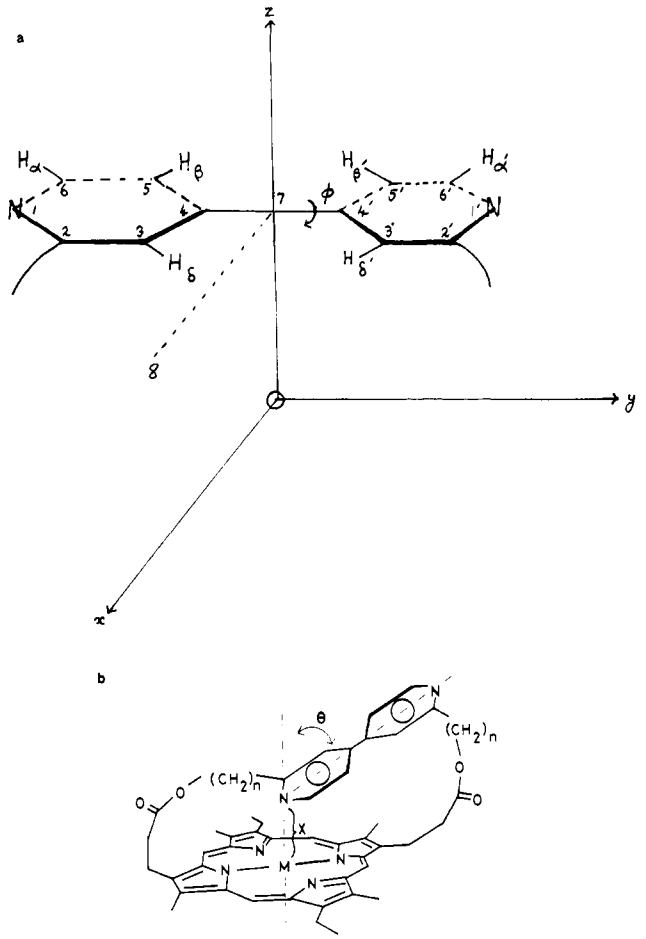

Figure 3. Definition of geometrical parameters in bipyridyl-capped porphyrins.

In the crystal of 2,2′-bipyridyl the pyridine rings are coplanar.[19] This situation would appear to be very reminiscent of that for biphenyl derivatives in which the dihedral angle between the phenyl rings varies from 0 to 40°, but commonly in unhindered biphenyl derivatives is ca. 30°,[20] due to the rather small rotational barrier about the central C–C bond. We therefore consider the dihedral angle between the bipyridyl rings as an additional variable parameter to be determined if possible. Parameters such as agreement factor (AF) and root mean square (rms) error, which are used as a test of the goodness of fit, have been described and defined previously by R.J.A.[12-17]

Free Base Porphyrins. Here we may reasonably assume that the twofold symmetry of the bipyridyl moiety is "effectively" preserved in the cap, i.e., that the central C–C bond is parallel to the porphyrin ring plane with the midpoint on the porphyrin C_2 symmetry axis. If this was not the case there would be two mirror image conformations about this axis in rapid equilibrium, giving the time-averaged geometry assumed. In this model there are only two parameters defining the cap position, the distance from the porphyrin and the angle of twist (ϕ) of each pyridyl ring (Figure 3a). The symmetry is preserved if the two pyridyl rings are either coplanar, or (more probably) if the angles of twist are equal and opposite (i.e., a propeller conformation).

The $\Delta\delta$ values for the protons were used in the computational search for the conformation with the best agreement factor (AF) as these will be less affected by other shift mechanisms than the ^{13}C shifts. The search gave for BP2 an interring distance of 3.7 Å with a 10° twist of each bipyridyl ring, i.e., an interring dihedral angle of 20° (Table II), and an AF of 0.0396. For BP3 and BP4 the corresponding values are recorded in Table II. The agreement is complete, but this is to be expected as three equations in two unknowns is not a very over-determined system. Strong support for the general accuracy of the solutions comes from the good agreement between the observed and calculated ^{13}C $\Delta\delta$ (Table I). For BP3 and BP4 the agreement is well within the experimental limits of error (ca. ±0.2 ppm) for all the carbons except possibly C_5 and C_6 (BP3) and C_4 (BP4).

It may be expected that carbons C-2 and C-4 could experience other shift contributions such as steric shifts, due to the different orientations of the side chains and the bipyridyl rings in the porphyrin complexes compared to the reference alcohols. Nevertheless, the agreement is sufficiently good to lend confidence to the geometries obtained, which will be considered subsequently.

For BP2 the agreement is much poorer, perhaps due in part to the necessity of using the BP3 diol as the reference compound (the BP2 diol being in short supply); more importantly, the unusual geometry renders the comparison with a model compound less valid. Nevertheless, it is clear from these calculations that BP2 has a quite different geometry from BP3 and BP4. Not only is the bipyridyl group much closer to the porphyrin, but also the bipyridyl nitrogens are seen in models to be less accessible to solvent. These differences are reflected in (a) the fact that we have to date been unable to N-methylate BP2 and (b) the observation of NOE's from cap to porphyrin (Figure 2). However, the results of protonation (described below) show clearly that it is possible for BP2 to take up a similar geometry to BP3 and BP4. It must be concluded, therefore, either that there is a favorable π–π interaction between cap and porphyrin in neutral BP2 or that this conformation is less strained than that taken up by BP3 and BP4.

The resonances of the porphyrin moieties in the free base compounds are unremarkable, being very similar to those in the quinone-capped porphyrins which we have previously described.[8] The methylene chains of the bipyridyl side give rise to complex multiplets which we have not analyzed in detail. In the metallated derivatives, however, their appearance is highly diagnostic of coordination states (see below).

Protonated Porphyrins. Addition of a few drops of deuterated trifluoroacetic acid to solutions of the free base porphyrins yielded the tetracations $BPnD_4^{4+}$. The ^1H spectra of these species show downfield shifted meso protons (δ 10.7) which are characteristic of protonated porphyrins; the bipyridyl cap protons are also dramatically shifted downfield. The shifts relative to a diprotonated bipyridyl reference compound are given in Table III.

Table II. Time-Averaged Geometries of Bipyridyl-Capped Porphyrins Obtained from Complexation Shifts

compound	d^a (d_N),[c] Å	φ^b (θ),[d] deg	rms (ppm)	AF
BP2	3.7	10	0.12	0.040
ZnBP2 + pyridine	3.8	0	0.04	0.016
ZnBP2				
BP3	5.5	−20	0.05	0.035
ZnBP3 + pyridine	6.0	−30	0.08	0.054
ZnBP3	(3.3)[c]	(85)[d]	0.08	0.041
BP4	6.1	−10	0.06	0.053
ZnBP4 + pyridine	7.2	−15	0.14	0.163
ZnBP4	(2.4)[c]	(0)[d]	0.15	0.062

[a] Distance from porphyrin center to the midpoint of the bipyridyl C–C bond. [b] Angle of twist of each pyridine ring, about the bipyridyl long axis (0° is coplanar with the porphyrin). When φ(3,4,7,8) is positive, this corresponds to a clockwise vector when looking along 7,4 (Figure 3a); H_β is then closer than H_δ to the porphyrin. When φ is negative, H_δ is closer. [c] Distance from the porphyrin center to bipyridyl nitrogen (see text). [d] Angle between the bipyridyl long axis and the porphyrin C_2 axis (see text).

Table III. Bipyridyl Proton Shifts in the $BPnD_4^{4+}$ Cations[a]

compound	H_α	H_β	H_δ
$BP2D_4^{4+}$	0.40	0.67	1.07
$BP3D_4^{4+}$	0.42	0.53	1.08
$BP4D_4^{4+}$	0.12	0.46	0.77

[a] Upfield shift in ppm relative to 2,2′-dimethyl-4,4′-bipyridyl-D_2^{2+} $(CF_3CO_2)_2^{2-}$: H_α δ 8.92, H_β δ 8.18, H_δ δ 8.17.

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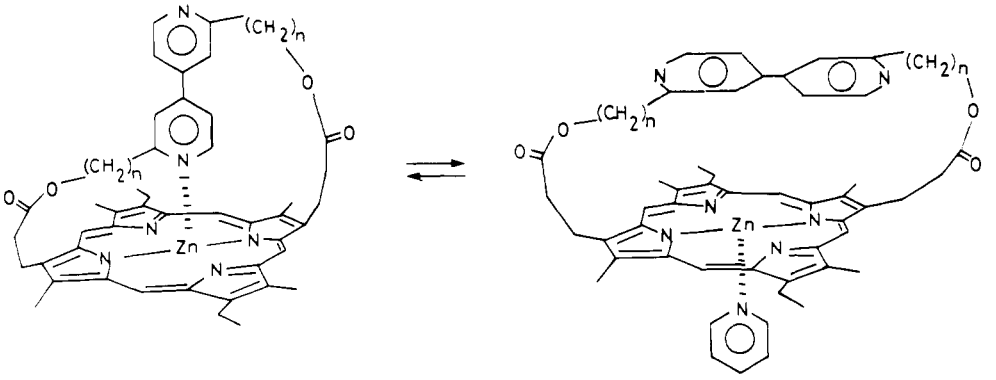

Figure 4. Schematic diagram of the conformational switch.

The most striking observation is that in all three cases the porphyrin-induced ring current shifts, relative to the reference compound, are very similar. This demonstrates that $BP2D_4^{4+}$ takes up virtually the same geometry as $BP3D_4^{4+}$ and $BP4D_4^{4+}$. Assuming a similar conformation to the free bases, and no substantial change in the porphyrin ring current on protonation,[21] the corresponding geometries obtained from a computational search were, for $BP2D_4^{4+}$ and $BP3D_4^{4+}$, −30° and 8.0 Å (AF 0.03), and for $BP4D_4^{4+}$, −40° and 9.4 Å (AF 0.23). This geometry is similar to that of BP3 and BP4, but with a larger porphyrin–bipyridyl distance which presumably results from electrostatic repulsion.

It appears, then, that there is no geometrical or steric barrier to BP2 taking up the BP4-like conformation with exposed pyridyl nitrogens. Protonation of both porphyrin and cap in BP2 leads to electrostatic repulsion between these moieties; this repulsion overcomes the attractive π–π interaction or strain which otherwise dictates the geometry of BP2. This is an example of a switch which is operated by protonation–deprotonation. In this case it is not yet as well characterized as the ligand-induced switching discussed below.

Zinc Porphyrins. When these compounds are examined in the presence of excess pyridine, it may be anticipated that the pyridine will compete successfully against the bipyridyl nitrogen for the zinc coordination site and in consequence the conformations of these complexes would be very similar to those of the analogous free bases, with perhaps some slight perturbations due to the zinc pyridine ligand. These expectations are confirmed by the observed shifts (Table I) which are very similar to those for the free bases. Analysis of these shifts on the same model as those of the free bases gives the conformational parameters shown in Table II and calculated shifts in Table I. The calculated shifts are in complete agreement with those observed, except possibly for ZnBP4. It may be significant that in this molecule there is the largest separation between the bipyridyl and porphyrin planes, and in this case there could be considerable conformational mobility of the pyridyl cap and the static model considered may not be entirely appropriate. Alternatively, there is the intriguing possibility that some pyridine molecules could fit into this cavity, and the increase in the bipyridyl–porphyrin separation on going from the free base to the zinc porphyrin is some support for this speculation.

It is pertinent to note here that there are many nonsymmetric conformations which would give equally good agreement between the observed and calculated shifts. For example, an alternative model would be to retain the bipyridyl long axis parallel to the porphyrin ring plane, assume a given angle of twist between the pyridyl rings, and then obtain the value of the inter-planar separation and the angle of twist of the bipyridyl entity which would give the best agreement factor. In this model the bipyridyl rings are no longer equivalent, but interconvert between two mirror-image conformers. This model gives as good agreement as the simpler symmetric model considered, with indeed almost identical interring separations, thus these results will not be documented.

However, these considerations are relevant to the analysis of the observed shifts of the zinc complexes without added pyridine, and again our approach is to envisage a chemically reasonable model and then use the observed shifts both to determine the geometry of the model and to confirm the correctness (or otherwise) of the model.

It would be anticipated that in the zinc complexes in the absence of pyridine, the bipyridyl nitrogens will occupy the vacant coordination site above the zinc atom, provided that this is sterically allowed (Figure 4). In ZnBP4 there is sufficient flexibility in the cap for this to be achieved, and the observed shifts demonstrate clearly that the conformation of the cap is very different from that of the other BP4 compounds examined. Thus we considered a conformation in which the bipyridyl cap long axis is coincident with the porphyrin C_2 symmetry axis, which is the optimum position for Zn···N coordination. In this model there is only one variable parameter, the Zn···N pyridyl distance, and due to the essentially cylindrical symmetry of the porphyrin ring current model the bipyridyl ring current shifts in this conformation are independent of the torsional angle. In this model the observed equivalence of the two bipyridyl rings must be due to rapid interconversion between the two identical conformations formed from the two bipyridyl nitrogens complexing in turn with the zinc. The observed $\Delta\delta$ values were input in the search for the best agreement factor, averaging the calculated shifts of the separate α, β, and δ protons of the two pyridyl rings. The best AF was obtained for a nitrogen to center distance of 2.4 Å, and the agreement is essentially complete, which is encouraging as this case is more over-determined than the previous one (one unknown in three equations). The calculated shifts and AF are given in Tables I and II.

The situation for the other zinc porphyrins is less clear-cut. In ZnBP2 the observed spectrum was broad and ill-resolved, precluding accurate measurements, but that of ZnBP3 could be recorded satisfactorily. It is clear that the short chains of ZnBP2 preclude any intramolecular binding, and aggregation occurs. In contrast, there is sufficient intramolecular interaction in ZnBP3 to prevent aggregation; in this case the carbon chains joining the bipyridyl cap to the porphyrin are too short to allow fully perpendicular binding of a pyridyl nitrogen to the zinc, thus we considered two possible models. In the first "static" model, the bipyridyl cap was assumed to complex at one nitrogen with the zinc, thus this nitrogen remained over the zinc atom, but the bipyridyl molecule was allowed to rotate from the optimum perpendicular orientation (Figure 3b). In this case the angle of twist of the bipyridyl rings affects the calculated shifts, and from the considerations given previously together with molecular models this angle was taken as 30°. The computational search was performed by varying both the nitrogen to zinc distance and the angle of the bipyridyl long axis with the porphyrin C_2 symmetry axis. Best agreement was obtained for a nitrogen to center distance of 3.3 Å and an angle of 85°, i.e., the bipyridyl cap is almost coplanar with the porphyrin, but the chains move so as to allow one of the bipyridyl nitrogen atoms to be coordinated with the zinc. Obviously there will be a number of closely related conformations which would also give reasonable AF's.

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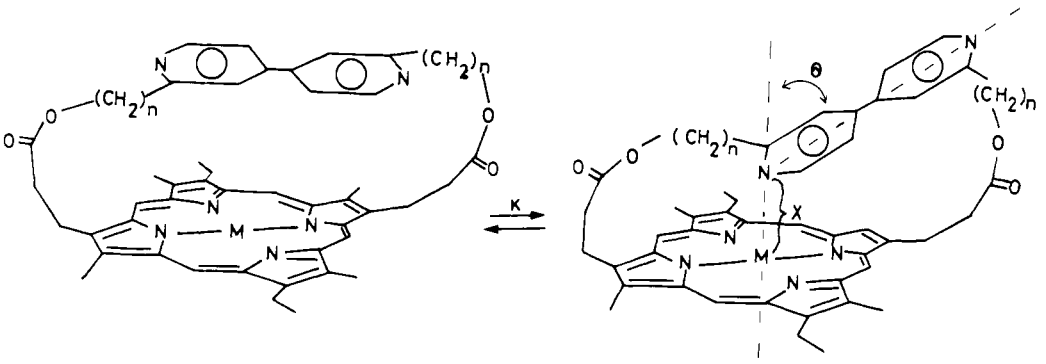

Figure 5. Proposed conformational equilibrium in ZnBP3.

Another quite different hypothesis is that in this molecule there is an equilibrium between a coordinated conformation and a non-coordinated one (Figure 5). In this model there are too many unknown parameters to be determined from only three observed shifts, thus we considered an equilibrium between the uncoordinated structure of BP3 and a twisted structure analogous to the above static model. Good agreement between the observed and calculated shifts was obtained for an equilibrium constant of 2.8:1 in favor of the non-coordinated structure over a twisted coordinated structure with a zinc to nitrogen distance of 2.5 Å and an angle of tilt of ca. 75°. The present NMR data alone cannot distinguish between these two possible models, but the Zn–N distance of 2.5 Å for the equilibrium model corresponds most closely to the distances in related molecules.

The resonances due to H_α in both ZnBP3 and ZnBP4 are substantially broadened in the absence of pyridine (Figure 1). This is presumably due to a dynamic process, but it is not yet clear whether that process is the flipping of the bipyridyl group end-on-end or is the free-bound equilibrium. Cooling a ZnBP4 solution increases the selective broadening, but even at 190 K a slow exchange spectrum is not reached. This very broad range of intermediate exchange indicates a large entropy of activation and is characteristic of a flexible system which passes through one or more strictly defined conformations.[22] Cooling of a ZnBP4/pyridine mixture shifts the equilibrium away from intramolecular to intermolecular coordination as expected.

As in the free base porphyrins, the methylene chains attached to the bipyridyl group give complex spectra, but they are nevertheless instructive and highly characteristic. Figure 6 shows the pyridine titration behavior of the high-field region of the ^1H spectrum of ZnBP4. In the intramolecularly bound state, the methylene chain protons adjacent to the bipyridyl group are substantially shielded and nonequivalent: in ZnBP4, H_f and $H_{f'}$ appear at δ 0.1 and 0.9 while in ZnBP3 the corresponding H_e and $H_{e'}$ resonate at δ 0.7 and 0.3. These upfield shifts are undoubtedly due to the porphyrin ring current, and the fact that they are largest adjacent to the bipyridyl provides yet further evidence for intramolecular binding. Notice, however, that the shielding is greater in ZnBP4, where the methylenes are placed more over the center of the porphyrin.

When pyridine is added, the bipyridyls are released and their adjacent protons become the least shielded in the region, H_f and $H_{f'}$ in ZnBP4 moving to δ 1.6 and H_e and $H_{e'}$ in ZnBP3 moving to δ 1.55 and 1.25. There are corresponding, but smaller shifts in the other methylene protons. These are also visible in Figure 6. In the presence of pyridine, this region of the spectrum is, in each case, very similar to the free base analogue.

In general, meso resonances in these compounds resonate in the normal δ 10.0 to 10.15 region irrespective of the coordination or metallation state of the porphyrin. However, in ZnBP3, *in the absence of pyridine*, the meso protons appear at δ 9.6 and 9.55. This shielding can only be due to the bipyridyl ring current, and it is striking independent evidence that the cap and porphyrin are indeed approximately parallel when bound together through zinc.[23] There are similar, but smaller, shifts of the other protons around the porphyrin periphery.

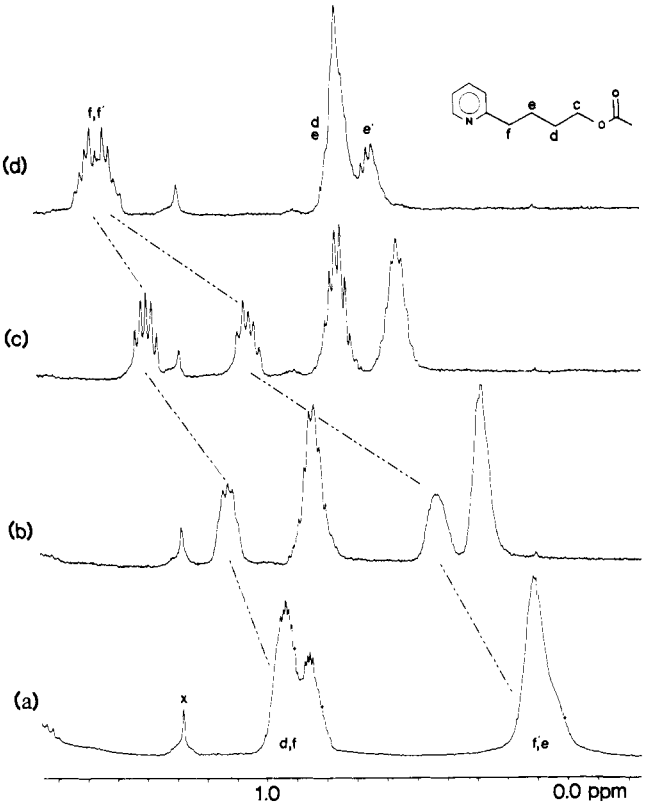

Figure 6. (a) ^1H spectra (400 MHz) of the highest field region of ZnBP4 in the absence of pyridine. (b–d) The same region as in part a in the presence of increasing concentrations of pyridine-d_5. X is an impurity.

Table IV. UV/Visible Spectral Absorption Maxima for Zinc Bipyridyl Porphyrins in CH_2Cl_2

compound	Soret λ_{max} (ϵ)[a]	β λ_{max} (ϵ)[a]	α λ_{max} (ϵ)[a]
ZnMeso-II-ester	402 (3.14)	530 (0.13)	568 (0.19)
+ pyridine	413 (3.18)	542 (0.16)	578 (0.12)
ZnBP2	404 (3.35)	532 (0.15)	570 (0.24)
+ pyridine	414 (3.35)	543 (0.18)	578 (0.15)
ZnBP3	403 (2.35)	534 (0.14)	570 (0.17)
+ pyridine	413 (3.13)	540 (0.16)	576 (0.12)
ZnBP4	414 (2.55)	539 (0.13)	576 (0.12)
+ pyridine	413 (2.85)	540 (0.14)	576 (0.12)

[a] λ_{max} in nm; $\epsilon \times 10^{-5}$.

(22) Chang, M. H.; Dougherty, D. A. *J. Am. Chem. Soc.* **1983**, *105*, 4102.

(23) Another possibility might be that intramolecular binding leads to distortion of the porphyrin macrocycle, and hence to reduced ring current [Wijesekera, T. P.; Prince, J. P.; Dolphin, D.; Winstein, F. W. B.; Jones, T. *J. Am. Chem. Soc.* **1983**, *105*, 6747]. However, the UV spectrum shows no sign of the anomalies reported for distorted porphyrins.

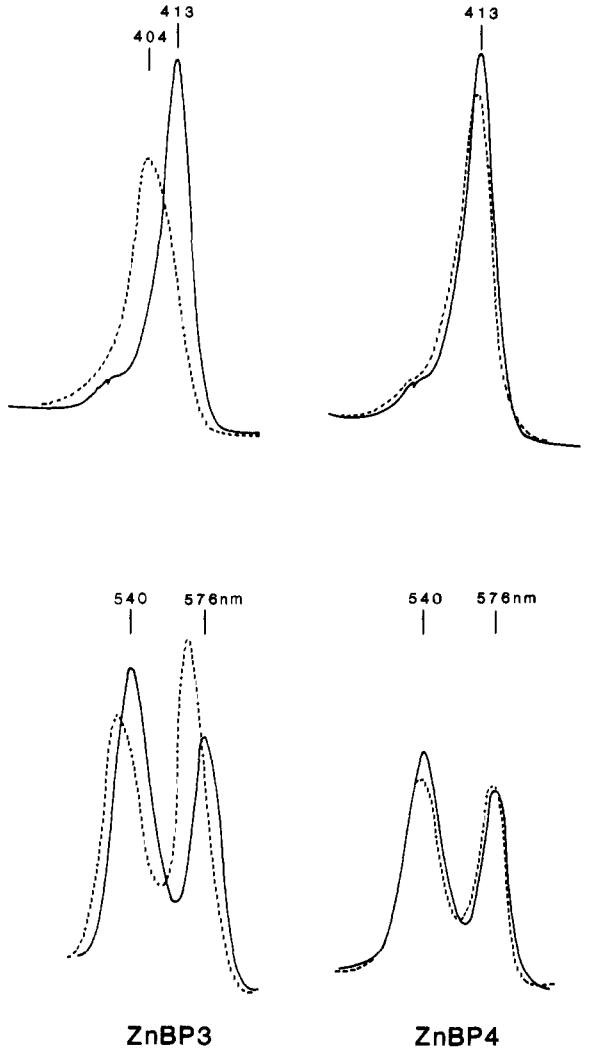

Figure 7. Soret, α, and β bands of ZnBP3 and ZnBP4 in the absence (---) and presence (—) of pyridine. Spectra are not normalized with respect to each other, but individual regions with and without pyridine are normalized to show intensity changes.

UV/visible spectroscopy confirms the general conclusions and allows a distinction to be made between the two possible binding models for ZnBP3. Four-coordinate zinc mesoporphyrins have a Soret absorption at ca. 400 nm, and α and β absorptions at ca. 568 and 530 nm, the former being the more intense.[24] In contrast, the absorption bands of zinc porphyrins bound to nitrogen ligands are red shifted to ca. 414, 540, and 578 nm, with the β band more intense than the α band. Thus the spectrum of ZnBP4 shows only minor changes on pyridine addition (Figure 7) while ZnBP3 shows similar changes to ZnBP2 and zinc mesoporphyrin II–dimethyl ester (Table IV and Figure 7). However, in the absence of pyridine, the Soret band of ZnBP3 is clearly asymmetric, broadened, and less intense than that of ZnBP2. This is almost certainly due to a small proportion of intramolecularly bound material absorbing at ca. 413 nm (Figure 7). Addition of pyridine restores the normal intensity and bandwidth of this absorption. Assuming that the ZnBP3 Soret absorption is the superposition of four-coordinate absorption at 404 nm and five-coordinate absorption at 413 nm, then the ratio of 4- to 5-coordinate material is approximately 3:1. This value is in extremely good agreement, probably fortuitously, with the equilibrium model obtained from NMR results. The β band of ZnBP3 is also slightly shifted from the pure four-coordinate position (Table IV).

Analysis of the chemical shifts of both porphyrin and added lutidine (or pyridine) as increasing amounts of the ligand were added gave the following estimates of binding constants: ZnBP3, 600; ZnBP4, 40 L M^{-1}. We have determined by UV/visible spectroscopy that the corresponding value for zinc mesoporphyrin II–dimethyl ester is approximately 2×10^4, demonstrating that in ZnBP3 the metal ion is bound intramolecularly to some extent, but that in ZnBP4 it is more effectively bound internally and so less available to an external ligand.

We can crudely estimate the strain energy involved in intramolecular binding. In the absence of any strain, and assuming the effective concentration of intramolecular pyridines to be of the order of 10 M, the expected binding constant for external pyridine should be approximately 0.1 L M^{-1}. The factor of 400 greater for ZnBP4 and 6000 for ZnBP3 reflects $\Delta\Delta G$ of ca. 15 and 22 kJ mol^{-1}, respectively. These values for the strain energies should be compared with the intrinsic binding energies of about 25 kJ mol^{-1} (i.e., $K \approx 20\,000$). If the effective molarity of the internal ligand is varied in the range 1 to 100 M, the corresponding variation in strain energy will be ± 6 kJ mol^{-1}.[25]

It is clear that there is a very narrow range of strain energies which will in fact allow a molecule to act as an effective switch: if the strain is too great then no binding will occur between metal and cap, and aggregation will occur. This is the situation for ZnBP2 and, as described below, MgBP3. If the strain is only slightly too large, then there will be sufficient binding to prevent aggregation, but there may be only a relatively small proportion of molecules actually found in the bound form. ZnBP3 apparently falls into this category.

By contrast, ZnBP4 is, fortuitously, almost perfect as a switch. The estimated strain energy of 15 kJ is sufficiently smaller than the binding energy to allow virtually complete intramolecular binding, but this is readily overcome by the unstrained complexation of an external ligand. If the strain were to be lessened by even a relatively small amount, impractically large quantities of external ligand would be required for switching.

Magnesium Porphyrins. In the absence of added ligand, MgBP4 has effectively the same shifts, and therefore geometry, as ZnBP4 (Table V). Addition of pyridine or lutidine produces the expected upfield shifts of the added ligand but only relatively small shifts in the porphyrin. There are insufficient data to allow any quantitative conclusions to be drawn, but it appears qualitatively that, as in the quinone analogues we have previously discussed,[3,8] there is some six-coordinate material formed in addition to one or both of the five-coordinate species. Similar equilibria between five- and six-coordination are observed in magnesium chlorophylls.[7,10]

Interestingly, MgBP3 is heavily aggregated, demonstrating that the strain involved is greater, relative to the binding energy, than that in ZnBP3. Whether this is due to a smaller intrinsic affinity of pyridine for Mg than for Zn or to a more stringent geometrical requirement for effective binding we do not know.

Table V. Bipyridyl Proton Shifts in MgBP3 and MgBP4[a]

compound	H_α	H_β	H_δ
MgBP3		aggregated	
MgBP3 + pyridine	0.7	1.1	2.2
MgBP4	3.8	1.45	1.45
MgBP4 + pyridine	1.7	1.1	1.35

[a] Upfield shift in ppm relative to reference compound.

Experimental Section

NMR spectroscopy was carried out at ambient temperatures with ca. 10^{-3} M solutions of porphyrin in deuteriodichloromethane. Solvent resonances were used as internal standards for both proton and carbon chemical shifts. Proton spectra of the bipyridyl diols were obtained at 80 MHz on a Bruker WP 80 instrument. Proton spectra of the capped porphyrins were obtained in Cambridge at 250 or 400 MHz with Bruker WM 250 or WH 400 instruments, using 16K data points over 3000 or 4800 Hz, respectively. NOE difference and COSY-45 spectra were

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(25) It would be possible to obtain more precise values for these and other thermodynamic quantities by appropriate variable temperature measurements. This has been done for similar, intramolecularly bound, pyridine-tailed porphyrins: Walker, F. A.; Benson, M. *J. Am. Chem. Soc.* **1980**, *102*, 5530.

acquired with standard software and conditions. Carbon spectra were obtained at 62.9 MHz on the WM 250 with 16K data points over 13 000 Hz. Titrations were carried out by addition of measured quantities of pyridine-d_5 or 3,5-lutidine solution to the NMR solution.

A 500-MHz COSY spectrum of BP4 and a two-dimensional ^1H-^{13}C correlation spectrum of BP2 were obtained by Dr. W. E. Hull on AM500 and AM400 instruments at Bruker Analytische Messtechnik, Karlsruhe.

No attempt was made to remove traces of residual water from porphyrin solutions, and its presence was clearly detectable in proton spectra. Therefore we cannot exclude its participation with a ligand. However, its relatively invariant chemical shift indicates that its effect is minimal.

Computations were carried out with programs which have been described previously.[12-14,16]

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Metal-Nucleotide Interactions. 3. ^{17}O, ^{31}P, and ^1H NMR Studies on the Interaction of Sc(III), La(III), and Lu(III) with Adenosine 5′-Triphosphate[1]

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Abstract: The interaction of adenosine 5′-triphosphate (ATP) with diamagnetic trivalent metal ions Sc(III), La(III), and Lu(III) was investigated by ^{17}O NMR, ^{31}P NMR, and ^1H NMR. All three techniques showed the formation of 1:2 M(III)/ATP complexes for all three metal ions. The exchange rate between free and bound ATP on the NMR time scale was fast for La(III) and Lu(III) but slow for Sc(III) ($<12\ s^{-1}$ at 30 °C). ^{31}P NMR results showed entirely different patterns of chemical shifts of ATP induced by the three metal ions. On the basis of our recent work [Huang, S. L.; Tsai, M.-D. *Biochemistry* **1982**, *21*, 951-959], the line-broadening effect in ^{17}O NMR is more reliable than the chemical shift effect in ^{31}P NMR in identifying the coordination between nucleotides and diamagnetic metal ions. The ^{17}O NMR results showed that binding of Sc(III), La(III), and Lu(III) induced a small chemical shift effect (5-15 ppm downfield shifts) and a large line-broadening effect for all of the three phosphates of ATP. Comparison of the relative magnitudes of the line-broadening effect for the α-, β-, and γ-phosphates of ATP suggested that the predominant macroscopic structure of $Sc^{III}(ATP)_2$, $La^{III}(ATP)_2$, and $Lu^{III}(ATP)_2$ is the α,β,γ-tridentate. Such a conclusion was further supported by ^1H NMR, which showed no indication of direct binding between M(III) and the adenine ring and showed significant upfield shifts for the resonances of H-2, H-8, H-1′, and others, which can be explained by the ring-current effect due to base stacking in $M^{III}(ATP)_2$.

Because of their significance in chemistry, biochemistry, and biology, the structures of metal ion-nucleotide complexes have been studied extensively by various physical techniques such as NMR (^{31}P, ^1H, ^{13}C, and ^{15}N), IR, UV, and others, as reviewed recently by Martin and Mariam.[2] However, the sites of coordination remain unresolved except for a few complexes such as $Co^{III}IMP$,[3] $Cr^{III}ATP$,[4] and $Co^{III}ATP$[4] which have been determined by X-ray crystallography. For the complexes of paramagnetic metal ions, the most widely used technique is the NMR paramagnetic relaxation method.[5] For the complexes of diamagnetic metal ions, ^{31}P chemical shifts have been used to deduce the binding of metal ions with the phosphate moiety of nucleotides,[6-10] and ^1H chemical shifts have been used to study the binding to the adenine moiety of ATP.[6,8-10]

The use of ^{31}P chemical shifts to elucidate the coordination sites of MgATP has generated controversial results.[6,7] Since ^{31}P chemical shifts of phosphate esters are very sensitive to conformation and the O-P-O bond angle,[11] there is no basis to directly correlate the metal-induced ^{31}P chemical shift to the site of coordination. As a possible substitute to the ^{31}P chemical shift method, we have shown that the diamagnetic Co(III) ion induces a large chemical shift effect and line-broadening effect on the ^{17}O NMR resonance of the directly coordinated oxygen.[12-15] The

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