Kinetics of the Acid Displacement of Magnesium Ion from Porphyrin[1]

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Abstract: The kinetics of displacement of magnesium ion from magnesium deuteroporphyrin dimethyl ester (MgP) by hydrogen ion ($10^{-6}\ M < (H^+) < 10^{-3}\ M$) have been studied for solutions acidified both with perchloric acid and with pyridine buffer. For perchloric acid in ethanol and methanol–water mixtures of 0–70 mole % water, the rate law found is $-d(MgP)/dt = k_1(MgP)(H^+)^3/[\rho_1 + (H^+)]$. The rate of the reaction parallels the coordinating power of the solvent: at 42° k_1 (M^{-2} sec^{-1}) $= 1.2 \times 10^3$ for ethanol, 3.1×10^5 for methanol, and $>10^7$ for water. In pyridine-buffered methanol containing up to 1 M water, catalysis by pyridine (py) and water leads to a three-term rate law $-d(MgP)/dt = (MgP)\{k_1(H^+)^3/[\rho_1 + (H^+)] + k_2(py)(H^+)^3/[\rho_2 + (H^+)] + k_3(py)(H_2O)(H^+)^2\}$. The values of the additional constants at 42° are $k_2 = 7.2 \times 10^8\ M^{-3}$ sec^{-1}, $k_3 = 2.7 \times 10^9\ M^{-4}$ sec^{-1}, $\rho_1 = 10^{-5}\ M$, and $\rho_2 = 5 \times 10^{-6}\ M$. The temperature dependence is quite small. For k_1, the apparent activation parameters are $\Delta H^{\ddagger} = 2.2$ kcal/mole and $\Delta S^{\ddagger} = -27$ eu, while for k_2 they are $\Delta H^{\ddagger} = 5$ kcal/mole and $\Delta S^{\ddagger} = -1$ eu. Phenol was found to have no effect on the rate while 8-hydroxyquinoline was slightly superior to pyridine as a catalyst. No primary salt effect was observed but Li^+ has a specific catalytic effect. A mechanism is suggested involving a succession of porphyrin protonations and magnesium solvations which combine to progressively displace the magnesium from the porphyrin. The intermediates are present in only minor concentrations and the final proton transfer is rate limiting only at low acidities. The role of pyridine and the alcohols as catalysts are discussed in terms of coordination of the magnesium.

The acid displacement of magnesium from porphyrins has been studied several times but not under conditions which could be described as essentially aqueous, that is, in solvents which are amphiprotic and ionizing such as the lower alcohols and water. These are the media of interest if correlations are to be made either with the biochemistry of chlorophyll and related compounds or with the coordination chemistry of ligand replacement reactions. The recent work of Baum and Plane[3] has shown that magnesium ion can be incorporated into deuteroporphyrin under such conditions and arrived at possible mechanisms to explain the observed rate law. The present study of the magnesium displacement was undertaken in the hope that it would lead to a better appreciation of the essential features of the proton–magnesium interchange. The displacement reaction is fundamentally simpler than the incorporation in that the concentration and prior coordination of the metal ion do not enter.

MacKinney and Joslyn[4] studied the acid dependence of the conversion of chlorophylls a and b to the metal-free pheophytins in acetone. The rate of displacement was first order in oxalic acid concentration (10^{-3}–10^{-1} M), but other acids differed considerably at least in the magnitude of their effect. First-order dependence was subsequently confirmed for the chlorophyll itself.[5]

Dissociation constants of magnesium porphyrins and chlorins have been determined in pure acidic media such as molten phenol, in addition to the acetic acid concentration required for fairly rapid magnesium displacement in dimethylformamide.[6] These results indicate that porphyrins and chlorins behave similarly in regard to demetalation with the porphyrins being somewhat more stable and inert. Displacement studies on metalloporphyrins[7] and phthalocyanines[8] have established that the magnesium chelate is one of the most labile that can still exist in aqueous type solution. This is convenient for the study of acid displacement since low concentrations of acid, whose properties are well understood, can be used.

The tin(IV) phthalocyanine demetalation has been studied in concentrated sulfuric acid and found to be first order in monoprotonated complex and second order in hydronium ion concentrations.[8] Displacement of Cu(II) from etioporphyrin by sulfuric acid in acetic acid is second order in the complex,[9] however. This result has been challenged on several grounds,[8] and the present study indicates that the use of pyridine to quench the acid might have promoted additional reaction.

The displacement of magnesium from porphyrin by hydrogen ion is an example of the large class of reactions known as acid-catalyzed chelate solvolysis. It is generally accepted that in these reactions the chelating ligands dissociate one bond at a time in order to reduce the otherwise prohibitively large activation energy. The porphyrin molecule, however, being cyclic and fairly rigidly planar, cannot literally unwrap itself from the magnesium ion, and yet some approximation to this process must occur in which the bonds are progressively weakened before the rate-determining step. Also, in most reactions of this type, it is presumed, even when there is no direct evidence, that the function, of the hydrogen ion is to attach to a free basic site and

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[1] Supported by Grant GM 11788 from the National Institutes of Health, U. S. Public Health Service.

[2] Supported by Postdoctoral Fellowship 1-F2-GM-34, 526-01 from National Institute of General Medical Sciences.

[3] S. J. Baum and R. A. Plane, *J. Am. Chem. Soc.*, **88**, 910 (1966).

[4] G. MacKinney and M. A. Joslyn, *ibid.*, **62**, 231 (1940).

[5] S. H. Schanderl, C. O. Chichester, and G. L. Marsh, *J. Org. Chem.*, **27**, 3865 (1962).

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

[7] J. E. Falk, "Porphyrins and Metalloporphyrins," Elsevier Publishing Co., New York, N. Y., 1964.

[8] B. D. Berezin, *Russ. J. Phys. Chem.*, **36**, 258 (1962).

[9] W. S. Caughy and A. H. Corwin, *J. Am. Chem. Soc.*, **77**, 1509 (1955).

thus labilize the remaining bonds; yet again, it is clear that this is not possible for a porphyrin complex, but porphyrin does have coordinating atoms capable of simultaneous bonding to cation and proton. In general, removal of magnesium from porphyrin may be expected to place unusual emphasis on acid catalysis, bond formation and bond breaking occurring in concert.

Experimental Section

Analytical grade anhydrous methanol (water content <0.1%) and absolute ethanol were dried over CaO, and purified pyridine was dried over sodium hydroxide pellets. The reagents were then obtained as the middle fraction from distillation in a dry nitrogen atmosphere. Ir spectra of the methanol indicated a water content of less than 0.05%. Phenol, which presumably contained no hypophosphorous acid as preservative, was recrystallized three times from chloroform and then triply sublimed. Salts were dried under vacuum at 150° for 2 days; all hydroscopic solids were transferred to methanol solution in a dry bag. Perchloric acid solutions were prepared by diluting the 71% acid with methanol.

Deuteroporphyrin dimethyl ester was prepared from hemin[3,7] and obtained in relatively pure form by chromatographing the washed porphyrin mixture twice on a Celite column. The deuteroporphyrin ester was eluted with a 2:1 hexane–chloroform mixture and thus separated from a loosely bound fraction having strong absorption at 645 mμ and the more tightly bound unesterified porphyrin. The visible spectrum and paper chromatographic properties were characteristic of the desired product which was then crystallized slowly from methanolic solution as purple needles melting at 225°.

The magnesium porphyrin was synthesized by heating deuteroporphyrin ester and anhydrous magnesium perchlorate together in a pyridine–acetone solvent so that the acetone evaporated very slowly. Complete conversion was ascertained by disappearance of the 494- and 617-mμ bands of the protonated form. The magnesium porphyrin was transferred to ether and washed with water until the absorption of pyridine at 250–260 mμ was no longer detectable in solutions where the magnesium porphyrin concentration was about 5×10^{-5} *M*. The pyridine concentration (in the kinetic runs) resulting from the magnesium porphyrin stock solution could therefore not exceed 10^{-7} *M*.

The stock acid solutions were analyzed by titration with NaOH standardized against potassium acid phthalate. The pyridine stock concentration was checked against this acid by potentiometric titration and found to be that expected from the dilution of the pure solvent.

The kinetics were followed on a Beckman DB spectrophotometer and 5-in. strip recorder running at 1 in./min. Essentially all of the experiments reported here were followed by watching the decay of the Soret band at 403 mμ. This decay generally covered about 60% of the 0–1.0 absorbance scale. Routine spectra were also measured on this instrument and occasionally checked against a Cary 14. The temperature of the cell compartments was controlled to better than 0.1° by a circulating thermostat. The magnesium porphyrin in methanol obeyed Beer's law in the concentration range 10^{-4}–10^{-6} *M* within 1%.

The reactants were brought to temperature separately in a two-pronged vessel sealed against evaporation. After rapid mixing the solution was delivered to the cell already in the spectrophotometer. Temperature drop was slight, but even near room temperature this procedure limited accurate runs to those with half-lives greater than 1 min.

In all runs, the concentration of porphyrin was far smaller than any other concentration involved so that all porphyrin species connected by labile equilibria, *e.g.*, neutral *vs.* monoprotonated forms, were held in fixed ratios. Under these conditions there are effectively but two colored forms, reactant metalloporphyrin and product "free" porphyrin, and hence, the Soret absorbance can be linearly related to the concentration of one of these forms. Also because of the concentration conditions, the rate is pseudo first order, with only the colored forms varying with time, and the data were therefore analyzed by the method of plotting against each other absorbances separated by a constant time interval.[10] Two separate time intervals were used in each case. Infinite-time absorbances were obtained from each and compared with each other and with the experimental value, if available.

Results

Constant-time-interval plots of absorbance, derived from experimental curves covering up to 90% of the total reaction, were in every case linear, indicating that the displacement is first order in total magnesium porphyrin concentration, (MgP), for all of the conditions investigated. The plots showed only small, random deviations from the best line. These were attributable to recorder response. As a check, runs were occasionally made at half or twice the usual $(\mathrm{MgP}) = 2.0 \times 10^{-6}$ *M* and the first-order rate constants agreed within the typical duplication error of a few per cent. The rate law

$$-\frac{\mathrm{d(MgP)}}{\mathrm{d}t} = k'(\mathrm{MgP}) \tag{1}$$

will therefore be implicit in the remainder of the paper and only the pseudo-first-order rate constant, k', will be discussed.

Perchloric Acid in Methanol. The dependence of the rate upon perchloric acid concentration in methanol does not correspond to a simple integral order. For the range of tractable acid concentrations ($\sim 3 \times 10^{-5}$ to $\sim 3 \times 10^{-4}$ *M*), k' appears to vary as $(\mathrm{HClO_4})^2$ at the higher acidities, but the order is clearly greater than two in the low part of the range. This observation is consistent with a rate law of the form

$$k' = \frac{k_1(\mathrm{H^+})^3}{\rho_1 + (\mathrm{H^+})} \tag{2}$$

where $(\mathrm{H^+})$ symbolizes the methylonium concentration, $(\mathrm{CH_3OH_2^+})$, since perchloric acid is a strong acid in methanol. A plot of $(\mathrm{H^+})^3/k'$ against $(\mathrm{H^+})$ should then be a straight line of slope $1/k_1$ and intercept ρ_1/k_1. The data presented in Figure 1, line A, do fit such a linear relation quite satisfactorily giving $k_1 = (3.1 \pm 0.1) \times 10^{-5}\ M^{-2}\ \mathrm{sec}^{-1}$ and $\rho_1 = (5.0 \pm 0.3) \times 10^{-5}$ *M* at 42°. These values and errors are derived from a least-squares fit to the best straight line, the errors being standard deviations. The assumption was made that the entire error resided in $(\mathrm{H^+})^3/k'$, which is certainly not the case, but of little consequence for the present data.

The data contained in Table I refer to experiments carried out using different stock solutions than those for the experiments of Figure 1. The value of k_1 at 42° is essentially the same, but ρ_1 is reduced by nearly a factor of one-half. This discrepancy can be explained as being the result of small amounts of residual water in the methanol, the effect of which (see line C in Figure 1) is to simply increase the intercept of the line and hence raise ρ_1 without changing k_1. The difference in the above quoted values of ρ_1 can be accounted for by only 0.03 *M* water. The upper limit set on the water content of both methanol preparations indicates that the value of ρ_1 for pure methanol is not very much lower than that given in Table I.

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[10] E. S. Swinbourne, *J. Chem. Soc.*, 2371 (1960).

Table I. Temperature Dependence of the First-Order Rate Constant for Demetalation of MgP by Perchloric Acid in Methanol

$(H^+) \times 10^3$, M	$k' \times 10^3$, sec^{-1}	$(H^+)^3 \times 10^9/k'$, M^3 sec	k_1, M^{-2} sec^{-1}	ρ_1, M
		$T = 42°$		
0.048	0.47	0.232		
0.096	2.36	0.374	3.2×10^5	2.7×10^{-5}
0.144	5.71	0.525		
		$T = 25°$		
0.048	0.41	0.258		
0.096	2.02	0.435	2.5×10^5	1.6×10^{-5}
0.144	4.62	0.650		

Table I also contains data obtained at 25°, using the same set of stock solutions as for 42°. Each experimental value listed is the average of two runs, which agreed within 2%. The variation with temperature is quite small. Apparent activation parameters calculated for k_1 are $\Delta H^{\ddagger} = 2.2$ kcal/mole and $\Delta S^{\ddagger} = -27$ eu. The quantity k_1/ρ_1, which will also be of interest, has the parameters $\Delta H^{\ddagger} = -3.7$ kcal/mole and $\Delta S^{\ddagger} = 0$.

Perchloric Acid in Ethanol. The addition of ethanol to the above methanol solutions inhibits the displacement reaction. The rate is inverse first order in ethanol for concentrations up to 4 M. Since mixed solvents are more difficult to discuss than the pure components, k' was measured in ethanolic solutions of perchloric acid, where it is a strong acid. As expected, the rate was considerably reduced over that for a corresponding methanol run, so that the experimentally suitable range of acid concentrations had a lower limit of about 2×10^{-4} M. This was the upper limit for methanol as solvent.

The ethanol data are presented in Table II. Up to about 10^{-3} M, k' varies linearly with $(H^+)^2$ but with a small negative intercept, and then increases more rapidly than this with increasing (H^+). The situation for the lower acidities is just that which might be expected from the previous methanol results assuming a similar ρ_1 value, so that now with $(H^+) \gg \rho_1$ only the second-order behavior is observed. The negative intercept, however, indicates probable third-order behavior at considerably lower acidities, and it seems reasonable to postulate a rate law of the same form as (2). A plot of $(H^+)^3/k'$ against (H^+) is strictly linear up to $(H^+) = 0.912$ M. A least-squares fit of the data gives $k_1 = (1.22 \pm 0.05) \times 10^3$ M^{-2} sec^{-1} and $\rho_1 = (4.0 \pm 2.2) \times 10^{-5}$ M. The point at $(H^+) = 1.37$ M appears to show some of the deviation which becomes pronounced at the higher acidities, but if it is included in the analysis, $k_1 = (1.45 \pm 0.07) \times 10^3$ M^{-2} sec^{-1} and $\rho_1 = (14.8 \pm 4.4) \times 10^{-5}$ M. As expected from the mathematical insignificance of the denominator constant for the experimental range studied, its value must be rather indeterminant. This is compounded, as for methanol, by the rate effect of small amounts of water. However, it seems safe to say that the ρ_1 values for the two alcohols do not differ markedly, for the value of 4×10^{-5} M is probably nearer the truth and may even be somewhat high. On the other hand, the numerator constants k_1 differ by over two orders of magnitude.

Table II. Determination of Rate Law Constants for Demetalation of MgP by Perchloric Acid in Ethanol

$10^3(H^+)$, M	$10^2k'$, sec^{-1}	$10^7(H^+)^3/k'$, M^3 sec
0.230	0.0055	2.18
0.456	0.0232[a]	4.10
0.684	0.0535[a]	6.00
0.912	0.097	7.80
1.37	0.250[a]	10.2
2.06	0.600[a]	
2.28	0.765[a]	
2.74	1.25[a]	

[a] Average of two runs agreeing within 1%.

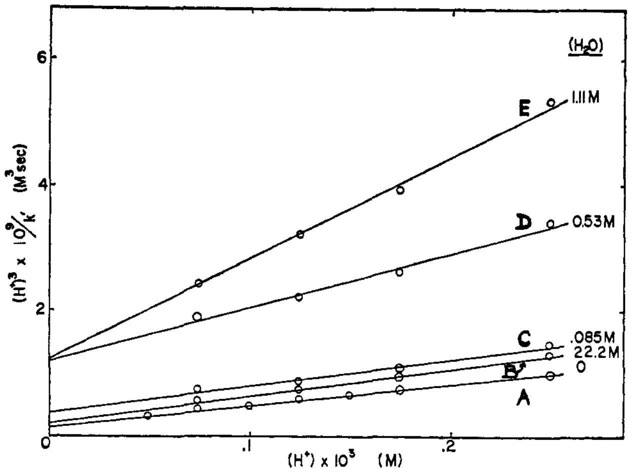

Figure 1. Rate of displacement of magnesium by perchloric acid in methanol–water media.

The deviation of k' from the values predicted by (2) at higher acidities does not correspond to a new term of simple order. Since this is the cation concentration range which leads to specific catalysis (see section on salt effects) and the experimental accuracy is diminishing, evaluation of this effect is not readily effected.

Pyridine Catalysis. The incorporation of magnesium ion into deuteroporphyrin in methanol solution was achieved readily[3] only through the strong catalytic action of certain bases. The most thoroughly studied of these bases was pyridine. A study of the effect of pyridine on the displacement reaction naturally suggests itself, although the particular pathways involved in the two investigations may not be the same because the acidities differ by 10^3. Pyridine is found to be an effective catalyst, with millimolar concentrations doubling the rate of the magnesium loss.

The procedure followed was to prepare a stock solution of pyridine, py, and pyridinium, pyH$^+$, by adding perchloric acid to pyridine in methanol. The rate was then measured as a function of the concentration of this buffer solution, for which $(H^+) \ll 10^{-3}$ $M \gtrsim (py) \gtrsim 10^{-2}$ M, giving a series of experiments in which the ratio $R = (pyH^+)/(py)$, and hence (H^+), remains constant. The three to six values of k' obtained at each R gave excellent linear plots as a function of (py), which was chosen as independent variable. Deviation from the line was quite small, and hence just the intercepts k_1^* and the slopes k_2^* of these lines are tabulated in Table III (* indicates a constant containing the hydrogen ion dependence).

Table III. Pyridine-Catalyzed Demetalation of MgP in Methanol at 42°

R	$10^2k_1^*$, sec^{-1}	$10^2k_2^*$, $M^{-1}\ \mathrm{sec}^{-1}$	k_2^*/R^2, $M^{-1}\ \mathrm{sec}^{-1}$	$10^{-4}R^3/k_2^*$, M sec
0.417[a]	0.0027	0.0060	0.035	1.20
0.430[d]	0.0019	0.0073	0.039	1.09
0.648[a]	0.006	0.0147	0.035	1.85
1.00[b]	0.005	0.0500	0.050	2.00
1.28[d]	0.005	0.087	0.053	2.40
1.44[a]	0.009	0.110	0.053	2.76
1.59[e]	0.005	0.157	0.062	2.54
2.33[d]	0.010	0.300	0.055	4.20
2.81[a]	0.013	0.457	0.058	4.85
3.00[b]	0.010	0.574	0.064	4.70
6.10[c]	0.052	2.45	0.066	9.2
6.10[a]	0.055	2.54	0.069	8.9

[a–d] The letters designate different sets of stock solutions. [e] Hydrochloric acid used.

The slopes k_2^*, arising from a new term first order in pyridine, clearly increase with acidity at a rate greater than R^2 but less than R^3. The hydrogen ion dependence discussed above is again suggested and is confirmed by the linearity of an R^3/k_2^* *vs.* R plot. The new term is, therefore

$$\frac{k_2(\mathrm{py})(\mathrm{H}^+)^3}{\rho_2 + (\mathrm{H}^+)} \tag{3}$$

The constants were determined by a least-squares fit of the data assuming, as before, that all of the error resides in R^3/k_2^*. In terms of R as variable, $k_2 = 0.072 \pm 0.002\ M^{-1}\ \mathrm{sec}^{-1}$ and $\rho_2 = 0.50 \pm 0.08$ at 42°. If the acid dissociation constant of pyridine is taken to be $1 \times 10^{-5}\ M$ (see below), then $(\mathrm{H}^+) = 10^{-5}R$ and $k_2 = (7.2 \pm 0.2) \times 10^8\ M^{-3}\ \mathrm{sec}^{-1}$ and $\rho^2 = (5.0 \pm 0.8) \times 10^{-6}\ M$.

These values, like k_1 and ρ_1, are also affected by water present in the reaction solutions. The effects of water on the rate in a pyridine-buffered solution are considered in detail in the next section, but the correction is readily made here. The water derived from the original 71% acid somewhat increases the slopes, k_2^*, but this small correction does not change the linearity. The alteration is greatest at the higher ratios R so that k_2 is lowered by about 6% and ρ_2 is essentially unchanged. Correction for the residual water in the solvent would lower both k_2 and ρ_2 by nearly the same degree up to a limit of 5%.

The pyridine-dependent rate term has been written in terms of the product of (py) and (H) rather than the equivalent factor 10^{-5}(pyH), implying that pyridine and hydrogen ion interact separately with the MgP in the transition state. There are several reasons for making this assumption rather than proposing the general acid catalyses. The direct testing of other acids is difficult to carry out because practical considerations require acids of pK = 2 to 6 and such acids are uncommon in methanol unless they are nitrogenous bases like pyridine. Nitric acid is quite suitable having pK = *ca.* 2 and an associated base which coordinates poorly. The rate was found to be independent of nitric acid concentration and entirely accounted for by the solvated hydrogen ion term (2), even though nitric acid should, by the Brønstead relation, be superior to pyridine as an acid catalyst. Also, the form of the rate law (3) is not consistent with general acid catalysis for the mechanism to be proposed since addition of pyH^+ in the final step would require pyridine dependence in the denominator. Instead, the coordination of pyridine to the magnesium is to be suspected, for the formation of such complexes is well documented.[11–13] Spectrophotometric measurements for methanol indicate that the monopyridinate complex is formed but accounts, at most, for only a few per cent of the total metalloporphyrin concentration under the conditions of the kinetic experiments, in keeping with the first-order behavior in pyridine. In addition, the above considerations combined with the fact that the incorporation reaction[3] is first order in (py) but inverse first order in (H^+) strongly implies that the over-all catalytic effect of pyridine is through association with the magnesium ion.

The intercepts of the k' *vs.* pyridine plots can, for the most part, be accounted for by the pyridine independent term, (2), already discussed. Comparison of similar k_1^* values from the two studies indicates that the acid dissociation constant of pyridine $K_{\mathrm{py}} = (\mathrm{H}^+)/R$ has the value $1 \times 10^{-5}\ M$. Spectrophotometric determination of K_{py} at 42° in methanol gave $(1.4 \pm 0.2) \times 10^{-5}\ M$. Any discrepancy could easily be the result of a small amount of ion pairing with the pyridinium, magnified by the high order in R (the form of the rate term 3 cannot be explained by ion pairing, however, even if it were not insignificant).

Comparison of k_1^* at the two extremes of the R values where the accuracy is fairly good shows that k_1^* clearly does not have the expected hydrogen ion dependence through the low end of the range. This may be due to a term of lower hydrogen ion order becoming prominent. The existence of such a term is to be expected so that the ratio of the forward and reverse rate expressions may correspond to the proper equilibrium quotient at $(\mathrm{H}^+) \cong 10^{-8}M$, where the incorporation[3] is inverse first order in (H^+).

The temperature dependence of k_2^* was examined for R = 1.28 and found to be quite small, as was the case for k_1^*. (At 25°, $k_2^* = 5.2 \times 10^{-4}\ M\ \mathrm{sec}^{-1}$.) The apparent activation enthalpy associated with k_2 will then be on the order of 5 kcal/mole and the apparent activation entropy −1 eu.

Water Catalysis in Pyridine Buffer. The rate of magnesium displacement was measured in pyridine-buffered methanol as a function of water concentration for $(\mathrm{H_2O}) < 1\ M$. Three series of such runs, each one corresponding to a different pyridine concentration and all referring to R = 6.17, are shown in Figure 2. In every case, k' was found to increase linearly with water concentration (the initial value being simply $k_1^* + k_2^*(\mathrm{py})$), and the slopes of these lines, in turn, increased linearly with pyridine concentration with zero

(11) J. B. Allison and R. S. Becker, *J. Phys. Chem.*, **67**, 2675 (1963).
(12) C. B. Storm and A. H. Corwin, *J. Org. Chem.*, **29**, 3700 (1964).
(13) D. M. Collins and J. L. Hoard, private communication.

intercept for all R values. Hence, a single additional term, $k_2^*(py)(H_2O)$, first order in both pyridine and water, is to be included in the rate law for pyridine solutions containing a small amount of water; no corresponding term appears involving water but not pyridine. The data presented in Table IV indicate that this new term, unlike the previous two, can be described as simply second order in hydrogen ion. The complete rate law, then, for displacement of magnesium ion from MgP in pyridine-buffered methanol containing only a few mole per cent water is

Table IV. Hydrogen Ion Dependence of the Pyridine–Water Term at 42°

R	k_3^*, M^{-2} sec^{-1}	k_3^*/R^2
0.65	0.118	0.280
1.44	0.540	0.260
2.81	2.10	0.266
6.10	9.6	0.258

$$k' = \frac{k_1(H^+)^3}{\rho_1 + (H^+)} + \frac{k_2(py)(H^+)^3}{\rho_2 + (H^+)} + k_3(py)(H_2O)(H^+)^2 \tag{4}$$

with possibly some terms of lower order in H^+ making a very minor contribution. The constant k_3 has the value 2.7×10^9 M^4 sec^{-1} for $K_{py} = 1 \times 10^{-5}$ M. If the pyridine–water term has in fact the same form as the others, *i.e.*, a constant in the denominator, then this constant ρ_3 must be 10^{-7} M or smaller.

The only evident effect of water for these experimental conditions is to add a pathway for reaction jointly catalyzed by the water and pyridine. It is fortuitous that this is so readily observed since the addition of water to methanol markedly increases the solvent basicity and should therefore correspondingly decrease the rate of a reaction of high order in hydrogen ion (as described in the next section). However, the presence of another base in addition to the MgP may provide a protonation equilibrium which is independent of solvent.[14] Apparently, MgP and pyridine are sufficiently similar for this to be the case. Were this not true to a good approximation, the linearity with respect to water could not be observed.

Water in Unbuffered Methanol. Unlike the situation in the pyridine buffer, the addition of water to perchloric acid solutions of MgP decreases the rate of displacement markedly. A reduction of one-half is produced by 0.2 M H_2O. The general variation of k' with the water content can be described as follows: as the water concentration increases, k' decreases, at a steadily diminishing rate, to a minimum value. This minimum value is less than one-tenth the initial value, the exact reduction depending on the hydrogen ion concentration, and occurs at about 15 mole % (4 M) water, apparently independent of (H^+) for 5×10^{-5} $M < (H^+) < 5 \times 10^{-4}$ M. Thereafter, k' increases, reattaining its initial value in the neighborhood of 60 mole % water and with steadily increasing slope greatly exceeds this by 80 mole % (the maximum concentration studied). Only for the small water concentrations, up to 0.2 M, can the variation be described by a simple order. In this range, the rate is inverse first order in (H_2O) with a slope that appears to be independent of (H^+).

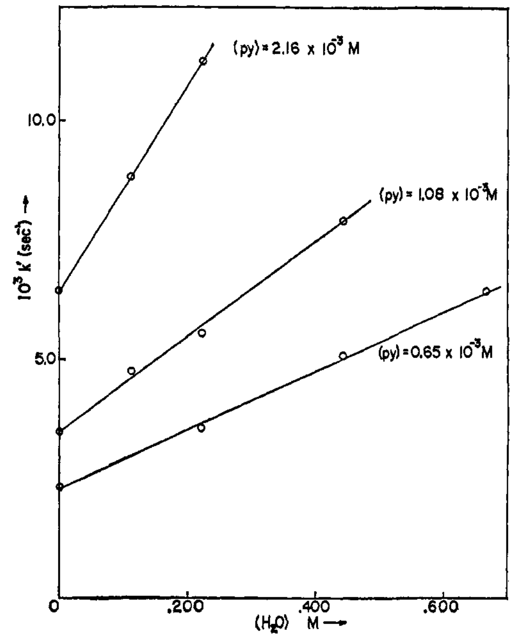

Figure 2. Rate of displacement of magnesium as a function of water concentration in pyridine-buffered methanol.

On the other hand, the dependence upon hydrogen ion concentration turns out to be surprisingly consistent. The data presented in Figure 1 show that, for solvent mixtures up to at least 60 mole % water, a plot of $(H^+)^3/k'$ *vs.* (H^+) is linear. Hence, the rate law proposed for pure methanol, (2), holds for water–methanol mixtures just as well and even for solutions in which the water predominates. This dependence can therefore be extrapolated to pure water with a fair amount of confidence. Of course, the constants k_1 and ρ_1 in (2) must now be interpreted as complicated functions of the solvent composition.

Analysis of the water dependence of the parameters k_1, ρ_1, and k_1/ρ_1, which is the reciprocal of the intercepts in Figure 2, does not seem to lead to any additional insights. Both k_1 and k_1/ρ_1 give a concave curve similar to that already described for k' but with two differences. The initial slope of k_1 is horizontal rather than having maximal negative values as do k' and k_1/ρ_1, while k_1/ρ_1 has a pronounced hood and nearly flat minimum extending over 0.5 $M < (H_2O) < 10$ M. The result of these differences is that ρ_1 behaves in an extremely complicated manner having a maximum at 0.4 M water, a minimum at 4 M, and probably another maximum at around 10 M water. The final value of ρ_1 in the limit of pure water appears similar to the other pure solvents, *i.e.*, 10^{-5} M or somewhat greater.

It is possible to say several things about this system, even though a mathematical formulation was unproductive. As already stated, the form of the hydrogen ion dependence is invariant to the solvent composition and appears to be of general validity for alcoholic

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(14) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959.

solutions. On the other hand, the form of the water dependence is strongly suggestive of the form of the acidity function for these media.[15]

Even though the neutral-base acidity function H_0 is not the only one involved in the present case, it seems highly probable that the appearance of a minimum rate at 15 mole % water reflects a reduced degree of protonation corresponding to the maximum in the mixed solvent basicity which is known to occur at this point. It is also well established that pure water is more basic than pure methanol and yet extrapolation indicates that the rate in pure water is probably 10^2 greater than in pure methanol. This result is inexplicable from the viewpoint of basicity, and the water must therefore be assigned a specific catalytic role. Pyridine buffer results show this catalysis is initially small, which is consistent with the present data, but for solutions in which water is a major constituent the catalysis becomes pronounced and appears to even approach an order greater than unity for water.

Salt Effects. For the experiments carried out in the absence of pyridine, the perchloric acid concentrations were so small as to preclude significant nonspecific salt effects. On the other hand, in pyridine buffer, ion concentrations reached 10^{-2} M where salt effects might be a reasonable possibility.

As the pyridine concentration increases at constant R, the ionic strength, μ, also increases in proportion due to the pyH$^+$ and ClO_4^-. A secondary salt effect is not to be expected for a neutral base like pyridine, but a primary salt effect is quite possible, since some step in the displacement presumably involves reaction between positive ions, for which a rate increase with μ is predicted. However, if salt effect were responsible for any significant fraction of the rate increase with pyridine, one would expect nonlinear behavior in accordance with the Debye–Hückel relation. The most direct test, of course, is the addition of an inert salt; however, there is a large specific salt effect due to the cation. This cation catalysis does level off in the neighborhood of $\mu = 0.1$ and further variation of μ does not seem to cause any noticeable primary salt effect.

For a reaction between positive ions, it is usually expected that anions will be specifically stabilizing. This was tested in the present case by comparison of ClO_4^- and Cl^-. One test was preparation of the pyridine buffer with HCl rather than $HClO_4$. The resultant k_2^* (see Table III) was 10% higher than the "best-line" value, which is somewhat greater than the experimental error. The other comparison contrasted the effect of LiCl and $LiClO_4$ in py buffer. The two salts increase the rate in parallel fashion, but the rate is again somewhat higher in the Cl^- solutions. It is probable therefore that a small specific anion effect does exist.

A truly sizeable salt effect does occur, however, in the lithium salt solutions, and this must be due to the presence of the Li^+. Both with and without pyridine buffer, the rate rises rapidly starting with $\sim 10^{-3}$ M Li^+ and then levels off at some higher value at 10^{-1} M Li^+. In unbuffered solution, the final k' is about threefold greater than the initial $k' = k'_0$. Under the same conditions, NH_4Cl gives a final k' less than twofold greater, while tetraethylammonium chloride does not ever show catalytic behavior but rather a gradual inhibition (20% decrease for 0.1 M Et_4N^+; a gradual rate reduction is the typical effect of inert organic molecules). Catalysis by salts such as $LiClO_4$ must therefore be associated with the presence of a small positive ion. In keeping with this, (pyH) < 10^{-2} M should have no effect as a cation and this is observed.

Table V contains a portion of the data for $LiClO_4$ addition to the unbuffered system. The initial linear increase followed by a leveling off was at first suggestive of the behavior of the "third" proton in (2), *i.e.*, the proton which gives rise to the denominator. There would then be an additional term for Li^+

Table V. Variation of the Rate as a Function of Added Salt at 42°

$(H^+) \times 10^3$, M		$(LiClO_4) \times 10^3$, M			
		0	4.5	13.5	22.4
0.050	$k' \times 10^3$	0.407	0.59	0.77	0.91
	k'/k_0	...	1.45	1.88	2.26
	$10^8(Li^+)(H^+)^2/\Delta$	...	6.1	9.2	10.8
0.100	$k' \times 10^3$	2.16	3.05	4.2	4.6
	k'/k_0	...	1.41	1.93	2.12
	$10^8(Li^+)(H^+)^2/\Delta$	...	5.3	6.8	9.1
0.150	$k' \times 10^3$	5.4	8.3	10.2	11.3
	k'/k_0	...	1.52	1.85	2.10
	$10^8(Li^+)(H^+)^2/\Delta$	...	3.6	6.4	8.5

$$\Delta = k' - k'_0 = \frac{k_{Li}(Li^+)(H^+)^2}{\rho_{Li} + (Li^+)} \tag{5}$$

A plot of $(Li^+)(H^+)^2/\Delta$ against (Li^+) should then be linear and (H^+) independent. The experimental data for $LiClO_4$ addition showed several times the usual reproducibility error but the plots do appear linear. However, as the data in Table V show, the lines are not (H^+) independent.

Actually this sort of two-pathway mechanism would demand competition between H^+ and Li^+ so that there would be a common denominator first order in both these variables. Then, even if a Δ were separable, the intercepts of the above-described plots would increase with (H^+), while clearly the opposite is the case.

A formulation consistent with the data is

$$k' = \frac{k_1(H^+)^3}{\rho_1 + (H^+)}\left[1 + \frac{\alpha_1(Li^+)}{\beta_1 + (Li^+)}\right] \tag{6}$$

This predicts that the ratio $r = k'/k'_0 = 1 + \alpha_1(Li^+)/\beta_1$ to $+ (Li^+)$ is independent of (H^+) and Table V shows this be the case. Also r will start at unity, increase linearly, and then level off, again in accordance with the data. Finally, a plot of $(Li^+)/(r - 1)$ *vs.* (Li^+) should be linear with intercept β/α and slope $1/\alpha$. In addition to the data given in Table V, for (Li) = 0.045 M, six runs at four different acidities give $r = 2.6 \pm 0.1$ and for (Li) = 0.093 M, three runs at three acidities give $r = 3.2 \pm 0.1$. These five points do fall on a straight line when plotted as above, to give $\alpha_1 = 2.5$ and $\beta_1 = 0.09$ M. The ratios r are unaltered by the presence

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[15] G. Kortum and K.-W. Koch, *Ber. Bunsenges. Physik. Chem.*, **69**, 677 (1965).

of water as well as H^+ (for a series of runs in 1.11 M H_2O, which decreases k' fivefold in magnitude).

The same kind of curvature is obtained in pyridine buffer solutions. The principle difference is a somewhat quicker achievement of the limiting k' value and a smaller magnitude for this value. Only the effect of varying (py) at constant $R = 3.0$ was tested and r proved to be invariant. Limiting values of r are 1.4 for $LiClO_4$ and 1.6 for LiCl.

Effect of Other Reagents. As previously mentioned, "inert" organic substances tend to reduce the rate of magnesium displacement for both the pyridine and nonpyridine pathways. The effectiveness of rate reduction at a given concentration (*e.g.*, 1 M) for four solvents studied is $CH_3CH_2OH > CH_3CN \simeq C_6H_6 > CCl_4$. Presumably, none of these, at 1 M concentration, reduces the ionizing power of methanol nor changes its basicity appreciably.

Phenol has been used as a catalyst in several metal-displacement studies.[6,16] It is of interest in the present study for this reason and because it is both an alcohol and has an aromatic ring like pyridine. A strong catalytic effect was observed for reagent grade phenol in the present systems, but this entirely disappeared when the hypophosphorous acid, used as a stabilizer, was eliminated. Carefully purified phenol has about the same effect as benzene.

Another compound resembling pyridine, and of interest for its vastly superior coordination of Mg, is 8-hydroxyquinoline. Comparison of their kinetic effect was made using buffer solutions of each having $r \simeq 1$. After adjustment for the somewhat greater basicity of the 8-hydroxyquinoline nitrogen, comparison of the same hydrogen ion concentration gave a value of $k_2^* = k'/(\text{base})$ about three times larger for the 8-hydroxyquinoline than for the pyridine.

Protonation Equilibria. The rate laws described above indicate an important step in the displacement process must be the protonation of MgP. Interpretation of the constant ρ in the denominator requires a knowledge of the extent to which the first protonation occurs, specifically whether ($MgPH^+$) is of the same magnitude as (MgP) or only a minor fraction thereof for the acid concentrations used; for in the first case $\rho_1 = K_1^{-1}$, the acid dissociation constant of $MgPH^+$, while in the second case $K_1^{-1} \gg \rho_1$.

Determination of the degree of protonation by the usual methods such as potentiometric titration was complicated by the methanolic solutions and particularly by the fact that sufficient H^+ to protonate the MgP was also sufficient to give demetalation. The procedure which was followed was a spectrophotometric indicator experiment using pyridine bands around 260 mμ. Pyridine serves this purpose nicely because it absorbs at a window in the MgP spectrum, its ρ_2 value is well characterized, and the absorption is intense enough that the spectrally appropriate pyridine concentration gives very slow reaction ($R = 1.6$, (py) $= 5 \times 10^{-5}$ M). Addition of MgP, of final concentration 8×10^{-5} M, should have reduced R to 0.61 and reduced the absorbance at 256 mμ by 20%. The experimental result was no reduction in absorbance and no charge in the vibrational structure of the band (uncertainty in the background from MgP would mask a small change). Hence, $K_1 \ll \rho_2$, which is not entirely unexpected, since K_1^{-1} for PH_3^+ is about equal to ρ_2 and MgP would not be expected to protonate as well as PH_2.

Another experiment carried out for the purpose of detecting $MgPH^+$ involved changes in the visible spectrum of MgP upon addition of perchloric acid. The spectrum changes with time as a result of $PH_2 + PH_3^+$ formation by displacement, but repetition allowed each portion to be extrapolated back to zero time. The changes were followed as a difference spectrum of MgP $+ H^+$ against MgP. Negative regions grew in at 537 and 574 mμ and positive at 490, 515, 555, and 595 mμ. The 490-mμ region shows a small negative absorbance (1%, expressed in per cent of total MgP absorption at 537 mμ for MgP *vs.* solvent), which represents conversion of PH_2 impurity to PH_3^+ initially. The following figures are corrected for this. The zero time absorbances are 515 mμ, 3%; 537 mμ, −1%; 555 mμ, 4%; 574 mμ, −1%; 595 mμ, 2%. Since one suspects that the extinction coefficients of $MgPH^+$ are not much greater than those of MgP, the positive–negative unbalance is undoubtedly an unbalance in the difference concentrations. It should also be pointed out that although the percentages, as expressed, are small, in the difference experiment they are doubled only after 20 min during which time the spectrum has been run five times (*e.g.*, 0.04 → 0.09 absorbance, 0–1.00 scale, in 20 min).

The initial spectrum appears to indicate formation of a few per cent of $MgPH^+$ for (H^+) $= 6 \times 10^{-5}$ M, which has a typical monocation spectrum. The acid dissociation constant is then somewhat greater than 10^{-3}.

Another spectrophotometric observation of interest is the enhancement of pyridine complexation of MgP in the presence of hydrogen ion. The decrease of the MgP Soret band at 404 mμ was measured as a function of pyridine concentration (up to 1.0 M) and pyridinium concentration ($R = 0.04, 0.06$). These small buffer ratios prevent magnesium displacement and give a negligibly small $MgPH^+$ concentration. Also, the small (pyH^+), if it were pyridine, would have no effect on the MgP spectrum, nor does it effect the PH_2 spectrum.

The experimental result, however, is a dramatic absorbance decrease upon addition of the pyH^+; *e.g.*, the fractional decrease, f, for (py) $= 0.50$ M of the total decrease found for pure pyridine is 5% for $R = 0$ but 10% for $R = 0.04$. For less than 10% of the total change possible, the observed decreases are proportional to (py), indicating formation of monopyridinate complexes. These data suggest that the far more stable species $pyMgPH^+$ forms in pyridine buffer in preference to both pyMgP and $MgPH^+$. In addition, if $pyMgPH^+$ is the principal species in the buffer solution, then the change is proportional to R as well as pyridine, and this is observed (for $R = 0, 0.04, 0.06$; $f/(\text{py}) = 0.10 \pm 0.01, 0.21 \pm 0.02, 0.29 \pm 0.02$).

The species $pyMgPH^+$ will amount to only a small fraction of MgP under the conditions of the other spectrophotometric and kinetic experiments. This is also consistent with not interpreting ρ as an acid dissociation constant, as is the observation that now (py) would occur in the denominator of (3).

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(16) S. C. Kiang, Ph.D. Dissertation, University of Utah, 1965.

Discussion

The rate terms, (2) and (3), both contain a fractional hydrogen ion dependence of the form, $(\mathrm{H}^+)^3/[\rho_i + (\mathrm{H}^+)]$. The possibility that this quotient represents considerable formation of MgPH^+ in a preequilibrium, in which the fraction of porphyrin in the protonated form would be $(\mathrm{H})/[K_1^{-1} + (\mathrm{H})]$ with ρ_1 being identified as the acid dissociation constant, can be rejected on the basis of the spectrophotometric experiments. The most reasonable mechanism appears to involve a sequence of steps producing steady-state intermediates. A number of steps at equilibrium precede the rate-determining step which will be either a third protonation or the step just prior to it when the acidity is sufficiently high to make the third protonation competitive with the reverse of this prior step. In its most abbreviated form, for any given term, this proposed mechanism is

$$\mathrm{MgP} + 2\mathrm{H}^+ + \mathrm{X} \underset{k_{n\mathrm{r}}}{\overset{K_1K_2\text{–}K_{n-1}k_{n\mathrm{f}}}{\rightleftharpoons}} \mathrm{XMgPH_2}^{2+} \qquad (7)$$

$$\mathrm{XMgPH_2}^{2+} + \mathrm{H}^+ \xrightarrow{k_{n+1}} \text{products} \qquad (8)$$

which by a steady-state treatment leads to the rate law

$$k' = \frac{K_1K_2\text{–}K_{n-1}k_{n\mathrm{f}}(\mathrm{X})(\mathrm{H}^+)^3}{k_{n\mathrm{r}}/k_{n+1} + (\mathrm{H}^+)} \qquad (9)$$

where X stands for all of the species other than H^+ appearing in the rate term (*i.e.*, pyridine and/or water). The constant ρ_i is interpreted as the rate constant ratio $k_{n\mathrm{r}}/k_{n+1}$, which determines the dominant rate-limiting step, k_i as the rate constant $K_1\text{–}K_{n-1}\cdot k_{n\mathrm{f}}$ for the limiting case of high (H^+) where the *n*th step is rate limiting, and k_i/ρ_i as the rate constant $K_1\text{–}K_nk_{n+1}$ for low (H^+) where the third protonation is rate determining.

It is clear from the slowness of the reaction, the value of $\Delta S^{\ddagger}$, the effect of solvent, and the appearance of coordinating agents in the higher order terms that solvations and perhaps rearrangements, not observable kinetically, must be involved in the lower order terms in addition to the protonations. The existence of such complexing steps prior to the rate-determining step is consistent with the idea that it is energetically impossible to break all of the magnesium to porhyrin bonds simultaneously so that instead solvent–magnesium bonds must be successively formed at the expense of the nitrogen–magnesium bonds. The question is when these steps occur relative to the second protonation and the first of the rate-determining steps. Certainly, several rapid processes occur after the final rate-determing step: complete solvation of Mg^{2+} and attainment of the $\mathrm{PH_2}$–$\mathrm{PH_3}^+$ equilibrium. Rapid exchange of the solvent from the weakly bound sixth "octahedral" position of MgP is also to be expected.

The existence of solvation steps for the nonpyridine pathway, (2), can be demonstrated readily from the magnitude of the associated constants. In methanol, the product $k_1\rho_1$ is essentially unity. Substitution of the corresponding expressions from the mechanistic interpretation gives

$$K_1/K_2 = k_{3\mathrm{f}}/k_{2\mathrm{f}}^2 \qquad (10)$$

where 1, 2, 3 identify the three stepwise protonations and f indicates forward direction. The ratios K_1/K_2 and $k_{2\mathrm{f}}/k_{3\mathrm{f}}$ would be expected to be greater than or equal to unity for successive formation of positively charged acids (near equality is a reasonable assumption in the present case since the lack of a primary salt effect indicates little interaction between the positive charges). Hence, the two sides of (10) fail to agree by at least the value of the rate constant for proton transfer, perhaps $10^7\ M^{-1}\ \mathrm{sec}^{-1}$. This argument is independent of the absolute value of the equilibrium constants; however, the same result is obtained directly from $k_1 = K_1k_{2\mathrm{f}} = 10^5$ if the value of $K_1 = 10^3$ is accepted. The conclusion follows that at least one other step besides protonations must be included for (2). Insertion of such a step either before or after the second protonation introduces new constants into both of the above relations permitting them to be reasonably satisfied.

Good evidence for the existence of a step specifically between the final two protonations comes from consideration of the magnitude of ρ_1. If the final two protonations are assumed to be consecutive, then $\rho_1 = k_{2\mathrm{r}}/k_{3\mathrm{f}}$, and introducing K_2 and the magnitude of ρ_1 in methanol

$$K_2 = 10^5k_{2\mathrm{f}}/k_{3\mathrm{f}} \qquad (11)$$

leading to the inequality $K_2 > 10^5$. Hence, K_2 would have to be at least a 100-fold greater than K_1. Since the monocation is observed for the parent deuteroporphyrin, *i.e.*, $K_1 > K_2$, and since K_1 is expected to be greater from general considerations, we are forced to conclude that the above assumption is incorrect and that a solvation step occurs between the second and third protonations. The rate law demands that this step approach equilibrium only for $(\mathrm{H}^+) \ll 10^{-5}\ M$ and would not be violated by additional nonequilibrium steps as long as only the first of these involves a variable concentration. The most concise formulation of the mechanism would introduce but a single solvation as the *n*th step in eq 7. This relieves the necessity for postulating any earlier solvations although their existence is indicated by analogy to the pyridine–water term. The magnitude of k_1 indicates that these solvations must be slower than the methanol exchange rate[17] of $10^4\ \mathrm{sec}^{-1}$ at 42° and hence involve some degree of molecular rearrangement.

An estimate of the true activation parameters for the rate-determining solvation *n* can be obtained by subtracting out the equilibrium thermodynamic values of the two prior protonations from the over-all parameters calculated for k_1. This is equivalent to making $\mathrm{MgPH_2}$ the initial reactant, but the activation parameters will still include the equilibrium values for any solvations preceding the *n*th step. For protonation of a neutral base,[14] $\Delta H^\circ \simeq \Delta F^\circ$, and if this is assumed to hold for both protonations with $K_1 = 10^3$ and $K_2 = 10^{-2}K_1$ as in the parent deuteroprophyrin,[6] then $\Delta H_n^{\ddagger} = 8$ kcal/mole and $\Delta S_n^{\ddagger} = -27$ eu. The large unfavorable entropy of activation is consistent with a solvation process. In addition, consideration of the over-all activation parameters for the final rate-limiting step, derived

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(17) S. Nakamura and S. Meiboom, *J. Am. Chem. Soc.*, **89**, 1765 (1967).

from k_1/ρ_1, in combination with the parameters for transfer of the solvated proton involved and the above estimates, indicates that $\Delta S_n{}^\circ \approx \Delta H_n{}^\circ \approx \Delta F_n{}^\circ \approx 0$. Hence, K_n, which might actually be a product of several solvation constants, is not very different from unity, in agreement with the value derived directly from $k_1/\rho_1 = K_1K_2K_nk_{n+1} = 10^{10}$. The solvation of $MgPH_2$ by methanol is therefore a fairly favorable process. If more than one solvation by methanol is involved in (2), the equilibrium thermodynamic values above are such as to suggest that they probably apply to each step separately as well as the aggregate. In this case, the estimated solvation activation parameters apply directly to the *n*th solvation.

Mention should be made of the possibility of interpreting the experimental rate law in terms of a push–pull type of mechanism where in the final step pyridine or methoxide would function as proton acceptors. Such a process would be atypical of chelate substitution reactions. Furthermore, for methoxide a total of four protons would have to be added in prior steps producing a 4+ species; also the concentration of methoxide ions is only 10^{-13} *M*. On the other hand, inclusion of pyridine in the final step gives the wrong rate law. The totality of evidence cited therefore is at variance with interaction between pyridine and protons being of catalytic importance but rather points to the coordination of pyridine with magnesium ion as the essential function. This must also be true of incorporation of magnesium, even though the complex cannot be directly observed.

In order to examine the catalytic effect of pyridine further, one can assume that the role of pyridine in the pyridine pathway is assumed by solvent in the nonpyridine pathway, and hence insert the solvent methanol concentration into (2). The constants k_1 and k_2 then have the same units and can be compared, k_2 being 10^5 greater than k_1. Yet pyridine is a much poorer complexing agent for magnesium ion than methanol[3] and is not even particularly superior to methanol in regard to coordination of the magnesium in MgP. The explanation of the effectiveness of pyridine must therefore reside in a weakening of the nitrogen–magnesium bonds either through an electronic rearrangement or creation of a favorable geometry. Electronic rearrangement is equivalent to a *cis* effect, which is generally quite small, and should be particularly so for a cation like Mg having low polarizability and devoid of specialized bonding. In fact, data obtained by Grinberg[18] for Pt(II) establish a trend which would assign a greater *cis* effect to alcohols.

Comparison of the two paths can also be made in terms of activation parameters (again inserting (MeOH) into (2) to allow comparison of $\Delta S^{\mp}$). Starting from $MgPH_2{}^{2+}$, for k_1 of the nonpyridine pathway, $\Delta H^{\mp} = 8$ kcal and $T\Delta S^{\mp} = 10$ kcal, while for k_2 of the pyridine pathway, $\Delta H^{\mp} = 11$ kcal and $T\Delta S^{\mp} = 0$. Hence, the catalysis by pyridine can be ascribed entirely to a very favorable entropy change for formation of the first activated complex of the pyridine pathway.

The establishment of a geometry especially favorable to the displacement process must therefore account for the major part of the rate increase due to pyridine. Presumably, the magnesium is held further out of the porphyrin plane so as to facilitate both solvation of the magnesium through elimination of steric hindrance and protonation of the nitrogens through separation of the positive charge. The idea that pyridine and hydrogen ion cooperate to promote this movement is supported by the special stability of $pyMgPH^+$ over pyMgP. Evidence in favor of increased opportunity for additional coordination when pyridine is present is provided by the enhanced catalytic effect of a water molecule when associated with pyridine in the activated complex. The pyridine–water term grows in much more rapidly than the corresponding methanol–water term as water is added to the solvent methanol, the latter term not even appearing in (4) for $(H_2O) < 1$ *M*. (This effect is even more pronounced for pyrophosphite.[19]) That an out-of-plane geometry might be fairly stable is not surpising since magnesium does not have stereochemical requirements favoring the square-planar arrangement and, for covalent binding might resemble beryllium in favoring a tetrahedral coordination, which can be approximated in the postulated intermediate. X-Ray structure determinations of zinc tetraphenylporphines show the Zn^{2+} to be 0.2 Å further out of the plane when pyridine, rather than water, is coordinated to the metal.[13]

On the other hand, the kinetic effectiveness of the alcohols compared among themselves correlates well with their known coordinating abilities. The generally observed order of complex stability, based for example on studies with magnesium(II),[17] chromium(III),[20] and the lack of phenol complexes,[21] is $H_2O > CH_3OH > CH_3CH_2OH > C_6H_5OH$. This same order is found for the proton basicities,[22,23] compared in a common solvent, which might be expected to apply for an alkaline earth ion. One kinetic comparison of the alcohols involves the relative magnitude of k_1 in (2) as obtained in the pure alcoholic solvents. k_1 for pure water is on the order of a 100 times greater than k_1 for methanol which is in turn 300 times greater than that for ethanol. If correction is made for the pure solvent proton basicities which have the ratio 1:0.13:0.33 for water, methanol, and ethanol respectively,[14] the intrinsic ratios of k_1 for these alcohols, independent of protonation, would be more like 10^4:1:10^{-2}. This conforms with the expectation that the organic alcohols will resemble each other more than water in coordinating ability. A second kinetic comparison can be made by means of the pyridine-catalyzed terms, which refer to experiments in which methanol alone acts as a solvent. If this solvent methanol concentration is included in (3) explicitly, then the constant k_3 for water–pyridine catalyses is 10^2 greater than k_2 for methanol–pyridine catalyses. The latter pathway is in turn inhibited by ethanol, implying that the ethanol also coordinates but less well; phenol does not show any effect at all. An additional indication of the importance of solvent basicity is the almost negligible effect of carbon tetrachloride on the rate. This molecule might very well associate with the

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(22) D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solution," Butterworth & Co., Ltd., London, 1965.

(23) C. E. Newall and A. M. Eastham, *Can. J. Chem.*, **39**, 1752 (1961).

periphery of the porphyrin but apparently does not affect the central region at all (a situation analogous to anionic detergent acceleration of copper incorporation[24]).

The possibility that the difference in rate associated with the alcohols is explainable through the solvation of the magnesium ion on the side opposite to its direction of displacement can be discounted. The rate of loss of this solvent molecule should be rapid considering the fast exchange of solvent with Mg^{2+} in general and the unfavorable nature of this site in MgP, particularly after the Mg^{2+} is partially displaced from the plane of the porphyrin. Even if inert binding were a possibility, the trend in rates observed for the alcohols in pyridine-buffered methanol is opposite to that for the rate of loss of the alcohol molecules, for studies of chromium(III) alcohol compexes[20,25] show that ethanol is replaced fastest and water slowest when compared in a common solvent. Another possibility is that the solvent on the opposite side could have a labilizing effect on the magnesium–nitrogen bonds. However, the *cis* effect is expected to be small and bound methanol and water have been shown to have identical kinetic effect on the replacement of other ligands on the first coordination sphere.[25]

Another comparison of interest is the relative value of ρ for the three terms in (4). As already mentioned, it seems reasonable to postulate the same fundamental mechanism for the water-catalyzed term and simply assign a ρ_3 value of $<10^{-7}$. On this basis $\rho_1 = \rho_2 \gg \rho_3$; that is, the replacement of methanol by pyridine has little effect, but replacement of an additional methanol by water has a pronounced effect. Comparison of both parameters for the pyridine terms, $k_3 = 10^2 k_2$ and $\rho_3 \leq 10^{-2}\rho_2$ suggests that inclusion of water increases the value of K_n through roughly equal and opposite changes in the forward and reverse rate constants of the nth step. The fact that pyridine does not have this dual effect suggests that the effect is not simply the result of coordination but rather that the water is actually added in the nth step itself. This would be the most reasonable place for a second coordination.

8-Hydroxyquinoline might have been expected to be an unusually good catalyst. It resembles pyridine and yet the stability constant of the mono complex of Mg^{2+} is at least 10^6 greater than that for pyridine as a result of its chelating ability. The pyridine–water term indicates that chelation might be possible in the present mechanism (addition of one 8-hydroxyquinoline to Cu(II) greatly catalyzes its incorporation into porphyrin[24]). The failure of 8-hydroxyquinoline to be markedly superior to pyridine could indicate insufficient driving force to deprotonate the hydroxyl group or it may indicate that the conformation required for effective catalyses is incompatible with chelation. The catalytic effect observed suggests monodentate attachment with the slightly more basic nitrogen of 8-hydroxyquinoline, compared to that of pyridine, giving a threefold rate increase.

In summary, the mechanism for displacement of the magnesium appears to involve a succession of protonations and ligations in which the two processes may alternate each facilitating the other. In this way, the bonding requirements of both the magnesium ion and the porphyrin nitrogens are met as the magnesium–nitrogen bonds are progressively weakened and the magnesium ion is removed from the plane of porphyrin. The intermediate formed subsequent to the first transition state may resemble the "stitting-atop" complex described by Fleischer and Wang[26] in having essentially two bonds between the magnesium and the porphyrin, but must differ in the greater strength of these bonds since the true "sitting-atop" complex is unstable in polar solvents. The system may then pass through this configuration after the final protonation.

Acknowledgment. The authors gratefully acknowledge the skilled technical assistance of Donna Derrig and Merna Fontes.

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