# Interaction between Porphyrins and Hydroxylated Compounds. Part 1. Study of Tetraphenylporphyrin Free Base and its N-Methyl Derivatives in the Presence of p-Nitrophenol

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The complexation of tetraphenylporphyrin free base ($P_I$) and its N-methyl ($P_{II}$) and $N_aN_b$-dimethyl ($P_{III}$) derivatives by p-nitrophenol is studied by u.v.–visible and i.r. spectroscopy in benzene and dichloromethane. $P_I$ and $P_{II}$ form a 2 : 1 and a 1 : 1 complex, respectively, with p-nitrophenol through intermolecular hydrogen bonding in benzene and an undissociative ion pair in dichloromethane. A study of the porphyrin concentration in the presence of excess of p-nitrophenol shows, in $CH_2Cl_2$, a self-association of $P_I$, which is described as the dimerization of the monocomplexed ion-pair species. Equilibrium constants are determined for several complexation reactions as well as for the dimerization process.

Nitrogenous bases and hydroxylated compounds are known to give hydrogen-bonded complexes, the evolution of which can lead to ion-pairs, depending on the dielectric constant of the medium or on the relative $pK_a$ values of the substrates, equation (1). Numerous papers [1] are devoted to the study of

$$-OH + N \rightleftharpoons -OH \cdots N \rightleftharpoons -O^{\delta-} \cdots^{\delta+} HN \quad (1)$$
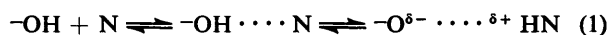
such systems. However, to the best of our knowledge, no information is available on the nature of the association sites between hydroxylated derivatives and compounds with numerous nitrogen centres, such as porphyrins, despite the importance of such systems in biological processes.[2] The present work is a spectroscopic approach to the interactions between p-nitrophenol (ArOH) and tetraphenylporphyrin ($P_I$) or its monomethyl and $N_aN_b$-dimethyl derivatives ($P_{II}$ or $P_{III}$) (Figure 1). For this study, two aprotic solvents, benzene and dichloromethane, have been selected, owing to the difference in their dielectric constants.

## Experimental

*Chemicals.*—Tetraphenylporphyrin $P_I$ (Strem) was used as received. Its purity was checked by t.l.c. and u.v.–visible spectroscopy.

N-Methyl- and $N_aN_b$-dimethyl-tetraphenylporphyrins were synthesized using iodomethane and tetraphenylporphyrin following the procedure described by Al-Hazimi et al.[3] They were purified by t.l.c. on silica (eluant MeOH–$CH_2Cl_2$ 1 : 9).

p-Nitrophenol (Prolabo) was sublimed under vacuum at 100 °C.

*Solvents.*—The solvents (Prolabo) were distilled twice from calcium chloride and kept under argon.

*Spectroscopic Measurements.*—U.v.–visible spectra were recorded on a Cary 219 spectrophotometer. Quartz cells of 10 or 1 mm optical path length were flushed with dry argon. All subsequent absorbances were normalized in the 10 mm optical path length cell. The temperature was 23 ± 1 °C.

I.r. spectra were recorded on a Perkin-Elmer 281 spectrophotometer with KBr cells of 0.1 mm optical path length.

## Results

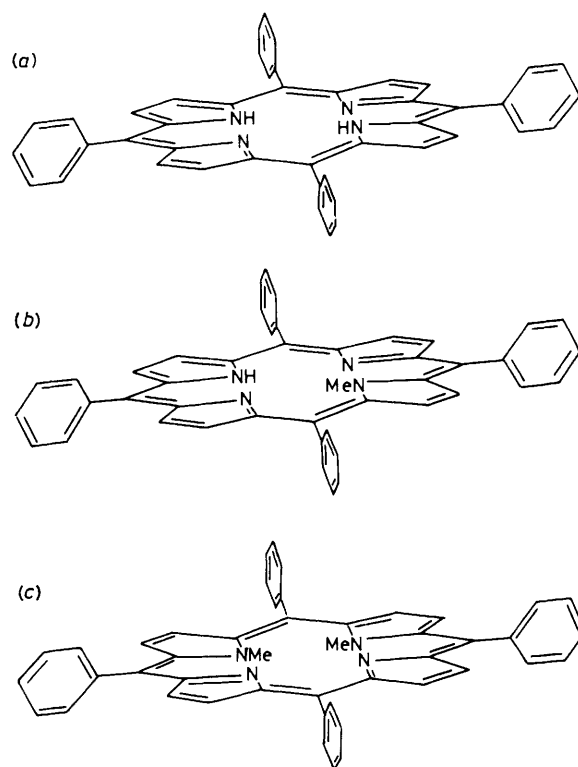*Complexation Equilibrium Constants of the Porphyrin–p-Nitrophenol System.*—(a) Benzene (D = 2.28). On addition



Figure 1. Schematic representation of $P_I$ (a), $P_{II}$ (b), and $P_{III}$ (c)

of a large excess of p-nitrophenol (0.03M < [ArOH] < 0.1M for $P_I$ and 0.003M < [ArOH] < 0.01M for $P_{II}$) to a ca. $10^{-5}$M benzene solution of porphyrin,† a red shift of the α, β, γ, and δ absorption bands of $P_I$ and $P_{II}$ is observed (Figure 2) and isosbestic points appear. No such modification is observed for the spectrum of $P_{III}$ under the same conditions. Obviously, a complex is formed between ArOH and $P_I$ and $P_{II}$. By analogy with results obtained on other nitrogenous bases, such as amines, the existence of such complexes can reasonably

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† The Beer–Lambert law has been checked up to the solubility limit of the porphyrin, ruling out any association phenomena.
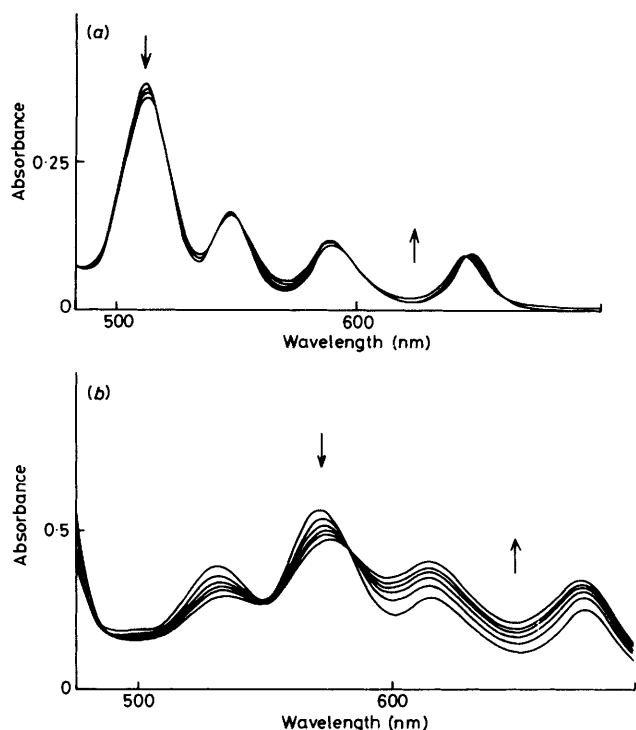
Figure 2. (a) Spectral modification on addition of p-nitrophenol to a solution of $P_I$ in benzene. Arrows indicate absorbance increase or decrease on increasing [ArOH] (in M): 0, 0.031, 0.050, 0.075, 0.084, 0.097. (b) Spectral modification on addition of p-nitrophenol to a solution of $P_{II}$ in benzene. Arrows indicate absorbance increase or decrease on increasing [ArOH] (in M): 0, 0.0025, 0.0043, 0.0061, 0.0079, 0.01

be ascribed to the formation of a hydrogen bond such as is shown in equilibrium (2).

$$n\text{ArOH} + P \underset{}{\overset{K_1}{\rightleftharpoons}} (\text{ArOH})_n \cdots P \qquad (2)$$

$$K_1 = \frac{[(\text{ArOH})_n \cdots P]}{[\text{ArOH}]^n[P]} \qquad (3)$$

The stoicheiometry $n$ of the complex and the formation equilibrium constant $K_1$ [equation (3)] are obtained using the modified Benesi–Hildebrand [4] equation, equation (4), where

$$\frac{1}{A_0 - A} = \frac{1}{A_0 - A_\infty} + \frac{1}{A_0 - A_\infty} \cdot \frac{1}{K_1} \cdot \frac{1}{[\text{ArOH}]^n} \qquad (4)$$

$A_0$ and $A_\infty$ are the absorbances of the porphyrin and the complex $(\text{ArOH})_n \cdots P$, respectively, and $A$ is the absorbance of the porphyrin-p-nitrophenol mixture in the presence of a given concentration [ArOH] of the hydroxylated compound, equation (5), where $\varepsilon_P$ and $\varepsilon_A$ represent the molecular extinc-

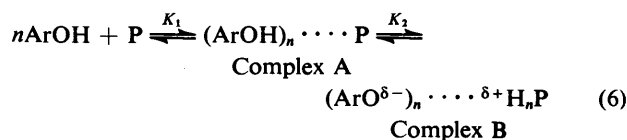$$A = \varepsilon_P[P] + \varepsilon_A[(\text{ArOH})_n \cdots P] \qquad (5)$$

tion coefficients of the porphyrin and its complex, respectively.

(b) Dichloromethane ($D = 9.08$). Identical measurements were carried out in dichloromethane, the dielectric constant of which is much higher than that of benzene. Spectral modifications for $P_I$ and $P_{II}$ are shown in Figure 3. $P_{III}$ undergoes no modification. Qualitatively, it is obvious that the gradual addition of p-nitrophenol to the porphyrin solution induces a more pronounced hyperchromic effect than is observed in benzene. As demonstrated in other nitrogenous
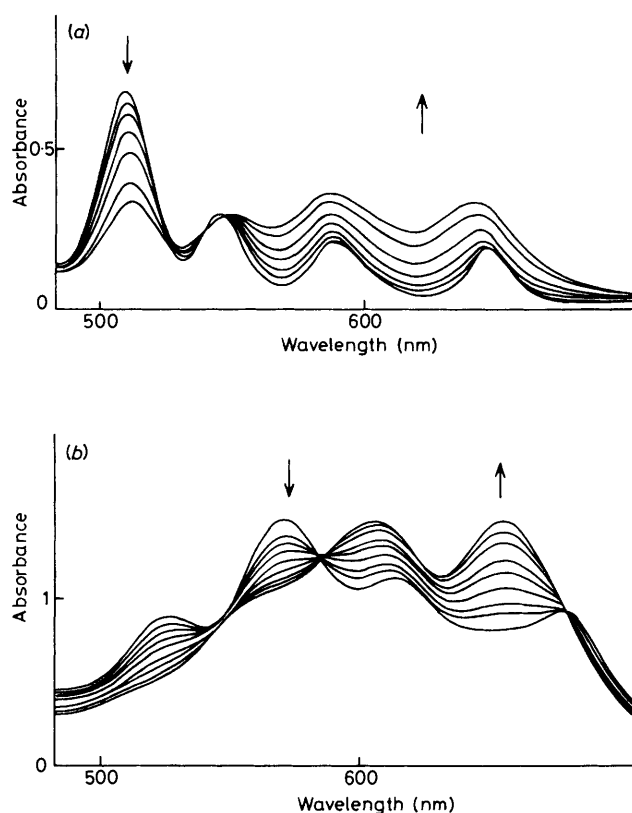
Figure 3. (a) Spectral modification on addition of p-nitrophenol to a solution of $P_I$ in dichloromethane. Arrows indicate absorbance increase or decrease on increasing [ArOH] (in M): 0, 0.07, 0.100, 0.144, 0.182, 0.234, 0.276. (b) Spectral modification on addition of p-nitrophenol to a solution of $P_{II}$ in dichloromethane. Arrows indicate absorbance increase or decrease on increasing [ArOH] (in M): 0, 0.0013, 0.0018, 0.0023, 0.0029, 0.0039, 0.005, 0.006, 0.007. Only the five last spectra have been retained for the calculation of equilibrium constants in order that the condition [ArOH] $\gg$ $[P]_0$ can be fulfilled.

derivatives, this observation stems from the interference of a new entity resulting from the tautomeric equilibrium between the hydrogen-bonded complex already found in benzene and the undissociative ion-pair,[5] equilibrium (6).

$$n\text{ArOH} + P \overset{K_1}{\rightleftharpoons} (\text{ArOH})_n \cdots P \overset{K_2}{\rightleftharpoons}$$

$$\text{Complex A}$$

$$(\text{ArO}^{\delta-})_n \cdots {}^{\delta+}H_nP \qquad (6)$$

$$\text{Complex B}$$

At 660 nm the absorbances of $P_I$ are almost identical in the two solvents. On addition of p-nitrophenol, a much larger increase in this absorbance is observed in dichloromethane than in benzene. The same phenomenon is observed at 620 nm for $P_{II}$. These wavelengths correspond to the absorption maxima of the protonated forms of these porphyrins and these observations give strong support to the formation of complex B. Using obvious notations, expressions (7) and (8) can be written.

$$[P]_0 = [P] + [(\text{ArOH})_n \cdots P] +$$
$$[(\text{ArO}^{\delta-})_n \cdots {}^{\delta+}H_nP] \qquad (7)$$

$$A = \varepsilon_P[P] + \varepsilon_A[(\text{ArOH})_n \cdots P] +$$
$$\varepsilon_B[(\text{ArO}^{\delta-})_n \cdots {}^{\delta+}H_nP] \qquad (8)$$

**Table 1.** Stoicheiometry and formation equilibrium constants for porphyrin–p–nitrophenol complexes

| Substrate | Benzene | | Dichloromethane | | |
| --- | --- | --- | --- | --- | --- |
| | Stoicheiometry of complex | $K_1$ [a] | Stoicheiometry of complex | $K_1$ [a] | $K_2$ [a] |
| $P_I$ | 2 : 1 | $113M^{-2}$ [c] | 2 : 1 | $3.4M^{-2}$ | 1.9 [c] |
| $P_{II}$ | 1 : 1 | $36M^{-1}$ [d] | 1 : 1 | $63M^{-1}$ | 2.0 [e] |
| $P_{III}$ | 0 : 1 | 0 | 0 : 1 | 0 | 0 |
| $Et_3N$ [b] | 1 : 1 | $1900M^{-1}$ | 1 : 1 | $440M^{-1}$ | 0.28 |

[a] See text. [b] Ref. 6; measured in iso-octane ($D = 1.94$) and 1,2-dichloroethane ($D = 10.65$). [c] Estimated at 635 nm ($\varepsilon_A = 2\,972$; $\varepsilon_B = 16\,450$) (uncertainty 35%). [d] Estimated at 570 nm (uncertainty 35%). [e] Estimated at 583 nm ($\varepsilon_A = 88\,808$; $\varepsilon_B = 60\,827$) (uncertainty 35%).

Using equation (9) for $A_1$, expression (10) is derived.

$$A_1 = \frac{\varepsilon_A + K_2\varepsilon_B}{1 + K_2}[P]_0 \qquad (9)$$

$$\frac{1}{A_0 - A} = \frac{1}{A_0 - A_1} + \frac{1}{A_0 - A_1} \cdot \frac{1}{K_1(1 + K_2)} \cdot \frac{1}{[ArOH]^n} \qquad (10)$$

The stoicheiometry $n$ and the overall constant $K_g = K_1(1 + K_2)$ are obtained from the slope and the intercept of the straight line representing equation (10). As a first approximation, the molecular extinction coefficient $\varepsilon_B$ of the ion pair can be taken as that of the protonated form of the porphyrin,[6] the values for which are known for protonated $P_I$ and protonated $P_{II}$. Values of $K_2$ are then calculated from equation (10) and are shown in Table 1. It should be noted that $\varepsilon_A$ is obtained from the value of $A_\infty$ in equation (4), after it has been checked that the molecular extinction coefficient for the pure porphyrin is practically unchanged in benzene and in dichloromethane.

The good linearity of the $\dfrac{1}{A_0 - A} = f\left(\dfrac{1}{[ArOH]^n}\right)$ curves in benzene as well as in dichloromethane implies the absence, or at least the non-interference, of parameters other than those taken into account in the present treatment.

*Self-association of Tetraphenylporphyrin.*—We checked that Beer's law is obeyed by $P_I$, $P_{II}$, and $P_{III}$ in dichloromethane. In benzene and in the presence of excess of p-nitrophenol, a linear relationship is still observed between the absorbance and the analytical concentration of porphyrin. However, the same study performed in dichloromethane with $P_I$ gives a pronounced deviation from linearity as shown in Figure 4 for concentrations of porphyrin higher than $3 \times 10^{-4}M$, while $P_{II}$ and $P_{III}$ show no such phenomena. A new entity is thus obtained, which can be ascribed by analogy with literature [7] results to the equilibrated formation of a dimeric species, equation (11).

$$2 \text{ Monomers} \underset{}{\overset{K_D^{obs}}{\rightleftharpoons}} \text{Dimer} \qquad (11)$$
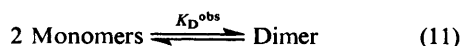
For an analytical concentration of porphyrin $[P]_0$, the classical relationship given in equation (12) can be written,[7]

$$\Delta A = \Delta\varepsilon \frac{4K_D^{obs}[P]_0 + 1 - \sqrt{1 + 8K_D^{obs}[P]_0}}{8K_D^{obs}} \qquad (12)$$
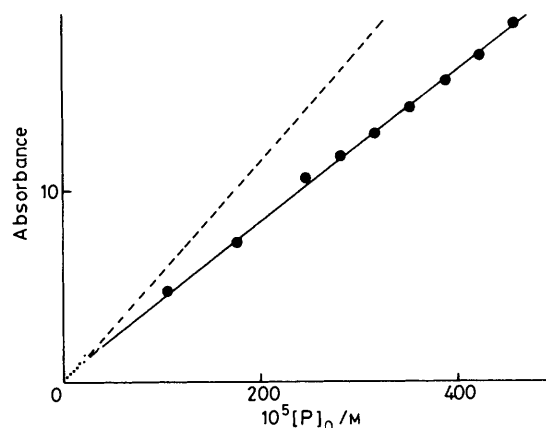


**Figure 4.** Concentration dependence of the absorbance of tetraphenylporphyrin in dichloromethane solution with added p-nitrophenol (0.23M). The straight line shows the Beer's law behaviour at 600 nm ($\varepsilon_{APP} = 5\,930$). The filled circles represent the experimental data and the line passing through the points is the theoretical graph
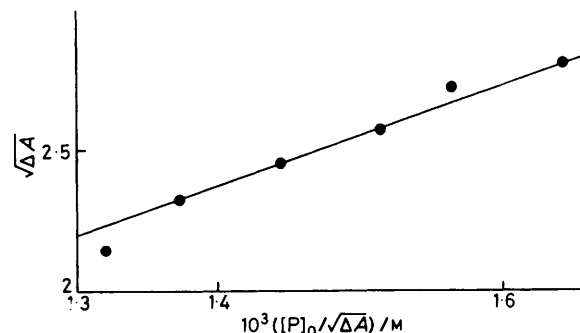


**Figure 5.** Determination of apparent dimerization constant $K_D^{obs}$ (for notation see text)

where $\Delta A$ represents the deviation of the absorbance from linearity and $\Delta\varepsilon$ is as given by equation (13).*

$$\Delta\varepsilon = |2\varepsilon_{APP} - \varepsilon_D| \qquad (13)$$

Relationship (12) can be rewritten in the form of equation (14) (see Appendix).

$$\sqrt{\Delta A} = \frac{\Delta\varepsilon}{2}\frac{[P]_0}{\sqrt{\Delta A}} - \frac{1}{2}\sqrt{\frac{\Delta\varepsilon}{K_D^{obs}}} \qquad (14)$$

Such a linear relationship between $\sqrt{\Delta A}$ and $[P]_0/\sqrt{\Delta A}$ is effectively verified in Figure 5, which strongly supports the equilibrated formation of a dimeric entity hypothesis. As is obvious from Table 2, the equilibrium constant $K_D^{obs}$ is extremely sensitive to the concentration of p-nitrophenol.
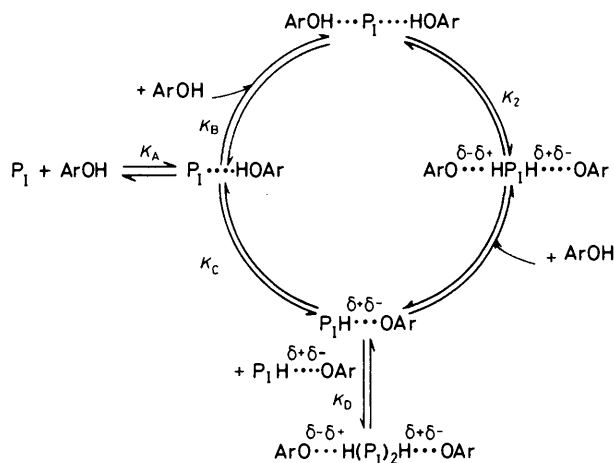
**Discussion**

*Complex Formation.*—The relatively important activation of the benzene ring of p-nitrophenol due to the presence of

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* $\varepsilon_{APP}$ is the apparent absorption coefficient of the monomeric species taken as the slope of the linear part of the curve of Figure 4 corresponding to small concentrations of porphyrin. $\varepsilon_D$ is the molecular extinction coefficient for the dimeric species.

**Table 2.** Variation of the observed dimerization equilibrium constant with the concentration of p-nitrophenol in $CH_2Cl_2$

| [ArOH]/M | 0.101 | 0.151 | 0.163 | 0.207 | 0.223 | 0.235 |
|---|---|---|---|---|---|---|
| $10^{-2}K_D^{obs}/M^{-1}$ | 2 | 19 | 29 | 38 | 47 | 50 |

ArOH$\cdots$P$_1\cdots\cdot$HOAr

+ ArOH

$K_2$

$K_B$

P$_1$ + ArOH $\xrightleftharpoons{K_A}$ P$_1\cdots\cdot$HOAr

$\overset{\delta-\delta+}{ArO}\cdots\overset{\delta+}{HP_1}\overset{\delta-}{H}\cdots\cdot\overset{\delta+\delta-}{OAr}$

$K_C$

+ ArOH

$\overset{\delta+\delta-}{P_1H}\cdots OAr$

$\overset{\delta+\delta-}{+ P_1H}\cdots\cdot OAr$

$K_D$

$\overset{\delta-\delta+}{ArO}\cdots H(P_1)_2\overset{\delta+\delta-}{H}\cdots OAr$

**Scheme.**

**Figure 6.** Plot of $K_D^{obs}$ versus $R$, where $R = \dfrac{[ArOH]^2}{(1 + K_g[ArOH]^2)^2}$. The filled circles represent the experimental data and the line is the theoretical graph

the hydroxy group allows the formation of a charge complex, as was observed by Gouterman and Stevenson,[8] in the tetraphenylporphyrin-trinitrobenzene system to be ruled out. Our results show that the interaction of $P_I$ and $P_{II}$ with p-nitrophenol gives hydrogen-bonded complexes, whose equilibrium can be shifted towards an ion pair when the dielectric constant of the medium increases. The strong increase in absorbance of the porphyrin-p-nitrophenol mixture in dichloromethane in the domain of the protonated forms of $P_I$ and $P_{II}$ supports an interaction between the n-doublet of the pyrollinic nitrogen and the phenolic hydrogen. The difference in the p$K_a$ values of p-nitrophenol (7.15[9]) and tetraphenylporphyrin (p$K_1$ = 4.37 and p$K_2$ = 3.85[10]) is additional support for this argument. Furthermore, a progressive disappearance on the i.r. spectrum of the valence vibration band $\nu_{NH}$ of the tetraphenylporphyrin (at 3 315 cm$^{-1}$ [11]) is observed when the concentration of p-nitrophenol varies from 0.1 to 0.27M. This result shows the formation of a second hydrogen bond, which is weaker than the first one, and which arises between the doublet of the phenolic oxygen (p$K_a \ll$ 0 [12]) and the pyrollic hydrogen of the porphyrin (2 < p$K_3$ < 7, 0 < p$K_4$ < 4 [13]). The concomitant formation of these two weak-energy bonds is facilitated by the flexibility of the tetraphenylporphyrin.[14] The pyrollinic nitrogens of $P_I$ have doublets that are not readily available due to the planarity of the macrocycle, which does not favour monocomplexation. However, the monocomplexed species induces a distortion of the macrocycle, thus favouring the formation of the 2 : 1 complex.

The monocomplexation of $P_{II}$ and the absence of the complexation of $P_{III}$ are consistent with the strong steric hindrance of the methyl group. Furthermore, there is no pyrollic hydrogen, which makes the formation of hydrogen-bonds such as $^-O\cdots\cdots HN$ in these compounds impossible.

The values of the complexation equilibrium constants for triethylamine, $P_I$, and $P_{II}$ are consistent with the relative availability of the doublets on the nitrogens, this factor being
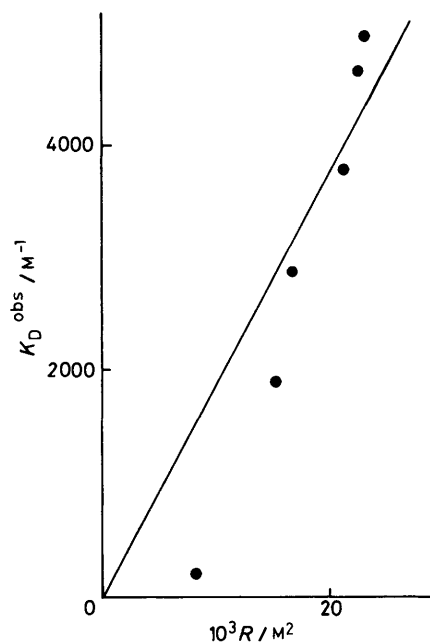
influenced by steric effects and the delocalisation of non-bonding orbitals.

*Dimerization.*—A comparative analysis of our various experimental results shows that no aggregation phenomena of tetraphenylporphyrin in benzene are observed, even in the presence of a large excess of p-nitrophenol. Furthermore, the protonated form of this porphyrin is known not to induce self-associations.[15] Therefore, the existence of a monomer-dimer equilibrium in an aprotic medium seems to be related to the formation of ion pairs between the porphyrin and p-nitrophenol. From these observations, the more likely hypothesis is still the dimerization of the monocomplexed species $P_IH^{\delta+}\cdots\cdot^{\delta-}OAr$. The general scheme is as given in the Scheme.

The mathematical analysis of such a scheme leads, as expected, to relationship (12), which Figure 5 shows is followed. From this scheme the apparent dimerization constant is readily expressed as equation (15), where $K_g = K_1(1 + K_2)$.

$$K_D^{obs} = \frac{(K_AK_C)^2K_D[ArOH]^2}{(1 + K_g[ArOH]^2)^2} \quad (15)$$

Figure 6 shows the good linearity of equation (16).

$$K_D^{obs} = f\left(\frac{[ArOH]^2}{(1 + K_g[ArOH]^2)^2}\right) \quad (16)$$

This observation gives additional support to the competition in $CH_2Cl_2$ between the dimeric species $ArO^{\delta-}\cdots\cdot^{\delta+}H-(P_I)_2H^{\delta+}\cdots\cdot^{\delta-}OAr$ and the dicomplexed porphyrin $ArO^{\delta-}\cdots\cdot^{\delta+}HP_IH^{\delta+}\cdots\cdot^{\delta-}OAr$. This competition, which strongly favours the dimeric species when the concentration of porphyrin increases, implies a dimerization equilibrium constant much larger than the overall complexation constant ($K_D \gg K_g$).

This is the first time that the dimerization of tetraphenyl-porphyrin has been demonstrated. This dimer can tentatively be described by the formation of intermolecular hydrogen bonds between the pyrollic and pyrollinic nitrogen atoms not complexed by $p$-nitrophenol. With such a model it becomes clear why $N$-methylporphyrins $P_{II}$ and $P_{III}$ cannot give these self-association phenomena, as the macrocycle no longer has pyrollic hydrogens available.

## Appendix

*Derivation of Relationship* (14).—The notations are as given in the text. Taking the square root of each side of relationship (12) and taking into account equation (17), equation (18) is easily obtained.

$$2(4K_D^{obs}[P]_0 + 1 - \sqrt{1 + 8K_D^{obs}[P]_0}) =$$
$$(\sqrt{1 + 8K_D^{obs}[P]_0} - 1)^2 \quad (17)$$

$$\sqrt{\frac{16K_D^{obs}\,\Delta A}{\Delta\varepsilon} + 1} = \sqrt{1 + 8K_D^{obs}[P]_0} \quad (18)$$

Returning to the square and rearranging gives equation (19).

$$\frac{2K_D^{obs}\,\Delta A}{\Delta\varepsilon} + \frac{\sqrt{K_D^{obs}}\,\sqrt{\Delta A}}{\sqrt{\Delta\varepsilon}} = K_D^{obs}[P]_0 \quad (19)$$

Multiplying each side by $\dfrac{\Delta\varepsilon}{K_D^{obs}\,\sqrt{\Delta A}}$ gives equation (20) or (21), which is relationship (14).

$$2\sqrt{\Delta A} + \sqrt{\frac{\Delta\varepsilon}{K_D^{obs}}} = \frac{[P]_0\Delta\varepsilon}{\sqrt{\Delta A}} \quad (20)$$

$$\sqrt{\Delta A} = \frac{\Delta\varepsilon\;[P]_0}{2\;\sqrt{\Delta A}} - \frac{1}{2}\sqrt{\frac{\Delta\varepsilon}{K_D^{obs}}} \quad (21)$$

## References

1 For a review see 'The Hydrogen Bond,' eds. P. Shuster, G. Zundel, and C. Sandorfy, North Holland, Amsterdam, 1976.
2 G. Jori, E. Reddi, E. Rossi, I. Cozzani, L. Tomio, P. L. Zorat, G. B. Pizzi, and F. Calzavara, *Med. Biol. Environ.*, 1980, **8**, 141.
3 H. M. G. Al-Hazimi, A. H. Jackson, A. W. Johnson, and M. Winter, *J. Chem. Soc., Perkin Trans. 2*, 1977, 98.
4 H. A. Benesi and J. H. Hildebrand, *J. Am. Chem. Soc.*, 1949, **71**, 2703.
5 J. Fritsch and G. Zundel, *J. Phys. Chem.*, 1981, **85**, 556.
6 H. Baba, A. Matsuyama, and H. Kokubun, *Spectrochim. Acta*, 1969, **25A**, 1709.
7 R. F. Pasternack, P. R. Huber, P. Boyd, G. Engasser, L. Francesconi, E. Gibbs, P. Fasella, G. C. Venturo, and L. de C. Hinds, *J. Am. Chem. Soc.*, 1972, **94**, 4511.
8 M. Gouterman and P. E. Stevenson, *J. Chem. Phys.*, 1962, **37**, 2266.
9 G. Kortum, W. Vogel, and K. Andrussow ' Dissociation Constants of Organic Acids in Aqueous Solution,' Butterworths, London, 1961.
10 S. Aronoff, *J. Phys. Chem.*, 1958, **62**, 428.
11 S. F. Mason, *J. Chem. Soc.*, 1958, 977.
12 E. M. Arnett, in ' Progress in Physical Organic Chemistry,' eds. S. G. Cohen, A. Streitwieser, and R. W. Taft, Interscience, New York, 1963, 223.
13 J. N. Phillips, *Rev. Pure Appl. Chem.*, 1960, **10**, 35.
14 A. Stone and E. B. Fleischer, *J. Am. Chem. Soc.*, 1968, **90**, 2735.
15 W. I. White in ' The Porphyrins,' ed. D. Dolphin, Academic Press, New York, 1978, 303.