A Spectroscopic Study of the Acid Ionization of Porphyrins

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N-Methyloctaethylporphyrin and the corresponding N-(3-bromo-n-propyl)porphyrin ionize in solutions containing aqueous sodium hydroxide to their monoanions by loss of a single proton. Octaethylporphyrin, aetioporphyrin I, and monoaza-aetioporphyrin I ionize to their dianions by loss of two protons. No evidence for the existence of appreciable concentrations of the monanions of the three compounds in solutions containing sodium hydroxide could be detected by visible spectrophotometry. N-Methyl substitution in a porphyrin increases the acidity of the remaining NH atom.

UNSUBSTITUTED porphyrins exist as the neutral compounds in aqueous sodium hydroxide solutions but ionize as acids in concentrated alcoholic solutions of alkoxides.[1-3] Dianionic alkali metal salts of porphyrins have been isolated.[4] Visible spectra of the dianions have been reported [3] and are similar to the spectra of the corresponding dications.[2] The ionization of porphyrins in strongly basic solutions usually involves the loss of the protons from both NH groups and therefore the formation of the monoanions is not observed.[3] The failure to observe monoanions implies that the ionization constant for the removal of the first proton from a neutral porphyrin is probably less than the ionization constant for the removal of the NH proton from the monoanion. The spectrum of a monoanion has been observed for N-methylaetioporphyrin, which has only one ionizable proton and therefore exists as the monoanion in sodium alkoxide solutions. [1,3] The pK_a value for the ionization of N-methylaetioporphyrin has been estimated to be ca. 14—15.[1]

The basicity of aqueous or alcoholic solutions of strong bases is greatly enhanced by the addition of dimethyl sulphoxide.[5-7] Solutions of bases in water-dimethyl sulphoxide or alcohol-dimethyl sulphoxide mixtures have been widely used as solvent systems in spectrophotometric studies of the ionization of many weak acids but not of porphyrins. The present paper reports an investigation of the ionization of two porphyrins, one aza-porphyrin and two N-monosubstituted porphyrins in solutions of aqueous sodium hydroxide in dimethyl sulphoxide.

EXPERIMENTAL

The porphyrins were prepared as before [8] and stock solutions (ca. 5×10^{-5} mol l⁻¹) in toluene were prepared. A solution of sodium hydroxide in water was standardized with anhydrous sodium carbonate via aqueous hydrochloric acid. Solutions for study were prepared from the solution of porphyrin in toluene, aqueous sodium hydroxide, water, and dimethyl sulphoxide. The solvent composition was water 10% v/v, dimethyl sulphoxide 82% v/v, and toluene 8% v/v and was the same for all measurements. The visible spectra of the porphyrins in the solvent mixture were measured as a function of sodium hydroxide concen-

tration using a Unicam SP 800 spectrophotometer with a thermostatted (25.0 ± 0.2 °C) cell compartment. Spectra were recorded as soon as possible after preparation of the solution because, particularly for aetioporphyrin I, slow, irreversible decompositions occurred.

RESULTS AND DISCUSSION

The five porphyrins whose ionization has been studied are 2,3,7,8,12,13,17,18-octaethylporphyrin, aetioporphyrin I, 2,3,7,8,12,13,17,18-octaethyl-21-methylporphyrin, 2,3,7,8,12,13,17,18-octaethyl-21-(3-bromo-n-propyl)porphyrin, and 2,8,12,18-tetraethyl-3,7,13,17-tetramethyl-20-azaporphyrin. All five macrocycles existed as the neutral compounds in the water–toluene–dimethyl sulphoxide solvent to which no sodium hydroxide had been added. The spectra were similar to the corresponding spectra of the porphyrins in toluene.[8]
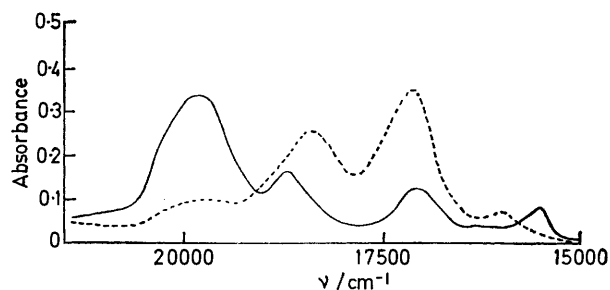

FIGURE 1 Spectrum of the neutral form (full line) and monoanion (dashed line) of N-methyloctaethylporphyrin. Sodium hydroxide concentrations were 0 and 0·02 mol l⁻¹ respectively

The addition of sodium hydroxide caused the ionization of the two N-monosubstituted porphyrins to their monoanions. The visible spectrum of the monoanion of N-methyloctaethylporphyrin is shown in Figure 1. The absorption maxima for the monoanion were at 19,750, 18,350, 17,100, and 16,000 cm⁻¹. The spectrum of the monoanion of N-(3-bromo-n-propyl)octaethylporphyrin was similar and showed maxima at 19,750, 18,300, 17,050 and 15,900 cm⁻¹.

The ionization of an N-monosubstituted porphyrin SH to its monoanion S⁻ in a solution containing sodium hydroxide may be represented by equilibrium (1). The equilibrium constant K_1 [equation (2)] is related

[1] W. K. McEwen, J. Amer. Chem. Soc., 1936, 58, 1124.
[2] J. E. Falk, ' Porphyrins and Metalloporphyrins,' Elsevier, Amsterdam, 1964, p. 26.
[3] T. I. Strelkova and G. P. Gurinovich, Biophysics, 1968, 13, 1164.
[4] H. Fischer and W. Neumann, Annalen, 1932, 494, 225.

[5] C. H. Rochester, Quart. Rev., 1966, 20, 511.
[6] K. Bowden, Chem. Rev., 1966, 66, 119.
[7] C. H. Rochester, ' Acidity Functions,' Academic Press, London, 1970.
[8] R. Grigg, R. J. Hamilton, M. L. Jozefowicz, C. H. Rochester, R. J. Terrell, and H. Wickwar, preceding paper.

to the ionization ratio $R = (c_{S^-}/c_{SH})$ of the porphyrin in a solution containing a concentration c_{OH^-} of hydroxide ions by equation (3) (a represents an activity and c a

$$SH + OH^- \rightleftharpoons S^- + H_2O \qquad (1)$$
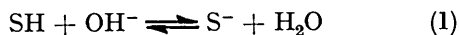
$$K_1 = (a_{S^-}a_{H_2O}/a_{SH}a_{OH^-}) \qquad (2)$$

$$-pK_1 = \log R - \log c_{OH^-} + \log \left(\frac{a_{H_2O}y_{S^-}}{y_{SH}y_{OH^-}} \right) \qquad (3)$$

concentration on the molar scale, and y represents an activity coefficient such that $a_i = c_i y_i$ for species i).
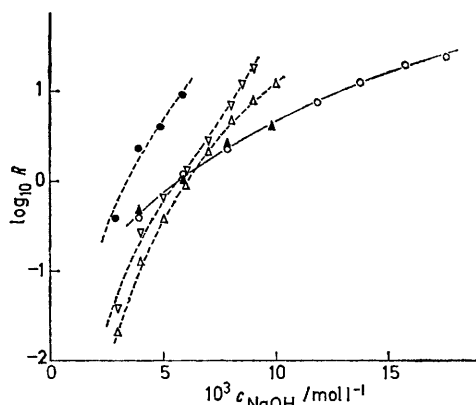

FIGURE 2   The variation of the ionization ratios R with sodium hydroxide concentration for △, aetioporphyrin I; ▽, octaethylporphyrin; ●, aza-aetioporphyrin I; ▲, N-methyloctaethylporphyrin; and ○, N-(3-bromo-n-propyl)octaethylporphyrin

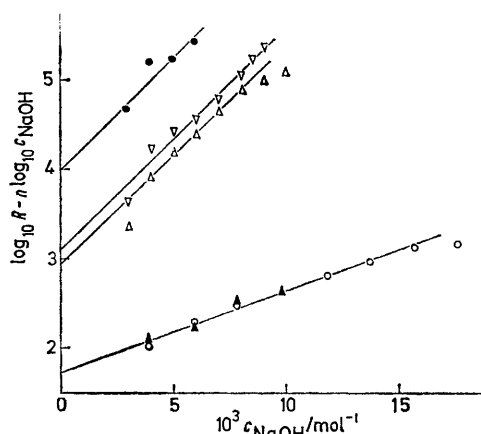

FIGURE 3   The evaluation of pK values by the extrapolation method: △, aetioprophyrin I ($n = 2$); ▽, octaethylporphyrin ($n = 2$); ●, aza-aetioporphyrin I ($n = 2$); ▲, N-methyloctaethylporphyrin ($n = 1$); and ○, N-(3-bromo-n-propyl)-octaethylporphyrin ($n = 1$)

Ionization ratios for the two N-monosubstituted porphyrins were deduced from optical density measurements by the standard method.[5,7] The variation of $\log_{10}R$ with sodium hydroxide concentration is shown in Figure 2. The results for the two porphyrins were similar which indicates that their acid ionization constants are nearly identical. The equilibrium constants K_1 were deduced by extrapolation of a graph of $\log_{10}(R/c_{OH^-})$ against c_{OH^-} to zero sodium hydroxide

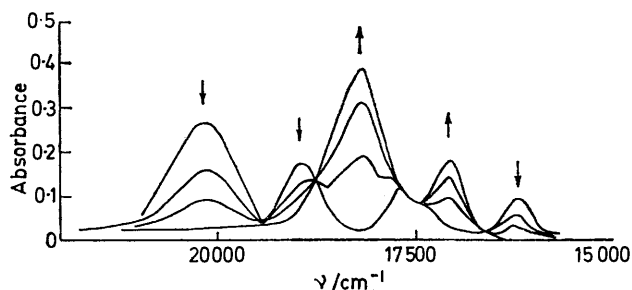concentration (Figure 3). Standard states may be chosen such that the activity coefficients of solute

FIGURE 4   Visible spectra of aetioporphyrin I in solutions for which the sodium hydroxide concentrations were 0 (neutral form), 0·006, 0·008, and 0·020M (dianion). Arrows indicate the direction of the absorbance changes for increasing NaOH concentration

species and the activity of water are unity in the pure solvent mixture ($c_{NaOH} = 0$). Hence [equation (3)] $-pK_1 = \log_{10}(R/c_{OH^-})$ when $c_{NaOH} = 0$. The intercept on the ordinate axis of Figure 3 gives $pK_1 = -1·73$ for both N-monosubstituted porphyrins. The positive slope of the curve gives a measure of the variation of $\log_{10}(a_{H_2O}y_{S^-}/y_{SH}y_{OH^-})$ with sodium hydroxide concentration. It is not surprising that the activity coefficient term in equation (3) is sensitive to such low concentrations of electrolyte in the particular solvent system being used.

Aetioporphyrin I, octaethylporphyrin, and aza-aetioporphyrin I ionize directly to their dianions in the presence of sodium hydroxide. The spectral changes which occurred with increasing sodium hydroxide concentration showed no evidence at any concentration of base for the existence of appreciable amounts of the monoanions. Typical spectra are illustrated in Figures 4 and 5. The isosbestic points support the conclusion that the monoanions are only present in the solutions in
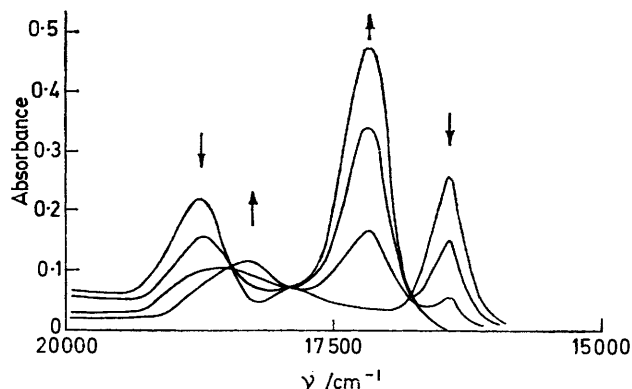

FIGURE 5   Visible spectra of aza-aetioporphyrin I in solutions for which the sodium hydroxide concentrations were 0 (neutral form), 0·003, 0·004, and 0·010M (dianion). Arrows indicate the direction of the absorbance changes for increasing NaOH concentration

negligible proportions. The spectral changes for octaethylporphyrin were similar to those for aetioporphyrin I. The absorption maxima of the dianions were at

18,150 and 17,000 cm^{-1} for octaethylporphyrin, 18,150 and 17,050 cm^{-1} for aetioporphyrin I, and 18,300 and 17,200 cm^{-1} for aza-aetioporphyrin I.

The ionization of a porphyrin SH_2 to its dianion S^{2-} involves the two proton transfer equilibria (4) and (5) for which the equilibrium constants K_1 and K_2 are given by equations (6) and (7). The ionization ratio $R = (c_{S^{2-}}/c_{SH_2})$ is therefore related to the sodium hydroxide

$$SH_2 + OH^- \rightleftharpoons SH^- + H_2O \qquad (4)$$

$$SH^- + OH^- \rightleftharpoons S^{2-} + H_2O \qquad (5)$$
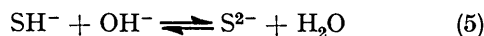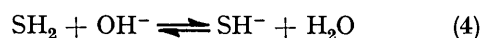
$$K_1 = (a_{SH^-} a_{H_2O}/a_{SH_2} a_{OH^-}) \qquad (6)$$

$$K_2 = (a_{S^{2-}} a_{H_2O}/a_{SH^-} a_{OH^-}) \qquad (7)$$

$$-(pK_1 + pK_2) = \log_{10} R - 2 \log_{10} c_{OH^-} + \log_{10} \left(\frac{a_{H_2O}{}^2 \, y_{S^{2-}}}{y_{SH_2} y_{OH^-}{}^2} \right) \qquad (8)$$

concentration by equation (8). The values of $\log_{10} R$ for the three porphyrins were parallel functions of sodium hydroxide concentration but varied approximately twice as rapidly with increasing concentration of base as the $\log_{10} R$ values for the N-monosubstituted macrocycles (Figure 2). The differences between the slopes of the curves in Figure 2 provide further evidence that aetioporphyrin I, octaethylporphyrin, and aza-aetioporphyrin I ionize to form their dianions in contrast to the two N-monosubstituted porphyrins which form their monoanions. Extrapolation of plots of $\log_{10} (R/c_{OH^-}{}^2)$ against c_{NaOH} to $c_{NaOH} = 0$ enabled values of $(pK_1 + pK_2)$ to be deduced [equation (8), Figure 3]. The values are -2.94 for aetioporphyrin I, -3.10 for octaethylporphyrin, and -4.00 for aza-aetioporphyrin I.

The NH atoms of aetioporphyrin I are slightly less acidic than those of octaethylporphyrin because of the electronic effect of substituting four ethyl groups for methyl groups in the 3, 7, 13, and 17 positions of the macrocycle. The acid ionization constant of the mono-cation formed by monoprotonation of aetioporphyrin I is similarly slightly less than the acid ionization constant of the monocation derived from octaethylporphyrin.[8] The monocation of aza-aetioporphyrin I is also more acidic than the monocation of aetioporphyrin I [8] which is in accord with the relative acidities of the neutral compounds observed here.

For N-methyloctaethylporphyrin $pK_1 = -1.73$ and for octaethylporphyrin $(pK_1 + pK_2) = -3.10$. The electronic effect of an N-methyl group would be expected to cause a slight decrease in the equilibrium constant K_1 for the ionization of the first NH proton. This leads to the prediction that $pK_1 < -1.73$ $(K_1 > 53.7)$ and therefore $pK_2 > -1.37$ $(K_2 < 23.4)$ for octaethylporphyrin. However if these values of K_1 and K_2 are correct then the monoanion of octaethylporphyrin should be spectroscopically detectable at certain concentrations of sodium hydroxide. The absence of any evidence for the monoanion in the spectra recorded in the present work suggests $pK_1 > -1.73$ for octaethylporphyrin and therefore that N-methyl substitution increases the acidity of the hydrogen atom on the unsubstituted NH group. The increase in acidity must be associated with the release of steric strain, present in the neutral compound, when the proton is lost from N-methyloctaethylporphyrin. McEwen [1] has shown that N-methylaetioporphyrin is similarly a stronger acid than aetioporphyrin I. However the estimate [1] of pK_a ca. 14—15 for N-methylaetioporphyrin would appear to be too low. Thus we have observed that 4-chloroaniline $(pK_a = 21.33$ in water at 25 °C) [9] and diphenylamine $(pK_a = 22.44)$ [9] were completely ionized in solutions of sodium hydroxide in toluene–water–dimethyl sulphoxide in the same concentration range as was used in the present study of the ionization of the porphyrins.

[9] D. Dolman and R. Stewart, *Canad. J. Chem.*, 1967, **45**, 911.