An Electron Spin Resonance Study of the Aggregation of Copper(II) Water-soluble Porphyrins

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Electron spin resonance measurements involving aqueous solutions of copper(II) tetraphenylporphyrintetrasulphonate have been carried out both at room temperature and 77 K to provide evidence for the process of aggregation. The addition of dimethylformamide or dimethyl sulphoxide to the aqueous solution containing the copper(II) chelate results in a breaking up of the polymer units into a distribution of species which include dimeric and monomeric species. The dimeric species are formed only to a minor extent. A similar study of solutions containing the copper(II) chelate of tetracarboxyphenylporphyrin showed that breakdown to monomeric species only occurred in solutions containing a high percentage of dimethylformamide or dimethyl sulphoxide, and that here, too, specific dimeric species did not occur in any great amount. The magnetic parameters have been determined for the monomeric chelates.

THE process of aggregation is of ubiquitous occurrence in solutions containing porphyrins and metalloporphyrins and a variety of techniques have been employed in its study.[1] Solutions containing metalloporphyrins may be described in terms of an equilibrium mixture containing polymeric, dimeric, and monomeric forms. The occurrence of the metalloporphyrins in the monomeric form is favoured in dilute solution (*ca.* 10^{-6}M). Increasing concentrations may well result in higher aggregates being formed. A number of studies have shown that the distribution in solution of polymeric, dimeric, and monomeric species of water-soluble metalloporphyrins may be altered in favour of monomeric species by the simple expedient of the addition of certain water-miscible organic solvents to the aqueous solution. It has been shown that the symmetrically substituted water-soluble copper(II) tetrasulphonated phthalocyanine (tspc) chelate is aggregated in aqueous solution, but that dimeric and monomeric species were formed by addition of dimethylformamide. Boyd and Smith[2] carried out e.s.r. measurements on 1.0×10^{-2}M-solutions of the copper(II) and vanadyl tspc chelates in an investigation designed to study the polymer, dimer, and monomer equilibrium processes by manipulating the solvent composition. The present investigation was carried out to determine the aggregation properties of the copper(II) chelates of the symmetrically *meso*-substituted porphyrins, tetrasulphonatotetraphenylporphyrin (tspp) and tetracarboxytetraphenylporphyrin (tcpp), in solutions of comparable concentrations (*ca.* 10^{-3}M) to those used in the similar studies of [Cu$^{\text{II}}$(tspc)]. Previous studies on the aggregation properties of [Cu(tcpp)] were carried out in dilute solutions (*ca.* 10^{-5}M) and examined the kinetics of dimerization.[3]

RESULTS

Tspp Chelates.—The e.s.r. spectrum of [Cu(tspp)] in water solution at room temperature consisted of a single absorption near $g = 2$. Addition of dimethylformamide brings about a resolution of the signal, an effect which reaches its maximum when the solvent contained 25% by volume of dimethylformamide. The signal at this stage is typical of that expected from monomeric copper(II) porphyrins tumbling in solution.

The e.s.r. spectrum due to an aqueous solution of [Cu(tspp)] at a sample temperature of 77 K consisted of a single isotropic resonance at $g = 2.06$ with a peak-to-peak derivative width of 90 G. The progressive addition of dimethylformamide to the solution prior to freezing to 77 K resulted in the diminution of the isotropic resonance and the simultaneous increase in intensity of copper(II) hyperfine and nitrogen superhyperfine structure. This structure was apparent even when the solution mixture contained only 5% (v/v) of dimethylformamide. When the solution mixture contained about 10% (v/v) of dimethylformamide, a weak signal was observed near $g = 4$. The intensity of this signal was critically dependent on the amount of dimethylformamide present. When the solution mixture contained more than 15% (v/v) of dimethylformamide, the signals in the $g = 2$ region due to the monomeric copper(II) porphyrin were readily discerned and comprised the major contribution to the spectrum.

The addition of dimethyl sulphoxide to the sqeous solution of [Cu(tspp)] brought about similar spectral changes, although no low-field component of the spectrum was observed. The signals at g *ca.* 2 were not completely resolved until the solvent contained about 50% (v/v) of dimethylformamide.

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[1] P. D. W. Boyd, T. D. Smith, J. H. Price, and J. R. Pilbrow, *J. Chem. Phys.*, 1972, **56**, 1253.

[2] P. D. W. Boyd and T. D. Smith, *J.C.S. Dalton*, 1972, 839.

[3] R. F. Pasternack, L. Frances, D. Raff, and E. Spiro, *Inorg. Chem.*, 1973, **12**, 2606.

Tcpp Chelates.—The e.s.r. spectrum of [Cu(tcpp)] in water at room temperature consisted of a single isotropic absorption at *g ca.* 2. Addition of dimethylformamide resulted in a resolution of the signal consistent with the formation of monomeric species when the solution contained more than 20% (v/v) of this solvent. The presence of monomeric species was not so readily discerned in solutions containing 20% (v/v) of Me_2SO, and the single isotropic line persisted in solutions containing up to 50% (v/v) of ethanol and acetonitrile.

The e.s.r. spectrum of an aqueous solution of [Cu(tcpp)] at a sample temperature of 77 K consisted of a single isotropic resonance at *g ca.* 2 with a peak-to-peak derivative width of only 60 G. The addition of dimethylformamide to the solutions prior to freezing to 77 K did not alter the signal in any way until the solvent contained more than 50% (v/v) of dimethylformamide. The [Cu(tcpp)] chelate is sufficiently soluble in dimethylformamide solutions to allow the e.s.r. spectrum to be recorded, and the spectrum in solutions containing 90% (v/v) of dimethylformamide was entirely due to monomeric species. The single line resonance also persisted at 77 K in aqueous solutions containing 50% (v/v) of any one of Me_2SO, methanol, ethanol, acetone, or acetonitrile. No resonances near *g ca.* 4 were observed in any of these solutions.

Interpretation of Results.—The signals observed at 77 K due to solutions of [Cu(tspp)] and [Cu(tcpp)] which contain high percentages of dimethylformamide or Me_2SO are characteristic of those observed for the monomeric copper(II) porphyrins where the unpaired electron of the copper(II) ion interacts with the four nearest nitrogen atoms.

The magnetic parameters determined by computer simulation of the e.s.r. spectra of the monomeric species are given in the Table and are based on the use of the spin Hamiltonian, equation (1), where the symbols have their usual meanings.

$$\mathscr{H} = g_{\parallel}\beta H_zS_z + g_{\perp}\beta(H_xS_x + H_yS_y) + A_{\parallel}S_zI_z + A_{\perp}(S_xI_x + S_yI_y) + Q\{I_z^2 - \tfrac{1}{3}I(I + 1)\} + \sum_{i=1}^{4}\{A_{\parallel}^{N}S_zI_{iz}^{N} + A_{\perp}^{N}(S_xI_{ix}^{N} + S_yI_{iy}^{N})\} \quad (1)$$

The superhyperfine interactions for all the four nearest-neighbour nitrogen atoms in the porphyrin plane were found to be equivalent and were described in terms of two hyperfine constants, $A_{\parallel}^{N}$ and $A_{\perp}^{N}$. In (1) I_{ix}^{N}, I_{iy}^{N}, and I_{iz}^{N} represent the nuclear spins of the individual nitrogen nuclei. The parallel axis here corresponds to the copper–nitrogen bond direction. The differences between $A_{\parallel}^{N}$ and $A_{\perp}^{N}$ given in the Table are just outside the limits of error. The parameters for [Cu(tspp)] are closely similar to those for copper(II) tetraphenylporphyrin in chloroform solution, as described by Manoharan and Rogers.[4] In particular, the coupling of the unpaired electron to the four in-plane nitrogens is the same to within the limits of error.

In order to obtain good agreement between the experimental and computed lineshapes in the parallel regions of the spectrum, the different nuclear magnetic moments of the two isotopes of copper had to be taken into account.

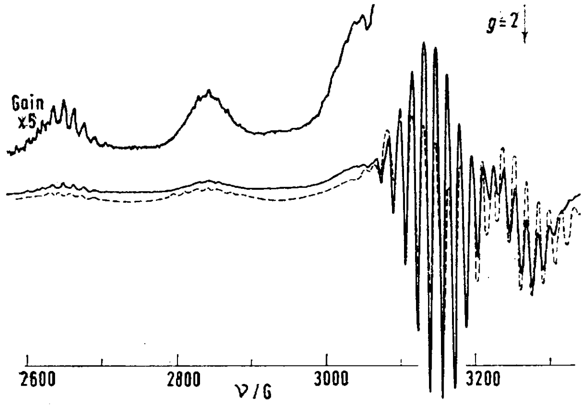
In each case the single isotropic absorption observed in frozen aqueous solution at 77 K can best be explained as arising from a type of 'exchange narrowing' effect resulting from the cumulative interaction of the electron spins of a large number of copper(II)-containing molecules stacked relatively close together. A similar spectrum was observed in frozen aqueous solutions containing the [Cu(tspc)] chelate.[2]

The weak lines observed at *g ca.* 4 in the case of the [Cu(tspp)] chelate are attributed to $\Delta M_s = \pm 2$ transitions arising from magnetic point dipole–dipole interactions in dimeric species. The associated $\Delta M_s = \pm 1$ resonances at *g ca.* 2 cannot be identified as they are obscured by the signals due to monomeric species.

Spin Hamiltonian parameters for the water-soluble porphyrins

Porphyrin	$g_{\parallel}$	$g_{\perp}$	$A_{\parallel}$	$A_{\perp}$	$A_{\parallel}^{N}$	$A_{\perp}^{N}$	Q
[Cu(tspp)] in 100%	2.204	2.069	208	<20	14	16	<4
dmf	±0.002	±0.002	±2		±1	±1	
[Cu(tcpp)] in 90%	2.206	2.071	206	<20	14	16	<4
dmf 10% H_2O	±0.002	±0.002	±2		±1	±1	

The values of the hyperfine constants $A_{\parallel}$ and $A_{\perp}$ are those for the isotope ^{63}Cu. The hyperfine coupling constant for the isotope ^{65}Cu is given by $^{65}A/^{63}A = 1.08$. All hyperfine coupling constants and the quadrupole interaction constant, Q, are given in $cm^{-1} \times 10^4$.



—— *X*-band e.s.r. spectrum at 77 K of [Cu(tspp)] (1.0×10^{-3}M) in dimethylformamide. Microwave frequency 9.141 GHz; — — — Computer simulated spectrum of [Cu(tspp)] using the parameters given in the Table

Some structural information may be obtained from the low-field signals if it is assumed that the magnetic parameters, *g*-values, and hyperfine constants will be the same as those relevant to the monomeric species. Thus, using the parameters given in the Table, and the theoretical treatment outlined previously,[1,2] the computer simulation of the experimental $\Delta M_s = \pm 2$ signal gives the distance between the copper(II) ions in the dimeric species as 4.5 ± 0.5 Å. This is similar to that found for the dimeric form of [Cu(tspc)].

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[4] P. T. Manoharan and M. T. Rogers, 'Electron Spin Resonance of Metal Complexes,' ed. Teh Fu Yen, Adam Hilger Ltd., London, 1969, p. 143—173.

It is argued that the effect of adding dimethylformamide or dimethyl sulphoxide is to break down the higher-order aggregates which exist in aqueous solution, and it is envisaged that the polymeric form will give rise to lower-order aggregates on the way to the monomeric stage. However, the mode of breakdown of the polymeric aggregate by addition of dimethylformamide or dimethyl sulphoxide is quite different in both the water-soluble porphyrins studied compared with that found in [Cu(tspc)]. Both the copper(II) and vanadyl tspc chelates, in the appropriate range of solvent composition, show easily observable signals in the *g ca.* 4 region, and these signals provide unequivocal evidence for the formation of dimeric species. Indeed, at certain solvent compositions, the dimeric species is the principal species present. A similar observation may be made for the unsymmetrically substituted porphyrins.[1]

By way of contrast, there is scant evidence for the presence of such dimeric species in the symmetrically substituted porphyrins. The distribution of species in solution is almost wholly due to monomeric or polymeric forms of the chelates.

EXPERIMENTAL

Tetraphenylporphyrin was prepared by a modification of method described in the literature.[5] Thus benzaldehyde (10 ml) and freshly distilled pyrrole (7 ml) were added to a refluxing solution of propionic acid (300 ml). After 30 min under reflux the solution was cooled to room temperature and filtered. The crude product was air dried and purified by column chromatography using alumina as adsorbent and chloroform as eluant followed by solvent extraction of the product (3.4 g) with benzene (Found: C, 85.9; H, 5.0; N, 9.1. Calc. for $C_{44}H_{30}N_4$: C, 85.9; H, 4.92; N, 9.12%).

Some concern has been expressed on the literature reports that pure materials can be obtained from the sulphonation of tetraphenylporphyrin.[6] In the present work tetraphenylporphyrintetrasulphonic acid was prepared by a modification of the method outlined in the literature.[7] Tetraphenylporphyrin (2 g) and concentrated sulphuric acid (30 ml) were ground together with mortar and pestle. The mixture was heated on a steam-bath for 4 h, stoppered, and set aside for 3 days. Addition of ice (100 g) resulted in a fine green precipitate being formed which was collected by centrifugation; this was repeatedly washed with acetone. Purification of the crude product was effected by column chromatography to eliminate the mono-, di-, and tri-sulphonated tetraphenylporphyrin. The column was packed with acid-washed Celite and chloroform–water–pyridine in the volume ratios 2 : 1 : 1, while a mixture of pyridine and chloroform was used as eluant. The product (1.2 g) was obtained as green flaky crystals (Found: C, 56.6; H, 3.5; N, 5.9; S, 13.6. Calc. for $C_{44}H_{30}N_4O_{12}S_4$: C, 56.52; H, 3.22; N, 5.98; S, 13.89%).

The copper(II) chelate of tpps was prepared as follows. An aqueous solution of tpps (1.0 g) was converted into the tetrasodium salt by addition of 0.1M-sodium hydroxide. To this solution was added an aqueous solution of cupric acetate (0.3 g) and the reaction mixture was heated for 1 h. Most of the water was removed to allow precipitation of the copper(II) chelate (0.9 g) which was purified by recrystallisation from dimethylformamide–benzene (Found: C, 43.0; H, 3.35; N, 4.5; S, 10.2. Calc. for $C_{44}H_{24}CuN_4Na_4O_{12}S_4 \cdot 8H_2O$: C, 43.20; H, 3.26; N, 4.59; S, 10.4%). The copper(II) chelate of tetracarboxyphenylporphyrin was prepared as described in the literature.[3]

X-Band e.s.r. measurements were carried out at room temperature and 77 K. The spectrometer and ancillary equipment was as described previously.[1]

[4/2395 *Received, 18th March,* 1974]

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[5] A. D. Adler, F. R. Longs, J. D. Finarelli, J. Goldmacher, J. Assour, and L. Korsakoff, *J. Org. Chem.*, 1967, **32**, 476.

[6] Dr. Yalman (Antioch College), comments on a paper by R. F. Pasternack, *Ann. N.Y. Acad. Sci.*, 1973, **206**, 628.

[7] J. Winkelman, G. Slater, and J. Grossman, *Cancer Research*, 1967, **27**, 2060.