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Propensity toward formation of higher aggregates in anionic and cationic iron tetraphenylporphyrin μ-oxo dimers: evidence from ^1H and ^{13}C NMR spectroscopy

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Abstract

The μ-oxo dimeric form of anionic iron(III) tetra(*p*-sulfonatophenyl) porphyrin, FeTSPP, and iron(III) tetra(*p*-carboxyphenyl) porphyrin, FeTCPP, as well as cationic iron(III) tetra(4-*N*-methylpyridyl) porphyrin, FeTMPYP, and iron(III) tetra(4-*N,N,N*-trimethylanilyl) porphyrin, FeTMAP, were investigated by ^1H and ^{13}C NMR methods in aqueous solution. Concentration dependence, chemical shifts, splitting patterns and line-broadening properties of phenyl/pyridyl and porphyrin β-pyrrolic resonances suggest the aggregation tendencies of these porphyrin dimers increase in the order TMPYP<TMAP<TSPP<TCPP. The diffused nature of positive charge in the *N*-methylpyridyl group of TMPYP makes this dimer least susceptible to aggregation. On the other hand, the steric/spatial dimensions of the localized charged groups in the *meso*-phenyl substituted TMAP, TSPP and TCPP porphyrins are most likely to affect their aggregation tendencies. The resolved splittings of *ortho*-phenyl protons observed at 50 mM concentration in the anionic systems suggest a tighter stacking of dimer/higher aggregates and slower formation/dissociation processes on the NMR time scale, than those found in the cationic analogs.

Introduction

Recent investigations have centered around the aggregation properties of both anionic and cationic water-soluble porphyrins as a means to approach the design of photosynthetic charge transfer complexes [1]. One of the most interesting characteristics of unhindered water-soluble ferric porphyrins is the formation of oxy-bridged dimers at intermediate pH (6–10) range [2]. These species serve as models for the antiferromagnetic spin coupling interactions between two metal centers which is operative in biological macromolecules including iron–sulfur proteins and cytochrome *c* oxidase [3]. The organic-soluble iron(III) tetraphenylporphyrin μ-oxo dimers have been the subject of extensive studies in the past two decades [4]; however, the water-soluble analogs have received less attention [5]. As part of our interest in the study of interaction between cofacially oriented metalloporphyrins in aqueous media, we were prompted to investigate the solution conformational characteristics of anionic FeTSPP and FETCPP as well as cationic FeTMPYP and FETMAP μ-oxo dimers TSPP: tetra(*p*-sulfonatophenyl) porphyrin, TCPP: tetra(*p*-carboxyphenyl) porphyrin, TMPYP: tetra(4-*N*-methylpyridyl) porphyrin, TMAP: tetra(4-*N*,*N*,*N*-trimethylanilyl) porphyrin by magnetic resonance techniques, Fig. 1.

Most aggregation studies of water-soluble porphyrins thus far have been directed at square-planar monomeric species (i.e. free base and Cu/Ni porphyrins) by using UV–Vis spectroscopy [6]. In this paper, ^1H and ^{13}C NMR spectral characteristics are utilized to show the

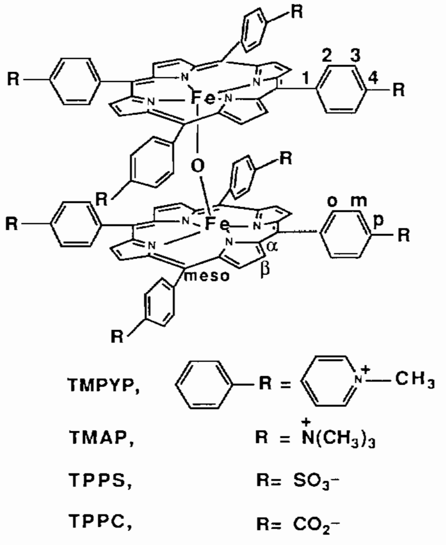

Fig. 1. Structures of μ-oxo dimers.

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propensity for aggregation of these square-pyramidal dimers through an analysis of peripheral charge density distribution, chemical shifts and splitting patterns of *ortho*- and *meta*-phenyl protons and carbons as well as chemical shifts and line-broadening properties of porphyrin β-pyrrolic protons.

Experimental

Materials

The cationic and anionic iron porphyrins were obtained from Midcentury Chemical Co., Posen, IL, as the chloride and the sodium salts, respectively, except for FeTCPP which was received in the acid form. The purity of these porphyrins was checked by thin-layer chromatography on Whatman reverse-phase glass-backed plates and ^1H NMR. FeTCPP was subject to further purification by dissolving the crude sample in ethyl acetate:acetone:methanol (1:1:1, vol./vol.) mixture followed by filtration through a short bed of celite to remove insoluble impurities. FeTMPYP was also further purified by column chromatography over Pharmacia Sephadex G-25 using methanol as the eluting solvent. The μ-oxo dimeric iron(III) porphyrins were prepared fresh before each experiment from the corresponding bis-aquo complexes in D_2O–DMSO-d_6 (9:1, vol./vol.) and the solution was adjusted to pH = 9 with NaOD/DCl. The 10% DMSO-d_6 in D_2O served as both to reference the resonance positions (water signal was suppressed) and to enhance solubility at 50 mM concentration for ^{13}C detection [7]. In order to investigate their tendencies toward formation of higher aggregates, the proton spectra were recorded at 3 and 50 mM concentrations and changes in chemical shifts and/or linewidths were compared [8].

Instrumentation

The ^1H and ^{13}C NMR spectra were obtained at 500.1 and 125.8 MHz, respectively, on a General Electric GN-500 instrument. pH adjustment was accomplished on a Radiometer model pH M26 with a Metrohm combination glass electrode. ^{13}C assignments for *ortho*- and *meta*-phenyl carbons as well as β-pyrrolic carbons were facilitated by recording the spectra under both proton coupled and decoupled modes. Only the ^{13}C spectra of FeTCPP and FeTMPYP μ-oxo dimers have been previously reported at 22.6 MHz by the pioneering work of Goff and Morgan; however, some of the earlier assignments have been reevaluated in light of application of higher-field instrument [9].

Results

The proton NMR spectral characteristics of the μ-oxo complexes at two different concentrations are provided in Table 1 in which β-pyrrolic hydrogens reveal attenuated diamagnetic-type chemical shifts, consistent with antiferromagnetic coupling mechanisms [10]. At these concentrations, the cationic FeTMPYP dimer experiences a uniform deshielding effect of all the resonances relative to those found in FeTMAP as well as the anionic systems. This is attributed in the TMPYP system to a partial delocalization of positive charge into the pyridinium ring and diminished tendency toward aggregation through interplanar electrostatic repulsion over a wider surface area [11]. All derivatives display a doubling of *meta*-proton signals at both concentrations, a diagnostic feature indicative of a five-coordinate complex [12]. This splitting is attributed to the unsymmetrical substitution of iron axial positions on the two sides of the porphyrin plane, displacement of iron from the porphyrin plane (~0.5 Å) toward the bridging oxygen and the slow rotation of phenyl rings at room temperature on the NMR time scale [13]. Thus, the earlier notion concerning the occupancy of the iron sixth axial position in the μ-oxo dimers by water may be ruled out for all derivatives, as also observed by Scheidt and coworkers for the solution and solid state of the FeTMPYP dimer [14]. At 3 mM concentration, *ortho*-protons remain as singlets in all complexes but at 50 mM, they split in the anionic systems (TPPS, $\Delta\delta = 128$ Hz; TPPC, $\Delta\delta = 200$ Hz) into two broad singlets and shift to higher field (av. $\Delta\delta = 1.0$ ppm). On the other hand, this resonance in the cationic analogs appear as broad ($\nu_{1/2}$ TMAP $\gg$ $\nu_{1/2}$ TMPYP) overlapping bands with no significant changes in chemical shifts at both concentrations. A close examination of changes in the chemical shifts and line-broadening properties of β-pyrrolic protons at these concentrations, Table 1, also reveal that as the concentration is raised from 3 to 50 mM, anionic systems display a distinct upfield shift (av. $\Delta\delta = 1.3$ ppm) and a more pronounced enhancement in linewidth (av. $\Delta\nu_{1/2} = 135$ Hz) of this resonance than those observed in the cationic complexes (av. $\Delta\delta = 0.15$ ppm; av. $\Delta\nu_{1/2} = 23$ Hz). This differences reflect the propensity of anionic species to undergo more extensive aggregation at higher concentration [15].

The ^{13}C NMR spectra, on the other hand, reveal two non-equivalent *ortho*-carbons in all derivatives at 50 mM concentration with splitting increasing in the order TMPYP (60 Hz) < TMAP (225 Hz) < TCPP = TSPP (338 Hz), Table 2. Moreover, *meta*-phenyl carbons also split in the anionic systems (63 Hz); whereas, this resonance remains as a singlet in TMAP and displays a small splitting for TMPYP (28 Hz). The more resolved splittings of *ortho*-hydrogens as well as *meta*-carbons in the anionic systems reflect a tighter stacking of dimer/higher aggregates with their formation/dissociation equilibria proceeding at slower rates on the NMR time scale, than those observed in the cationic species. Thus,

TABLE 1. ^{1}H NMR chemical shifts (δ, ppm) and linewidth ($\nu_{1/2}$, Hz) characteristics of the porphyrin μ-oxo dimers at different concentrations[a]

Porphyrin	β-Pyrrolic hydrogen		Aryl hydrogen				Methyl	
	3 mM	50 mM	*ortho*		*meta*		3 mM	50 mM
			3 mM	50 mM	3 mM	50 mM		
TMPYP	14.1(85)	14.1(87)	8.1	8.0	9.0/9.3	9.0/9.4	4.4	4.4
TMAP	13.4(157)	13.7(201)	7.3	7.5	7.8/8.1	7.9/8.2	3.8	3.8
TSPP	13.5(100)	12.5(198)	7.5	6.5/6.8	8.0/8.2	7.8/7.9		
TCPP	13.4(130)	11.8(301)	7.4	6.0/6.3	8.1/8.2	7.5/7.8		

[a] In D_2O–DMSO-d_6 (9:1) solution, pH = 9, 0.1 M in $NaNO_3$, 25 °C, ref. to DMSO(δ = 2.50 ppm).

TABLE 2. ^{13}C NMR chemical shifts of μ-oxo dimer of water-soluble iron porphyrins[a]

Porphyrin	Pyrrole carbon		*meso*	Aryl carbon				Methyl	COO^-
	α	β		1	2	3	4		
TMPYP	244.9	216.4	115.4	154.3	139.0 138.2	145.8 145.6		49.7	
TMAP	241.7	216.4	125.5	137.3	146.3 144.5	120.3	148.6	59.0	
TSPP	239.7	216.2	137.3	[b]	146.1 143.4	125.8 125.3	144.5		
TCPP	237.5	215.2	124.9	[b]	145.8 143.1	128.8 128.3	137.3		175.7

[a] Porphyrins 0.05 M in D_2O-DMSO-d_6 (9:1) solution, 25 °C, ref. to DMSO-d_6(δ = 39.5 ppm). [b] Not observed or hidden under C-4 signal.

^{1}H and ^{13}C data both suggest that aggregation in this series increases in the order TMPYP < TMAP < TSPP < TCPP. Indeed, this phenomenon has already been explained in terms of localized peripheral negative charges in TCPP and TSPP and a more diffused positive charge in TMPYP [16]. Tendency of TMAP toward aggregation seems to approach those of anionic derivatives in view of the analogous location of the charged center at the *para*-phenyl position and absence of substantial positive-charge delocalization into the phenyl ring. Consequently, the steric/spatial dimensions of the charged centers (i.e., $N(CH_3)_3+ > SO_3- > CO_2-$) are most likely to contribute to the extent of aggregation in the *meso*-phenyl substituted porphyrins.

Discussion

X-ray studies on the FeTPP μ-oxo dimer have revealed that aromatic *meso*-phenyl groups of interacting porphyrins are parallel, allowing the porphyrin planes to get sufficiently close (~4.5–5.0 Å) to form the oxo bridge; however, interaction between phenyl groups, which are nearly perpendicular (60–90°) to the plane of porphyrin ring, prevent the closer approach to the van der Waals distance of separation (~3.4 Å) [17]. The tilting of *meso*-phenyl groups into the porphyrin plane and increased phenyl–porphyrin resonance interaction has been observed with diprotonated TPP which is facilitated by the deformation of the pyrrole rings [18a]. The increase in the degree of coplanarity between the phenyl ring and the porphyrin plane may account for the overall smaller splittings and more equivalent *ortho*- and *meta*-protons and carbons in cationic systems; however, these species will then be more susceptible to aggregation owing to the decrease in steric barrier rendered by perpendicular phenyl rings [18b].

Electron-releasing *para*-phenyl substituents are known to increase the rate of phenyl ring rotation in TPP complexes [19]. The presence of electron-donating carboxylate and sulfonato groups should then promote averaging of the phenyl resonances to the AA'BB' spin pattern; however, the enhanced splitting of *ortho*-protons at higher concentration in the anionic complexes relative to cationic analogs reveal a ABCD-type spin system in the former. An alternative explanation for the non-equivalence of *ortho*-phenyl protons in anionic systems is the slow inversion of the iron atom such as that observed for monomeric Tl(III)TPP(OAc) [20]. The inversion is not however expected to be significant for the dimeric species that are bridged via strong-field metal axial-ligands [21]. Additionally, since the spontaneous rate of bond dissociation/formation is faster in anionic dimers [22], a larger non-equivalency of *ortho*-protons should be observed for the cationic dimers, instead.

It is well known that the electronic effects of *para*-phenyl groups can alter the basicity of the porphyrin nitrogens [23]. In a recent study on FeTPP μ-oxo dimers, Helms *et al.* have associated the effect of an electron-withdrawing *para*-substituent with decrease in the axial iron–oxygen bond length and increase in antiferromagnetic coupling interaction [24]. The positively-charged FeTMPYP and FeTMAP dimers should be considerably less basic than the negatively-charged FeTSPP and FeTCPP dimers and will thus favor a shorter iron–oxygen–iron bond distance and form stronger μ-oxo dimers. Indeed, it is documented that the anionic FeTSPP dimer dissociates 17 times more rapidly than the cationic FeTMPYP dimer [25]. The shorter axial bonding in the cationic systems may induce closer interplanar interaction in these dimers and the peripheral electrostatic repulsion may force the phenyl groups to rotate away from each other and change the phenyl–porphyrin dihedral angles. If this phenomenon was operative, however, one pair of *ortho*- and *meta*-hydrogens and carbons which project into interplanar cavity will then experience quite a different ring current effect relative to the other pair directed outward.

Kano *et al.* have reported the concentration-dependant self-aggregation of free base TMPYP [15b]. They demonstrate that at concentrations above 10 mM, H_2TMPYP stack up to form loose higher aggregates where porphyrin-to-porphyrin distance is around 10 Å which results in the broadening of the porphyrin proton NMR signals. They attribute this broadening to monomer–dimer equilibrium with formation and dissociation processes occurring at slow rates. By the same analogy, the diastereotopism for *ortho*-phenyl protons at 50 mM concentration in the anionic dimers suggest a tighter packing of dimer/higher aggregate complex, which is consistent with their propensity for aggregation, rendering these protons oriented on the two sides of the porphyrin plane more non-equivalent than those observed in the corresponding cationic species and slow formation/dissociation processes which accounts for the broadening nature of the signals.

Conclusions

^{1}H and ^{13}C NMR assignments are given for two examples of anionic and cationic iron tetraphenylporphyrin μ-oxo dimers. Concentration-dependant NMR data suggest that the anionic dimers aggregate more extensively at high concentrations than the cationic species owing to the localized nature of the negative charge in the former relative to TMPYP and smaller steric/spatial dimensions of their charged groups with respect to TMAP. Further study is underway to measure dimer/higher aggregates equilibrium constants in this series and to shed more light on their solution geometrical arrangement as they display porphyrin–porphyrin heteroaggregation due to both the dimer as well as dimer/higher-order aggregate assembly, which may differ substantially from those observed in the free base and square-planar metalloporphyrin self-aggregates.

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