16.62, 16.43, 16.40, 16.45; (2,6-dimethyl-d_6-pyridine) 16.26, 16.33, 16.48, 16.32, 16.56. 16.45.

The mean values and the average deviations are summarized in Table I.

Statistical Analysis.[52] A statistical analysis of the data was carried out to establish whether the observed differences between ΔH_H and ΔH_D were significant. The procedures were similar to those used in the preceding paper.[8] The results are summarized in Table III and support the conclusions previously reached based on a visual examination of the average values and average deviations reported in Table I.

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[52] We are indebted to W. J. Hammar and D. VanderJagt of the Department of Chemistry, Purdue University, for this analysis.

Stability Constants of Magnesium Porphyrin–Pyridine Complexes. Solvent and Substituent Effects[1]

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Contribution from the Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218. *Received January 14, 1966*

Abstract: The stability constants for the reaction, magnesium porphyrin monopyridinate + pyridine $\leftrightarrows$ magnesium porphyrin dipyridinate, have been determined for a series of variously substituted magnesium porphyrins. Comparison of the substituent effects observed in the case of the magnesium porphyrins to those obtained earlier for nickel porphyrins provided insight into the nature of the metal-to-porphyrin bonding. The effect of substitution in the 4 position in the pyridine ring was also examined. These results suggest that d–π bonding between transition metals in porphyrins and pyridine ligands is not very important.

There has been considerable controversy in the literature concerning the state of solvation of chlorophyll in the leaf and in solution. The differences of opinion have been based primarily on spectral observations. One group of investigators has held that the divergence of the spectrum in the leaf from that in solution can be best accounted for by its state of aggregation while the other group has preferred to consider the chlorophyll as occurring in the leaf in combination with a protein, as does heme in hemoglobin.

The question of chlorophyll aggregation in solution was investigated by Katz, Closs, Pennington, Thomas, and Strain.[3] They concluded that the chlorophyll molecules were aggregated in noncomplexing solvents by way of intermolecular complexing between the carbonyl groups on the periphery of the chlorophyll ring and the magnesium at the center of another molecule.

Wei, Corwin, and Arellano[4] observed that magnesium porphyrins readily form dipyridine complexes. Corwin and Wei[5] found that magnesium porphyrins and chlorins form monoaquo and monomethanol complexes, substantiating earlier observations of Fischer[6] who prepared methanolate complexes of magnesium porphyrins, and of Byrne, Linstead, and Lowe[7] who studied the hydration of magnesium phthalocyanin.

Miller and Dorough[8] made a quantitative study of the magnesium tetraphenylporphin and chlorin stability constants in pyridine–benzene mixtures. They obtained their stability constants by analyzing changes in the visible spectrum of the magnesium tetraphenylporphin and chlorin as the pyridine concentration was changed. These observations have led us to examine the complexing of magnesium porphyrins with nitrogen bases.

Results and Discussion

Although the magnesium porphyrins readily form dipyridinate complexes, solution of the magnesium porphyrin in a variety of solvents, including pure pyridine, does not yield the spectrum of the pure dipyridinate. Instead a spectrum having two Soret peaks and a more subtly altered visible spectrum is obtained. Dilution of the ligand increases the intensity of the shorter wavelength Soret peak and decreases the intensity of the longer wavelength Soret peak. This behavior is characteristic of an equilibrium between two different states of ligancy in solution, analogous to that described by Baker, Brookhart, and Corwin[9] for Ni(II) and Cu(II) porphyrin–piperidine complexes. The spectra of magnesium deuteroporphyrin IX dimethyl ester in a complexing solvent (pyridine) and a noncomplexing solvent (2,6-lutidine) are shown in Figures 1 and 2.

The stereoelectronic effect of the ligand on the porphyrin π system proposed earlier by Corwin,

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[1] (a) Porphyrin Studies. XXXV. Paper XXXIV: C. B. Storm and A. H. Corwin, *J. Org. Chem.*, **29**, 3700 (1964); (b) taken in part from the Ph.D. dissertation of C. B. Storm, The Johns Hopkins University, Baltimore, Md., 1965. This work was supported in part by Research Grant GM 06691 from the National Institutes of Health.

[2] National Institutes of Health Predoctoral Fellow, 1962–1965.

[3] J. J. Katz, G. L. Closs, F. C. Pennington, M. R. Thomas, and H. H. Strain, *J. Am. Chem. Soc.*, **85**, 3801 (1963); G. L. Closs, J. J. Katz, F. C. Pennington, M. R. Thomas, and H. H. Strain, *ibid.*, **85**, 3809 (1963).

[4] P. E. Wei, A. H. Corwin, and R. Arellano, *J. Org. Chem.*, **27**, 3344 (1962).

[5] A. H. Corwin and P. E. Wei, *ibid.*, **27**, 4285 (1962).

[6] H. Fischer, L. Filser, and E. Plotz, *Ann.*, **495**, 26 (1932).

[7] G. T. Byrne, R. P. Linstead, and A. R. Lowe, *J. Chem. Soc.*, 1017 (1934).

[8] J. R. Miller and G. D. Dorough, *J. Am. Chem. Soc.*, **74**, 3977 (1952).

[9] E. W. Baker, M. S. Brookhart, and A. H. Corwin, *ibid.*, **86**, 4587 (1964).

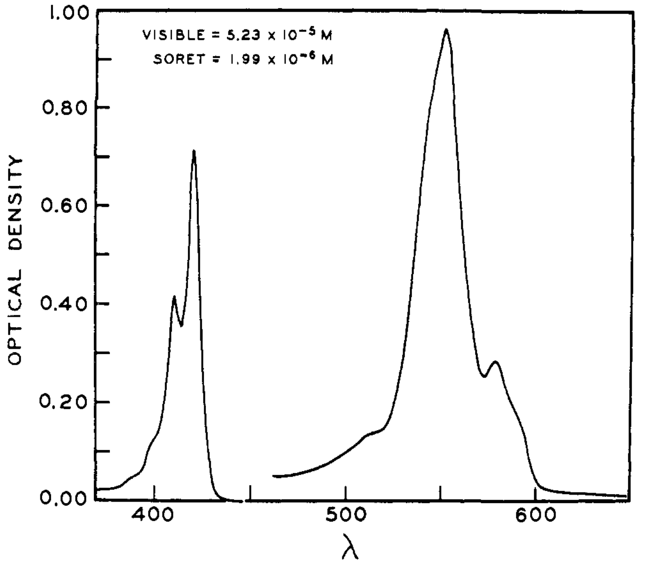

Figure 1.

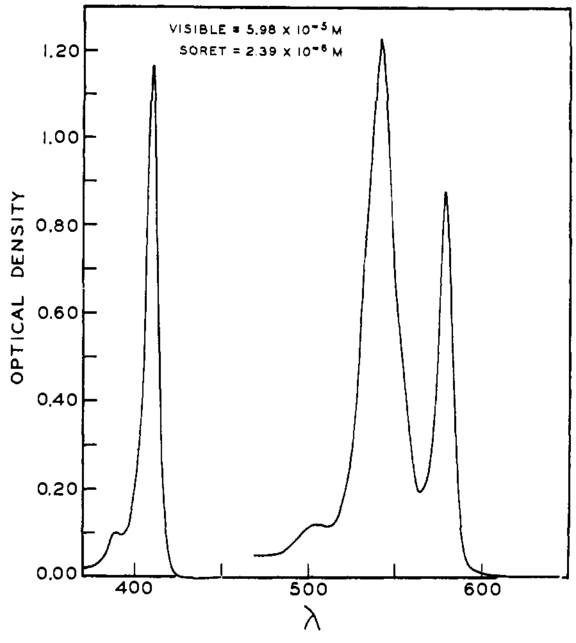

Figure 2.

et al.,[10] accounts for the appearance of the two different Soret bands in the magnesium porphyrin pyridinate complexes. From the work of Wei, Corwin, and Arellano[4] and Miller and Dorough[8] the equilibrium, magnesium porphyrin monopyridinate (PL) + pyridine (L) $\leftrightharpoons$ magnesium porphyrin dipyridinate (PL_2), was presumed to be the most likely one to exist.

To obtain further information pertaining to the state of ligancy of the magnesium porphyrins a simple vacuum balance was constructed. A sample of magnesium tetraphenylporphin dipyridinate was placed in the balance and evacuated to 10 μ for a period of 24 hr. No change in weight was observed. Heating the sample to 160° while still at 10-μ pressure brought about a slow but steady decrease in weight. After 72 hr a weight change had occurred that corresponded to a loss of 1 mole of pyridine. Heating to higher temperatures for longer periods of time brought about no further decrease in weight. The spectrum of the recovered material was identical with that of the magnesium tetraphenylporphin monopyridinate. This is in agreement with the earlier data[3,4,8,11] that the minimum coordination number of the magnesium in the porphyrin system is five, *i.e.*, that it exists as the monopyridinate in noncomplexing medium. If a porphyrin substituted with polar functional groups is taken, *i.e.*, magnesium deuteroporphyrin IX dimethyl ester, a weight change is observed on the vacuum balance that corresponds to a loss of 2 moles of pyridine per mole of magnesium porphyrin dipyridinate. This is accounted for by intermolecular complexing of the carbomethoxy groups, as observed by Katz, *et al.*[3]

In an attempt to elucidate the effects of structural variation on the stability constants of the magnesium porphyrin–pyridine complexes we have determined the stability constants for nine different porphyrins. The structures of these porphyrins are given in Table I.

Since the magnesium porphyrin is never converted completely to the dipyridinate complex and there is some overlap between the absorption peaks of the mono- and dipyridinate complexes, it is not feasible to determine the extinction coefficient of the dipyridinate directly. Without knowing the extinction coefficient of the dipyridinate, it is not possible to determine its concentration and thereby the stability constant. We have therefore chosen to determine the extinction coefficient and stability constant by a graphic method.

If we represent the equilibrium as

$$PL + L \rightleftharpoons PL_2$$

$$K = \frac{[PL_2]}{[PL][L]}$$

If we let the concentration of the dicomplex = C, the total concentration of the porphyrin = C_p, and the initial ligand concentration = C_L, then

$$K = \frac{C}{(C_p - C)(C_L - C)}$$

but $C_L >> C$, so

$$K = \frac{C}{(C_p - C)(C_L)} \qquad (1)$$

If we let the optical density of the dicomplex = OD_{II} and let the extinction coefficient of the dicomplex = ϵ_{II}, then from Beer's law

$$OD_{II} = \epsilon_{II}Cl \qquad (2)$$

Solving eq 1 and 2 for C, equating, and rearranging, one obtains (for unit path length)

$$\frac{C_pC_L}{OD_{II}} = \frac{1}{K\epsilon_{II}} + \frac{C_L}{\epsilon_{II}} \qquad (3)$$

Jaffé[12] suggests the linearity of such a plot as a test for the proposed stoichiometry. This is essentially the equation proposed by Benesi and Hildebrand[13] to

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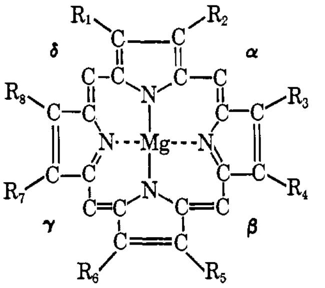
(10) A. H. Corwin, D. G. Whitten, E. W. Baker, and G. C. Kleinspehn, *J. Am. Chem. Soc.*, **85**, 3621 (1963).

(11) C. B. Storm and A. H. Corwin, *J. Org. Chem.*, **29**, 3700 (1964).

(12) H. H. Jaffé and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy," John Wiley and Sons, Inc., New York, N. Y., 1962, p 580.

Table I[a]



Compd		R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	α	β	γ	δ
1	Mesoporphyrin IX dimethyl ester	M	E	M	E	M	PrM	PrM	M	H	H	H	H
2	Etioporphyrin II	M	E	E	M	M	E	E	M	H	H	H	H
3	Protoporphyrin IX dimethyl ester	M	V	M	V	M	PrM	PrM	M	H	H	H	H
4	Desoxophylloerythrin monomethyl ester	M	E	M	E	M	CH_2CH_2	PrM	M	H	H		H
5	Dinitrodeuteroporphyrin IX dimethyl ester	M	NO_2	M	NO_2	M	PrM	PrM	M	H	H	H	H
6	Mesoporphyrin IX dicholesteryl ester	M	E	M	E	M	PrCh	PrCh	M	H	H	H	H
7	Tetraphenylporphin	H	H	H	H	H	H	H	H	Ph	Ph	Ph	Ph
8	Dichlorodeuteroporphin IX dimethyl ester	M	Cl	M	Cl	M	PrM	PrM	M	H	H	H	H
9	Deuteroporphyrin IX dimethyl ester	M	H	M	H	M	PrM	PrM	M	H	H	H	H

[a] M = CH_3; E = CH_2CH_3; PrM = $CH_2CH_2COOCH_3$; V = $CHCH_2$; Ph = C_6H_5; Ch = $CH_2CH_2COOC_{27}H_{45}$.

analyze charge-transfer equilibria. After determining the extinction coefficient of the dicomplex from eq 3, the data are most conveniently presented in the form

$$\frac{C_p\epsilon_{II}}{OD_{II}} = \frac{1}{KC_L} + 1 \qquad (4)$$

The data are presented according to eq 4 in Figure 3.

The Benesi–Hildebrand equation has been the subject of some discussion in the literature in recent years.[14] The analysis given by Hammond is particularly useful.[15] He demonstrates that for the equation to be applicable, a series of ligand concentrations should be available such that $(C_{L1})(C_{Ln}) \approx K^{-2}$. Our ligand concentrations vary from *ca.* 2 to *ca* 12 *M* and the values of the stability constants are around 0.2. Thus the stability constants we are interested in fall in the range where the errors in the equation are a minimum.

As electron-withdrawing substituents are placed on the periphery of the porphyrin ring, the half-band-widths of the transitions become markedly wider. This leads to a decrease in the resolution of the two Soret peaks. For two of the compounds in Table I (**5** and **8**) the resolution was so poor that the stability constants were estimated using another equation. Using the notation indicated earlier one can substitute directly into the equilibrium expression from Beer's law and obtain

$$K = \frac{OD_{II}}{OD_I}\frac{\epsilon_I}{\epsilon_{II}}\frac{1}{C_L} \qquad (5)$$

Since these two porphyrins are converted to a large extent to the dipyridinate in pyridine solution, the extinction coefficient of the dicomplex may be estimated from the spectrum in pyridine. The results are given in Table II. The correlation coefficients and error analysis for the lines in Figure 3 and the data in Table II are given in Table III.

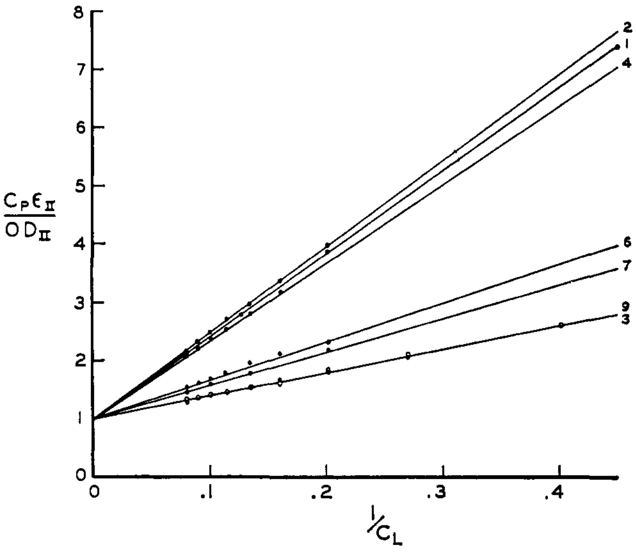


Figure 3.

In deuteroporphyrin IX dimethyl ester, the 2 and 4 positions on the periphery of the porphyrin ring are substituted by hydrogen atoms. In Table I compounds **1**, **3**, **5**, and **8** may be considered as 2,4-disubstituted deuteroporphyrin IX dimethyl ester derivatives.

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(13) H. A. Benesi and J. H. Hildebrand, *J. Am. Chem. Soc.*, 71, 2703 (1949).

(14) W. B. Person, *ibid.*, 87, 167 (1965), and references contained therein.

(15) P. R. Hammond, *J. Chem. Soc.*, 479 (1964).

Table II

Compd[a]	$\epsilon_{I} \times 10^{-5}$ [b]	$\epsilon_{II} \times 10^{-5}$ [c]	K[c]	K[d]	I[e]
1	5.53	4.66	0.070	0.070 ± 0.007	0.988
2	4.55	4.07	0.068	0.068 ± 0.006	1.005
3	3.21	2.82	0.242	0.247 ± 0.022	1.014
4	4.96	3.87	0.074	0.075 ± 0.006	0.977
5	1.58	1.45	0.326[f]		
6	4.97	4.16	0.142	0.146 ± 0.014	1.015
7	6.74	6.56	0.161	0.168 ± 0.011	1.024
8	0.66	0.68	0.282[f]		
9	5.01	4.65	0.228	0.243 ± 0.019	1.041

[a] For the structures of these magnesium porphyrins see the corresponding numbers in Table I. [b] Magnesium porphyrin monopyridinate in 2,6-lutidine. [c] Calculated from the least-squares analysis of $C_pC_L/OD_{II} = (1/K\epsilon_{II}) + (C_L/\epsilon_{II})$ (eq 3). [d] Calculated from the least-squares analysis of $C_p\epsilon_{II}/OD_{II} = 1 + (1/KC_L)$ (eq 4). [e] Intercept from least-squares analysis of equation given in *d*. $I = 1.000$ in theory. [f] Calculated from $K = OD_{II}/OD_I \times \epsilon_I/\epsilon_{II} \times 1/C_L$ (eq 5).

Table III. Correlation Coefficients and Error Analysis ± % in K[d]

Compd	r[a]	r[b]	At 95% level	Standard error[c]
1	0.9968	0.9999	32.4	10.3
2	0.9993	0.9999	30.0	9.1
3	0.9973	0.9976	28.1	8.9
4	0.9987	0.9917	27.6	8.6
6	0.9961	0.9914	29.1	9.0
7	0.9906	0.9808	21.0	6.5
9	0.9989	0.9965	25.8	7.8

[a] Correlation for $C_pC_L/OD_{II} = (1/K\epsilon_{II}) + (C_L/\epsilon_{II}^0)$. [b] Correlation for $C_p\epsilon_{II}/OD_{II} = 1 + (1/KC_L^0)$. [c] 50% level. [d] Estimated error 6%.

Baker[16] has shown that the stability constants for such nickel porphyrin–pyridine complexes may be correlated by a Hammett plot. A plot of log (K/K_0) against $\Sigma\sigma p$ gives a ρ value of 1.65, indicating a moderate electronic effect. When the results for the magnesium porphyrin–pyridine complexes are plotted according to the Hammett equation, no linear relationship is indicated. The electron-withdrawing groups do not have nearly the effect of stabilizing the complex that they do in the nickel case. The electron-donating group is about as effective in the magnesium case as it is in the nickel case.

This large difference in behavior of the Ni(II) and Mg(II) derivatives indicates that there is a fundamental difference in the way in which the substituent on the periphery of the porphyrin ring interacts with the metal at the center of the porphyrin ring. Nickel(II) has a d^8 configuration. In the square-planar Ni(II) porphyrin complex the d_{xz} and d_{yz} orbitals are fully occupied. These orbitals are of the correct symmetry and are placed in an ideal position to overlap with the porphyrin π orbitals. In the Fe(III) tetraphenylporphin, Eaton and LaLancette[17] have shown by nmr studies that the metal d electrons are delocalized into the porphyrin π system. It is easy to see then how an electronic effect could be transmitted from the periphery of the porphyrin ring to the metal d_{xz} and d_{yz} orbitals. It is the electron density in the d_{z^2} orbital, however, that provides the barrier to further complex formation. In the square-planar porphyrin complex the d_{z^2} and d_{xz} and d_{yz} orbitals are of nearly the same energy.[18] In the octahedral Ni(II) porphyrin dipyridinate the d_{z^2} orbital is of much higher energy than the d_{xz} and d_{yz} orbitals. We suggest that electron-withdrawing groups on the periphery of the porphyrin ring cause a delocalization of electron density from the metal d_{xz} and d_{yz} orbitals. This in turn provides a greater area for the electrons in the d_{z^2} orbital to occupy, which is the equivalent of saying that the energy of the d_{z^2} orbital will be lowered. Since the energy of the d_{z^2} orbital is highest in the octahedral complex, the stabilizing effect would be greatest in the octahedral complex.

Since Mg(II) has no d electrons this mechanism of electron withdrawal could not operate. We have observed that the Mg(II) porphyrins are relatively insensitive to electron-withdrawing groups. This implies that electron withdrawal by a σ route is not very important in altering the electron density at the metal.

Desoxophylloerythrin monomethyl ester differs from etioporphyrin II and mesoporphyrin IX dimethyl ester mainly in that it has a two-carbon bridge between the 6 position and the γ-methine position (ring V). The closing of the isocyclic ring diminishes the hold of the porphyrin on the magnesium.[5] The additional steric strain imposed on the system seems to have little effect on its affinity for the last pyridine molecule.

The effect of esterifying mesoporphyrin IX with cholesterol instead of methanol is surprising. It is not likely that an electronic effect could be directly transmitted over such a distance. MacCragh, Storm, and Koski[19] found that copper porphyrins were predominately dimerized in 10^{-4} *M* solutions from 77°K almost to room temperature unless the solvent molecules had a large π system. They suggested that the dimerization was taking place through π–π bonding. However, on esterification with a bulky group such as cholesterol the dimerization was almost completely impeded. Caughey and Corwin[20] observed in demetalation studies of copper porphyrins that the copper porphyrin solutions did not follow Beer's law strictly and that there was a second-order dependence on copper porphyrin in the kinetic relation. Thus it appears that metalloporphyrins can exist as π dimers even at 10^{-6} *M* concentrations. If the magnesium porphyrin monopyridinate exists in part as a π dimer and the dimer has a spectrum closely resembling that of the monomer, then the equilibrium would be displaced in the direction of the monomer and make the observed stability constant smaller than it would be in the absence of the π dimerization.

The stability constant determined for the magnesium tetraphenylporphin is somewhat less than expected. Removing eight electron-donating alkyl groups and adding four electron-withdrawing phenyl rings on the bridge positions would be expected to have a larger effect than is observed.

The solvent that we used as a diluent also had a

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(16) E. W. Baker and A. H. Corwin, Abstracts of Papers, 149th National Meeting of the American Chemical Society, Detroit, Mich., 1965.

(17) D. R. Eaton and E. A. LaLancette, *J. Chem. Phys.*, 41, 3534 (1964).

(18) C. A. Coulson, "Valence," Oxford University Press, New York, N. Y., 1961, p 281.

(19) A. MacCragh, C. B. Storm, and W. K. Koski, *J. Am. Chem. Soc.*, 87, 1470 (1965).

(20) W. S. Caughey and A. H. Corwin, *ibid.*, 77, 1509 (1955).

marked effect on the magnitude of the stability constant. Miller and Dorough[8] examined the magnesium tetraphenylporphin case in the visible portion of the spectrum. They used benzene–pyridine mixtures and determined a value of 0.577 ± 0.03 for the same stoichiometry as we propose here. The ratio of the value determined using benzene as a diluent to that obtained using 2,6-lutidine as a diluent is 3.60. We examined the stability constant for magnesium mesoporphyrin IX dimethyl ester in these two solvents also. In this case the ratio was 5.02. This places our observations in good general agreement with those obtained earlier by Miller and Dorough from the visible portion of the spectrum. We have also used acetone, and pinacolone as diluents. The same result is obtained with these two diluents as with 2,6-lutidine, although there is a spread of 13 units in their dielectric constants.[21] A further decrease of four units to that of benzene causes a large change in the stability constant. Evidently the dielectric constant is not the critical variable in this case.

In the esr studies of the copper porphyrins cited earlier[19] acetone and chloroform were found to be more effective in breaking up the porphyrin dimers than was benzene. The position of the equilibrium will be determined by the relative solvation energies of the three species involved, *i.e.*, the magnesium porphyrin monopyridinate (**1**), pyridine (**2**), and the magnesium porphyrin dipyridinate (**3**). Species **1** and **2** still appear more polar to the surrounding solvent molecules than species **3**, which will present the backside of two pyridine molecules and the periphery of the porphyrin ring to the solvent. More polar solvent molecules will solvate species **1** and **2** more effectively than **3**, requiring more energy to disrupt the solvent shell, and will result in a lower association constant. Conversely benzene will solvate species 3 most effectively, since this species presents a nonpolar facade to the surrounding solvent.

We have further studied the effect of substitution in the pyridine ligand. The stability constants for the complexing of various 4-substituted pyridines with magnesium deuteroporphyrin IX dimethyl ester have been determined. These results are given in Table IV. Philips has studied the complexing of various substituted pyridines with ferrous porphyrins.[22] He observed that the stability of the complex was inversely related to the ligand base strength, *i.e.*, that a substituent that increased the pyridine base strength decreased the stability of the complex. In the ferrous porphyrin–pyridine complexes this was cited as evidence of the importance of metal d to pyridine π bonding. Indeed the substituted pyridine π-electron affinities are in the correct order to support such a hypothesis.[23]

We have observed the same inversion of expected order in the case of the magnesium porphyrin–4-substituted pyridine complexes. Since there are no d electrons present in Mg(II) this effect cannot be ascribed to changes in metal d to pyridine π bonding. It is interesting to note that Corwin and Wei[5] observed a similar phenomenon in equilibrium demetalation studies of magnesium porphyrins. Electron-withdrawing groups on the periphery of the porphyrin ring increased the strength of the hold of the porphyrin on the magnesium, the opposite effect to that which one would expect if the magnesium nitrogen bond were ionic. On the basis of these studies Corwin and Wei[5] concluded that the magnesium was covalently bonded to the porphyrin nitrogens. The same explanation would hold equally well for the additional ligand to metal bonds.

Table IV. Stability Constants of 4-Substituted Pyridine–Magnesium Deuteroporphyrin IX Dimethyl Ester Complexes

4-Substituent	$\epsilon_I \times 10^{-5}$	$\epsilon_{II} \times 10^{-5a}$	K^a	K^b	I^b
Methyl	5.08	4.22	0.163	0.159	0.968
Ethyl		4.22	0.152	0.150	1.001
Vinyl		4.25	0.091	0.090	0.981
Methoxycarbonyl		2.93	0.362	0.347	0.980
Hydrogen	5.01	4.65	0.228	0.243	1.041

[a] From least-squares analysis of eq 3. [b] From least-squares analysis of eq 4. $I = 1.000$ in theory.

Since the optical density corresponding to the mono complex (OD_I) is proportional to the concentration of that species and the optical density corresponding to the di complex (OD_{II}) is proportional to the concentration of that species, a plot of ln $[OD_{II}]/[OD_I]$ against $1/T$ would give the ΔH for the reaction. The thermodynamic constants for the compounds given in Table I are given in Table V. The resolution of the bands in the Soret region for the magnesium dinitrodeuteroporphyrin IX dimethyl ester was too poor to obtain a temperature-dependent plot. The ΔH's are all of the same order of magnitude and do not seem to vary in any rational manner with the structure of the porphyrin. The ΔH's are quite low, an observation consistent with the extremely facile ligand exchange observed by Storm and Corwin.[11]

Table V. Thermodynamic Constants for Pyridine–Magnesium Porphyrin Complexes

Compd	ΔF,[a] kcal/mole	ΔH,[b] kcal/mole	ΔS, kcal/deg mole
1	1.60	−3.98	−18.4
2	1.62	−2.92	−15.0
3	0.84	−4.25	−16.8
4	1.56	−2.55	−13.7
5	0.68	−3.99[c]	
6	1.16	−3.77	−16.3
7	1.08	−2.37	−11.4
8	0.76	−3.90	−15.4
9	0.85	−3.89	−15.6
2[d]	1.42	−2.28	−12.0
2[e]	1.42	−2.46	−12.6

[a] $\Delta F = -RT \ln K$ at 30°. [b] $d(\log OD_{II}/OD_I)/d(1/T) = -\Delta H/R(2.303)$. [c] Estimated using a$\Delta S = -15.4$. [d] In piperidine $K = OD_{II}/(OD_I)(L)$. [e] In pyrrolidine $K = OD_{II}/(OD_I)(L)$.

The ΔS values are of the correct order of magnitude for the localization of 1 mole of solvent. Davies, Singer, and Staveley found a decrease of 13 to 17 entropy units for attachment of the third mole of ligand when no water of hydration was released in the

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(21) A. A. Maryott and E. R. Smith, "Table of Dielectric Constants of Pure Liquids," National Bureau of Standards, Circular 514, U. S. Government Printing Office, Washington, D. C., 1951.

(22) J. E. Falk, "Porphyrins and Metalloporphyrins," Elsevier Publishing Co., New York, N. Y., 1964, p 50.

(23) E. M. Kosower, "Molecular Biochemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 183.

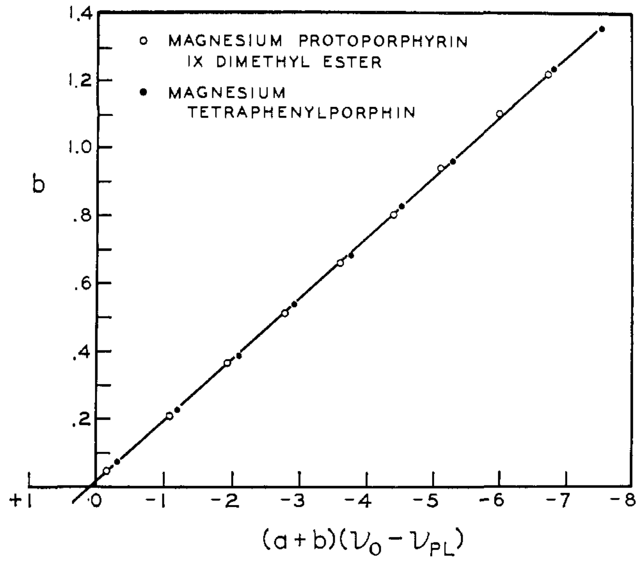

Figure 4.

complexation of EDTA with Cd, V, and Zn. Baker, Brookhart, and Corwin[9] found an entropy decrease of 11 to 12 entropy units per mole of added ligand for the complexing of piperidine to copper and nickel porphyrins.

Although piperidine and pyrrolidine are some 10^6 times stronger as bases than pyridine, the stability constants for these bases are only about twice as large and the thermodynamic properties of the complexes are also quite similar to those of the pyridine complexes. This relationship might be regarded as abnormal until it is realized that the complexes formed by pyridine and piperidine are of different charge types. The pyridine nitrogen, when bonding to a metal, becomes positively charged. The piperidinium species formed by a similar process readily loses its proton to give a neutral complex. Because of the much greater polarity of the charged nitrogen, its electron-attracting character would be expected to greatly strengthen the bond to the metal in comparison to an uncharged nitrogen in media of suitably low dielectric contants. In addition, the pyridine and piperidine ligand molecules have very different steric requirements.

The following ligands showed no tendency to form a disolvate according to the Soret spectrum: 2-picoline, dimethylaniline, N-methylformamide, N,N-dimethylformamide, 4-cyanopyridine, 2,6-lutidine, imidazole, and potassium cyanide.

Storm and Corwin[11] observed that the protons in ligands attached to the magnesium porphyrins showed large shifts to high field due to the well-known porphyrin ring current effect. The position of the ligand proton resonances are dependent on the amount of the ligand present in the solution because the observed resonances are the average resultants of the different magnetic environments affecting the ligand. The exchange has been demonstrated to be rapid even at quite low temperatures. Using the concentration dependence of the ligand proton resonance, it should be possible to calculate the stability constant for the equilibrium involved.[24]

For the equilibrium established earlier

$$\underset{a-x}{PL} + \underset{b-x}{L} \rightleftharpoons \underset{x}{PL_2}$$

$$K = \frac{x}{(a-x)(b-x)}$$

Given an initial concentration of PL = a and L = b the equilibrium concentrations are given above. The observed averaged chemical shift will be

$$\nu_0 = \frac{a-x}{a+b}\nu_{PL} + \frac{b-x}{a+b}\nu_L + \frac{2x}{a+b}\nu_{PL_2} \qquad (6)$$

where ν_{PL}, ν_L, and ν_{PL_2} are the chemical shift of the pyridine α protons in their different environments.

Using the approach of Mather, *et al.*,[24] one obtains

$$\nu_0 - \nu_{PL} = \frac{b-x}{a+b}\Delta_{PL} + \frac{2x}{a+b}\Delta_{PL_2} \qquad (7)$$

where $\Delta_{PL} = \nu_L - \nu_{PL}$ and $\Delta_{PL_2} = \nu_{PL_2} - \nu_{PL}$. In general $b >> x$; solving the equilibrium expression for b (neglecting x with respect to b) and substituting in eq 7, one obtains

$$(a+b)(\nu_0 - \nu_{PL}) = b\Delta_{PL} + \frac{2Kab}{1+Kb}\Delta_{PL_2} \qquad (8)$$

If we assume that $Kb << 1$ in eq 8, we may write

$$(a+b)(\nu_0 - \nu_{PL}) = b(\Delta_{PL} + 2Kab\Delta_{PL_2})$$

We know that a is small; if K is in the same range as determined in the ultraviolet, it is also small. If the difference in absorption frequency of PL and PL_2 is small, the Δ_{PL} term will dominate the slope. A plot of $(a+b)(\nu_0 - \nu_{PL})$ against b will then have a slope of $\Delta_{PL} - 2Ka\Delta_{PL_2}$. Figure 4 shows such a plot for the α-pyridine protons in the magnesium protoporphyrin IX dimethyl ester and magnesium tetraphenylporphin complexes.

Least-squares analysis of the nearly coincident lines in Figure 4 gives intercepts of 0.074 and 0.032 (theory 0.00) and slopes of −5.58 and −5.61, respectively. These slopes lie within the experimental error in determination of the Δ_{PL} term. This result then means that the $2Ka\Delta_{PL_2}$ term is indeed small and that the geometry of the dipyridine complex is similar to that of the monopyridine complex.

We may solve eq 6 for x and obtain

$$x = \frac{(a+b)\nu_0 - a\nu_{PL} - b\nu_L}{2\nu_{PL_2} - \nu_{PL} - \nu_L}$$

If $\nu_{PL_2} \approx \nu_{PL}$ this expression simplifies to

$$x = \frac{(a+b)\nu_0 - a\nu_{PL} - b\nu_L}{\nu_{PL} - \nu_L}$$

After determining x by the above equation, we can calculate K from the equilibrium expression.

With this scheme the K's were calculated from the nine points determined for the magnesium tetraphenylporphin–pyridine titration in deuteriochloroform. The K's varied from 4.0 at b = 0.05 *M* to 0.08 at b = 1.08 *M*. This is similar to the problems encountered by Freed and Sancier[25] in their attempts to calculate pyridine–chlorophyll stability constants. The K's cal-

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[24] R. Mathur, E. D. Becker, R. B. Bradley, and N. C. Li, *J. Phys. Chem.*, 67, 2190 (1963).

[25] S. Freed and K. M. Sancier, *J. Am. Chem. Soc.*, 76, 198 (1954).

Table VI

Compound[b]	Formula	% C[a] Calcd	% C[a] Found	% H Calcd	% H Found
Mg mesoporphyrin IX dimethyl ester dipyridinate	$C_{46}H_{50}N_6O_4Mg$	71.27	71.34	6.50	6.55
Mg etioporphyrin II dipyridinate	$C_{42}H_{46}N_6Mg$	76.51	76.23	7.05	7.01
Mg protoporphyrin IX dimethyl ester dipyridinate	$C_{46}H_{46}N_6O_4Mg$	71.63	70.82	6.02	5.96
Mg desoxophylloerythrin monomethyl ester dipyridinate	$C_{44}H_{47}N_6O_2Mg$	73.77	73.42	6.63	6.66
Mg dinitrodeuteroporphyrin IX dimethyl ester dipyridinate	$C_{42}H_{40}N_8O_8Mg$	62.36	62.12	5.00	5.03
Mg mesoporphyrin IX dicholesteryl ester dipyridinate	$C_{98}H_{134}N_6O_4Mg$	79.27	78.91	9.03	9.06
Mg tetraphenylporphin dipyridinate	$C_{54}H_{38}N_6Mg$	81.56	80.96	4.85	4.90
Mg deuteroporphyrin IX dimethyl ester dipyridinate	$C_{42}H_{42}N_6O_4Mg$	70.14	69.85	5.90	5.89

[a] All microanalysis was done by Mr. Joseph Walter, The Johns Hopkins University, Baltimore, Md. [b] There was not a sufficient amount of the magnesium dichlorodeuteroporphyrin IX dimethyl ester dipyridinate available for elemental analysis.

culated in their case varied from 12 to 4.5 over a pyridine concentration of 0.008 to 1.76 *M* using *n*-propylbenzene as a diluent. Adding pyridine to chloroform would be expected to bring about large changes in the solvent properties. Although normally both chloroform and pyridine are thought of as good solvents for porphyrins, the magnesium porphyrins were observed to crystallize out of the pyridine–chloroform-*d* solutions when the pyridine concentration approached 1 *M*. We believe that the failure to obtain satisfactory *K* values from this method at present is primarily due to solvent–ligand interactions.

Our results showing the facile exchange of the ligands attached to the magnesium porphyrins indicate that extreme caution must be used in interpreting reports of the isolation of native chlorophyll–protein complexes.[26] Furthermore the state of solvation of the chlorophyll molecule must be considered in terms of the existence of both mono- and disolvates, although the disolvate would certainly be present in only small amounts.

Experimental Section

The least-squares analysis, correlation coefficients, and statistical analysis of the data were carried out in the usual manner.[27]

The raw data from which these results were extracted are contained in the Ph.D. dissertation of Carlyle B. Storm, The Johns Hopkins University, Baltimore, Md., 1965, and may be obtained from University Microfilms Inc., Ann Arbor, Mich.

The magnesium porphyrins were synthesized from the free-base porphyrins by the magnesium hexapyridine diiodide-pyridine method described by Wei, Corwin, and Arellano.[4] They were purified by chromatography over 80% magnesol-20% cellulose, using 10:20:3 ethylene dichloride-hexane-methanol as eluent. The eluate was filtered through a fine sintered glass funnel, taken to dryness on a rotary evaporator, and recrystallized from hot pyridine-isooctane. The net yields ran about 80%. The analytical and spectral properties of each of the compounds are given in Tables VI, VII, and VIII. The references pertaining to the preparation of the free base porphyrins are given in ref 22.

Table VII. Magnesium Porphyrin Spectra in 2,6-Lutidine

Compd	Soret, λ_{max}[a] ($\epsilon \times 10^{-5}$)[b]	Visible, λ_{max} ($\epsilon \times 10^{-4}$)
1[d]	410 (5.53)	510 (Sh),[c] 548 (2.04), 582 (1.98)
2	410 (4.55)	498 (0.23), 545 (1.98), 580 (1.79)
3	422 (3.21)	510 (0.25), 552 (1.99), 590 (1.95)
4	411 (4.96)	503 (Sh), 543 (2.11), 578 (1.69)
5	413 (1.58)	515 (Sh), 551 (1.72), 588 (1.04)
6	410 (4.97)	500 (Sh), 543 (2.08), 581 (2.03)
7	426 (6.74)	520 (0.43), 560 (2.26), 600 (1.17)
8	414 (0.66), 418 (0.64)	520 (Sh), 557 (0.30), 581 (0.10), 590 (Sh)
9	410 (5.01)	505 (Sh), 542 (2.00), 578 (1.46)

[a] In mμ. [b] In l. mole^{-1} cm^{-1}. [c] Sh = shoulder. [d] Numbers refer to compounds in Table I.

Table VIII. Magnesium Porphyrin Spectra in 12.36 *M* Pyridine

1[a]	410[b]	420	510 (Sh)	550	556	582	595 (Sh)[c]
2	410	422	510 (Sh)	549	555	582	594 (Sh)
3	422	432	520 (Sh)	555 (Sh)	562	595	
4	411	421	510 (Sh)	543	550 (Sh)	576	583 (Sh)
5	405 (Sh)	425	520 (Sh)	561	595		
6	410	422	510 (Sh)	546	551	578	590 (Sh)
7	426	432	533 (Sh)	565 (Sh)	572	618	
8	415 (Sh)	428		567	597		
9	410	420	515 (Sh)	545 (Sh)	552	578	591 (Sh)

[a] Numbers refer to compounds in Table I [b] Position of λ_{max} in mμ. [c] Sh = shoulder.

The stability constants of the magnesium porphyrin–pyridine complexes were determined in the following manner. A stock solution of the magnesium porphyrin to be used was made up in a pyridine solution to a concentration that was *ca.* five times that

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(26) A. Takamiya, H. Obata, and E. Yakushiji in "Photosynthetic Mechanisms of Green Plants," Publication 1145, B. Kok, Ed., National Academy of Sciences, National Research Council, Washington, D. C., 1963, p 479.

(27) (a) L. G. Parratt, "Probability and Experimental Errors in Science," John Wiley and Sons, Inc., New York, N. Y., 1961, p 128; (b) C. A. Bennett and W. L. Franklin, "Statistical Analysis in Chemistry and the Chemical Industry," John Wiley and Sons, Inc., New York, N. Y., 1954, p 36.

required for an optical density of 0.70 to 1.00. A 1-ml aliquot of this solution was transferred to a 5-ml volumetric flask and diluted to the mark with previously prepared pyridine–2,6 lutidine solutions. This enabled us to work at constant porphyrin concentration and known pyridine concentration. The point in pure 2,6-lutidine was obtained by evaporating the 1 ml of pyridine–porphyrin stock solution to dryness with a stream of dry nitrogen and dissolving the magnesium porphyrin remaining in 2,6-lutidine.

In the case of the stability constant determinations using 4-substituted pyridines as ligands a slightly different method was used. A solution of magnesium deuteroporphyrin IX dimethyl ester in 2,6-lutidine was made up to such a concentration that it was *ca.* five times that required to obtain an optical density of 1.00 to 1.25. One-milliliter aliquots of this solution were then placed in 5-ml flasks and measured amounts of the 4-substituted pyridine added. The 5-ml flask was then filled to the mark with 2,6-lutidine.

The two peaks in the Soret (OD_{I} and OD_{II}) are close enough together so that neither one is completely resolved. The OD_{II} peak must be corrected for the residual absorption by OD_{I}. The spectrum in 2,6-lutidine was taken and the ratio of the peak height at the λ_{max} to the place where the OD_{II} falls was determined. This ratio was then used to determine the residual OD_{I} absorption in OD_{II} at the different ligand concentrations. This was accomplished by multiplying the observed OD_{I} by the earlier determined ratio and subtracting the result from the observed OD_{II}.

The Soret region of the solutions was recorded using a Beckman DK-2 Ratio recording spectrophotometer equipped with a constant-temperature cuvette holder. One-centimeter glass-stoppered matched quartz cuvettes were used. The temperature was held at 30 ± 0.5°. The thermodynamic data were obtained on 12.36 *M* pyridine solutions by varying the temperature of the cuvette holder. All spectra were run twice at 5-min intervals to ensure temperature equilibration. The magnesium porphyrin solutions were made up fresh before each stability constant determination. The magnesium porphyrins are unstable so it is not possible to use the same solution even 24 hr later. All determinations were made in duplicate and the two sets of points were treated together in the statistical analysis.

The pyridine used was Baker Analyzed reagent grade. It was distilled from potassium hydroxide at atmospheric pressure through a Vigreux column. A center cut was taken (bp 115–116°) and stored over Linde 5A molecular sieve. The presence of any water in the reagents caused nonlinearity of the plots and nonreproducible results.

The 2,6-lutidine was purified from Eastman practical grade. It was first stored in a freezer at *ca.* −15°. The unfrozen portion was rapidly decanted off and discarded. The remainder was allowed to thaw completely and then recrystallized twice more, discarding the liquid phase each time. The remainder from the crystallization was then distilled at atmospheric pressure from potassium hydroxide and a center cut was taken (bp 143–144°). This was then stored over Linde 5A molecular sieve. The nmr spectrum of the 2,6-lutidine prepared in this way showed no spurious peaks when compared to the literature spectrum.[28]

The 4-substituted pyridines were obtained from the Reilley Tar and Chemical Co. All were quite brown when first opened. Passage over alumina and vacuum distillation from potassium hydroxide gave water white material. The distilled materials were stored over Linde 5A molecular sieve. The nmr spectra were in all cases consistent with the structure of the ligand and showed no spurious peaks.

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(28) N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "High Resolution NMR Spectra Catalogue," Varian Associates, Palo Alto, Calif., 1962.

Chemical Transformations of Ibogaine

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Contribution from the Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts. *Received February 19, 1966*

Abstract: Ibogaine has been converted to the naturally occurring ester alkaloid voacangine by a four-step sequence. Treatment of ibogaine with *t*-butyl hypochlorite yielded the chloroindolenine which combined with potassium cyanide to give 18-cyanoibogaine and an isomeric nitrile resulting from an amusing rearrangement. Vigorous base hydrolysis of the former nitrile followed by esterification with diazomethane furnished voacangine. The chloroindolenine served also as a convenient intermediate for the preparation of 18-methoxy- and 18-hydroxyibogaine.

The molecular structures of a number of Iboga alkaloids[1] contain a carbomethoxy group and in the course of structural studies it was found that the carboxylic acids derived from the esters suffer ready decarboxylation to the parent Iboga bases.[2,3] This evidence strongly suggested that the carbomethoxy groups were located at C_{18} in the ester alkaloids. We have recently completed total syntheses of racemic ibogamine and ibogaine and planned from the outset to use the two bases as relays for the synthesis of the corresponding ester alkaloids.[4]

The starting material chosen for such transformations was ibogaine (**5**)[5,6] which is readily available from natural sources. It was suspected that the hypothetical imine (**7**) would be highly electrophilic and combine with cyanide ion to yield the nitrile (**8**) which in turn could be transformed to voacangine (**9**) by standard operations. The method chosen for the genesis of the unstable imine (**7**) was suggested by the acid-catalyzed conversion of 11-hydroxytetrahydrocarbazolenine (**1**) to the dimer (**4**) which probably proceeds through the imine (**2**) and further intermediates, *e.g.*, **3**.[7] Initiation of imine formation clearly requires a suitable leaving group and in practice we employed chloroindolenines which are easily prepared from indoles and *t*-butyl hypochlorite.[8,9] Treatment of ibogaine (**5**)[10] with

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