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Formation and Dissociative Breakdown of Chlorophyll and Its Synthetic Analogues in Solution

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A critical survey is made of studies on the mechanism, kinetics, and thermodynamics of the formation and the dissociation of chlorophyll, its metal analogues, and other metal porphyrins. Consideration is given mainly to results published during the past decade. Special attention is paid to complexes of the most important natural porphyrin—chlorophyllic acid. A list of 120 references is included.

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I. INTRODUCTION

Research on chlorophyll and structurally similar complexes of other porphyrins has entered a new stage during the past twenty years. The comprehensive study of the properties of this numerous group of complexes is progressing as one of the most important links in the chain of diverse problems waiting to be solved on the path to mastery and conscious control of photosynthesis. Until recently the most intensely studied physicochemical properties were the optical and electrophysical properties of chlorophyll, its analogues, and products of their reversible chemical reactions[1-20]. Many interesting results have been obtained by infrared[3-5,10,12,18,19], nuclear magnetic resonance, and electron spin resonance spectroscopy[4-6,12]. A special place is occupied by investigations on the electronic absorption spectra and spectral luminescent properties of chlorophyll, its structural analogues, and their photoreduced forms[1,4-11]. Scale investigations on the properties of photoreduced forms of chlorophyll and other porphyrin compounds, made in the Soviet Union by Krasnovskii, Evstigneev, and others[6,11,15-17,20], have formed the basis of fertile new insights into the rôle and nature of the transformations of the inner-complex pigment system in the photosynthesising apparatus of plants while functioning in the living cell.

Products of the dark reduction and the photoreduction of metal analogues and structural analogues of chlorophyll, as well as of the complexes formed by association with metal salts, have been widely studied during recent years[10,19,20]. Results of paramount importance have been obtained in this field. However, they are not directly connected with the subject of the present Review, and therefore will not be covered. Naturally, in view of what has been said, the Reviewers do not aim to give any complete list of references on these questions. Such a list can be found in the reviews cited above.

Experimental researches on the physicochemical properties of chlorophyll and other tetrapyrrole pigments during the past decade have been accompanied by quite fruitful theoretical investigations[21-29]. A critical survey of scientific results on the structure of these molecules obtained by spectroscopic methods and theoretical calculation will be found in the monograph by Gurinovich et al.[5]

Chlorophyll and other metal porphyrins utilise their coordinating properties in their formation and decomposition, as well as their functioning in vegetable and animal organisms, so that the investigation of these properties is of considerable interest. Although the first attempts at quantitative examination of the dissociation of chlorophylls-a and -b in solution were made more than thirty years ago[30-32], since then the formation of metal analogues of chlorophyll from metal salts and the corresponding "ready made" porphyrin molecules, as well as their dissociation, have been studied almost entirely qualitatively or at best semi-quantitatively. The results of these numerous attempts were summarised in Phillips' review[33]. Systematic studies of the formation and the decomposition of chlorophyll-like inner-complex compounds were begun about fifteen years ago. They can be regarded as originating with the appearance of papers by Kukhtevich[34,35], Caughey and Corwin[36], Fleischer[37], and one of the present Reviewers[38]. Within a short time numerous data were obtained on the coordination properties of chlorophyllic acid and other porphyrins, and on the mechanism of the formation and the decomposition of structural analogues† and metal analogues‡ of chlorophyll in various solvents. There is at present no review of the porphyrins in which due attention is paid to quantitative investigations of coordination properties.

The well known and extremely comprehensive and interesting monograph by Falk[8] discusses only out-of-date results of semi-quantitative kinetic investigations of the dissociation and formation of metal porphyrins, so that judgments and conclusions based on them are often unsound. The aim of the present paper is to examine critically research results on the coordination properties of porphyrins and to elucidate the main laws governing the formation and the breakdown of chlorophyll and other metal porphyrins in solution.

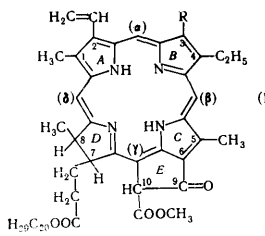
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† Structural analogues of chlorophyll are taken to be porphyrins and their derivatives of similar structure to chlorophyllic acid, i.e. most tetrapyrrole pigments with conjugation in the macro-ring.

‡ Metal analogues of chlorophyll are taken to be inner-complex compounds of metals with chlorophyllic acid other than the magnesium complex.

II. FORMATION OF METAL AND STRUCTURAL ANALOGUES OF CHLOROPHYLL IN SOLUTION

Most complexes of chlorophyllic acid (I), otherwise termed phaeophytin ($H_2\Phi$)



(I) R = CH_3; chlorophyllic-a acid; R = CHO; chlorophyllic-b acid

are formed by heating metal salts (MX_2) with phaeophytin dissolved in an organic solvent. The procedure suggested by Zalesky[39] has been widely used up to the present time. Glacial acetic acid (HOAc) is used as solvent, with a large excess of the metal acetate as the salt. The phaeophytin is complexed by heating the mixture on a boiling waterbath for 2 h. It has since been shown[40] that such treatment produces no changes in the phaeophytin molecule, and glacial acetic acid is one of the most favourable media[41] for the formation of metal analogues ($M\Phi$) of chlorophyll:

$$H_2\Phi + MX_2 \rightleftarrows M\Phi + 2HX. \quad (1)$$

Formation of $M\Phi$ takes place most rapidly in glacial acetic acid. Zalesky's method can be used to obtain stable copper(II), cobalt(II), nickel(II), iron(II), manganese(II), palladium(II), silver(II), and zinc(II) complexes. Organic solvents of other types—alcohols, esters, ethers, ketones, pyridine, quinoline, dimethylformamide—are used to prepare the cadmium(II), mercury(II), lead(II), silver(I), and certain other complexes, which are unstable even in weakly proton-donating media[41]. However, complexes of alkali and alkaline-earth metals (other than magnesium) cannot be obtained by this method, for reasons which will become clear from the subsequent discussion. Nor can treatment of the porphyrin with the metal alkoxide in alcohol or pyridine, generally adopted for other porphyrins[42], be used to prepare alkali-metal analogues of chlorophyll, owing to the instability of the cyclopentanone ring (E) of chlorophyllic acid in the presence of alkaline reagents[43]. Beryllium(II), calcium(II), strontium(II), and barium(II) analogues of chlorophyll also have not yet been prepared.

Chlorophyll itself, the progenitor of all metal phaeophytins, can be obtained by introducing magnesium into the phaeophytin molecule by means of a Grignard reagent[33,42] or a magnesium subhalide prepared from magnesium and iodine in dry pyridine[44]. Later results[45] seem to allow hope that the magnesium ion may be introduced directly into the phaeophytin molecule from solutions of its salts in organic solvents. The actual possibilities of this method will be discussed below. First we shall examine the formation of complexes from natural porphyrins—chlorophyllic-a acid.

1. Formation of Metal Analogues of Chlorophyll in Solution

The most detailed study has been made of the formation of complexes of chlorophyllic acid. The first attempt at a quantitative kinetic study of reaction (1) was made by Baker and Hodson[46], who measured the rates of formation of nickel phaeophytinate $Ni\Phi$ in methanol. They were able to obtain only empirical rate constants and an empirical kinetic equation of fractional order, which was attributed to unjustifiably severe experimental conditions and inaccurate measurements. These results were subjected to critical discussion by Berëzin and Sosnikova[38], who made a series of investigations[47-52] aimed at establishing the kinetics of the formation of metal analogues of chlorophyll in ethanol using the iron(II), cobalt(II), nickel(II), copper(II), zinc(II), silver(II), cadmium(II), mercury(II), and palladium(II) complexes as examples. Experiments were made with chlorophyllic acid under mild conditions between 15° and 50°C. The concentration of the metal salts was varied from 0.00025 M to 0.025 M. Reaction (1) took place in the presence of a considerable excess of the salt, since the concentration of phaeophytin-a did not exceed 0.000025 M. The reaction was of the first order with respect to salt concentration at all concentrations of copper(II) acetate, iron(II) chloride, and cobalt(II) chloride. With other metals the order with respect to salt concentration fell below unity as the concentration increased. The first order of reaction (1) with respect to phaeophytin was strictly maintained in ethanol with all the salts studied at all the temperatures. The general character of the kinetic dependence of reaction (1) on salt concentration is illustrated in Fig. 1 for the formation of cadmium(II) phaeophytinate[48]. Fig. 2 shows the typical dependence for most salts of the order of reaction (1) on salt concentration, illustrated by the formation of the cadmium complex from the acetate.

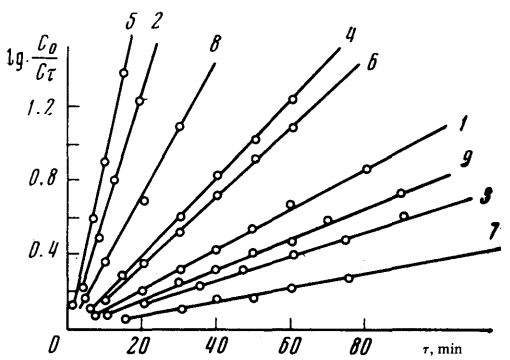


Figure 1. Rates of formation of cadmium phaeophytinate-a at different salt concentrations c and temperatures (°C): 1) 0.0025 M CdI_2 at 30°; 2) 0.0025 M CdI_2 at 40°; 3) 0.00025 M $Cd(NO_3)_2$ at 30°; 4) 0.00025 M $Cd(NO_3)_2$ at 40°; 5) 0.0025 M $Cd(NO_3)_2$ at 30°; 6) 0.0025 M $CdCl_2$ at 30°; 7) 0.00025 M $CdCl_2$ at 30°; 8) 0.0025 M $CdCl_2$ at 40°; 9) 0.00025 M $CdCl_2$ at 40°.

It was concluded from the results[38,48-50] that, at low concentrations of metal salts (below 0.0005 M), reaction (1) conforms to the second-order kinetic equation

$$-\frac{dc_{H_2\Phi}}{dt} = k_v \cdot c_{H_2\Phi} \cdot c_{MX_2}. \quad (2)$$

Values of k_V in Egn. (2) obtained at salt concentrations of 0.00025 M and below can be regarded as true rate constants. At higher concentrations k_V has smaller values, which are in some measure arbitrary (concentration rate constants).

Among the many causes of the "concentration" dependence of the rate constants discussed in the literature[53] two—the change in properties and structure of the solvent with increase in the salt concentration, and also the change in the geometrical configuration of the coordination sphere of the reactant salt with increase both in its own concentration and in that of a foreign electrolyte—must probably be regarded as the most significant. In several cases additional causes—association of the salts and also weak interaction between the salt and side-chains of the porphyrin—may no doubt operate[53]. The latter leads to "weighting" of the porphyrin molecule and changes the reactivity of its main coordination centre—the four cyclic nitrogen atoms.

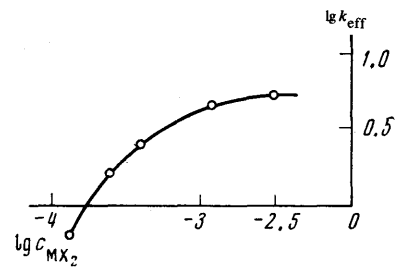


Figure 2. Concentration dependence of rate of formation of cadmium phaeophytinate.

Determinations[48-53] of the principal kinetic parameters for the formation of nine metal analogues of chlorophyll-a showed (Table 1) that "concentration" dependence of the rate constant is absent with certain salts, e.g. copper(II) acetate and cadmium(II) nitrate, iodide, and chloride; reaction (1) obeys the kinetic equation (2) at all concentrations of these salts. With other salts, e.g. cobalt(II) nitrate, the rate constant is almost independent of concentration. Finally, the "concentration" dependence is large with zinc(II) nitrate, cadmium(II) acetate, and nickel(II) nitrate. Such specific behaviour of different salts is explained by differences in the stability of particular coordination structures of the salts in organic solvents. Table 1 shows that, under comparable conditions, the rate of reaction (1) depends little on the electronic structure, charge, or radius of the cation.

The mean rate constant of reaction (1) for salts of eight metals is $(9.8 \pm 6.4) \times 10^2$ M^{-1} h^{-1}.

The rate of formation of the nickel complex is around 10%, and that of cobalt phaeophytinate around 1%, of the average for the remaining complexes. The activation energy is more sensitive to the nature of the cation than is the rate, and varies from 10.6 kcal for copper(II) acetate to 31 kcal for cobalt(II) chloride. In conformity with the kinetic compensation effect, which is strictly observed[54] in the series of metal phaeophytinates, the entropy of activation varies correspondingly from −26 to +30 e.u. for the above salts. The rate of formation of phaeophytinates depends substantially on the anionic composition of the medium[48-52]. In the case of the cadmium and cobalt salts the reaction velocity diminishes[53] in the sequence of anions $NO_3^- > Cl^- > CH_3COO^-$ (Table 1). The instability constants of the cadmium and cobalt salts with these anions decrease in the same sequence: i.e. the stability of the M–X bond in solution increases. The nature of the bond between the anion X^- and the cation probably has an indirect effect on the stability of the solvent sheath of the salt MX_2Solv_{n-2}§, determining the rate and other kinetic parameters of reaction (1). The effect of the structure of the coordination sphere in the initial salt on the formation of metal analogues of chlorophyll has been studied[50,51] by measuring the rate of formation of copper phaeophytinate at various temperatures with various complex salts of copper—malonate, succinate, citrate, and alaninate—in 90% ethanol and in ammoniacal–ethanolic media, in which the above salts have satisfactory solubility. Inspection of the experimental results (Table 2) indicates that replacing the anion X^- in the coordination sphere of the salt MX_2 changes the reaction velocity not more than tenfold, independently of the type of coordination (linear, cyclic, or inner-complex) of the organic anion as ligand, of the stability of its bond with the cation. Alanine and citrate form very stable chelate complexes with the Cu^{2+} ion[55], yet they react with chlorophyllic acid just as easily as does copper acetate. From these facts it may be concluded that reaction (1) takes place with the undissociated salt MX_2, and the stage of activation of the salt involves loss of a solvent molecule—not of an anion—from the coordination sphere of the cation.

Table 1. Kinetic parameters of the formation of metal analogues of chlorophyll

$$H_2\Phi + MX_2 \rightarrow M\Phi + 2HX$$

in ethanol at 25°C.

Metal salt	Rate constant $10^{-2}k_v$, M^{-1} h^{-1}	Activation energy, kcal $mole^{-1}$	Entropy of activation, e.u.
$FeCl_2$	4.48±0.23*	13.8±1	−16±3
$CoCl_2$	0.018±0.002**	31.0	+30
$Cu(OAc)_2$	0.011±0.001*	23.9	+6.1
$Co(NO_3)_2$	0.106±0.012*	24.0	+11
	0.068±0.008**	18.0	−10.5
$Ni(NO_3)_2$	0.34±0.04*	15.5	−15.4
	1.42±0.28***	23.6	+14.4
$Cu(OAc)_2$	59.1±0.6	10.6±1.2	−26±4.0
$Cu(NO_3)_2$	91.3±5.5*	12.9±1.2	−13±3.0
$Zn(NO_3)_2$	2.30±0.20*	14.1±0.5	−16.2±1.6
	15.0±2.0***	14.1±0.7	−12.5±2.0
$Cd(OAc)_2$	15.1±1.2***	13.4±1.5	−15±5.0
	3.37±0.08*	16.5±0.7	−7.5±2.5
$Cd(NO_3)_2$	26.0±1.7	16.2±0.2	−4.5±0.7
CdI_2	5.25±0.40	19.6±1.7	+4±7.0
$CdCl_2$	18.5±0.8	11.1±0.5	−22±2.0
HgI_2	23.0±3*	13.4±2	−14±7.0
$HgCl_2$	21.9±2.4*	—	—
$AgNO_3$	2.66±0.15*	19.0±0.2	+34±0.5
$PdCl_2$	4.76±0.15*	18.0±1	−2±3.0

*Concentration of salt 0.0025 M.
**Concentration of salt 0.025 M.
***Concentration of salt 0.00025 M.

Saturation of 90% ethanol with ammonia (Table 2) lowers the rate of reaction (1) by factors of 10–20, with increase in the energy and the entropy of activation, which was explained[50] both by rearrangement of the inner coordination sphere of the Cu^{2+} ion from a solvate to an ammine and by rearrangement of the solvent structure around this

§ Solv = solvent molecule; n = maximum coordination number of cation under specific conditions.

sphere. The high energies and entropies of activation in aqueous–alcoholic and ammoniacal–alcoholic media were explained by the formation of a second and subsequent solvation spheres in the vicinity of coordinated water or ammonia, which is impossible in the case of alcohols.

Table 2. Formation of copper phaeophytinate from various complex copper salts in ethanol at 25°C.

Cu salt	$10^{-3}k_v$, M^{-1} h^{-1}	E, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.	Ethanol
$Cu(OAc)_2$	5.91	10.6	−26	Absolute
$Cu(NO_3)_2$	4.67 *	41.7	+82	90%
$Cu(NO_3)_2$	0.445 *	42.5	+80	90% + NH_3
Cu(Malonate)	1.23 **	13.2	−16	90%
Cu(Malonate)	0.0273 **	41.8	+73	90% + NH_3
Cu(Succinate)	0.150 **	28.4	+31	90% + NH_3
Cu(Citrate)	0.390 **	21.9	+11	absolute
Cu(Alanine)	2.06 **	6.5	−37	90%

*Concentration of salt CuX_2 is 0.0025 M.
**Salt concentration 0.00025 M.

Table 3. Kinetic parameters of formation of mercury(II) phaeophytinate at 25°C.

Salt	Concn., 10^3c, M	$10^{-3}k_v$, M^{-1} h^{-1}	E, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.	Solvent
$HgCl_2$	0.25	28.0	13.9	−5	ethanol
$HgCl_4^{2-}$	0.25	very slow	—	—	ethanol
$HgCl_2$	0.25	0.58	56.4	+101	methanol
$HgCl_2$	0.50	0.43	48.7	+129	methanol
$HgCl_4^{2-}$	0.25	0.67	12.7	−16	methanol
$HgCl_4^{2-}$	2.50	0.046	11.3	−26	methanol
HgI_2	2.50	0.230	13.4	−14	ethanol
HgI_4^{2-}	2.50	very slow	—	—	ethanol
HgI_2	2.50	0.021	13.1	−22	methanol
HgI_4^{2-}	0.25	0.068	21.8	+14	methanol

The kinetics of reaction (1) with chloride and iodide complexes of mercury was studied in order to determine the effect of the number of coordination sites of the cation occupied by simple anions[51]. Table 3 shows that decrease in the number of solvent molecules located in the coordination sphere of Hg^{2+}, from two for HgX_2 to zero for HgX_4^{2-}, strongly inhibits reaction (1) in ethanol, whereas in methanol $Hg\Phi$ is formed at the same rate from $HgCl_2$ and $HgCl_4^{2-}$, and the rate from HgI_4^{2-} is even higher than from HgI_2. An explanation for such unusual behaviour of mercury salts will be given in discussing the mechanism of reaction (1) in later sections.

Here, however, we must note the extraordinarily strong dependence of the rate of formation of phaeophytinates on the nature of the solvent. This becomes obvious when it is remembered that the solvent forms the structure of the coordination sphere of the salt MX_mSolv_{n-m}, and determines the strength of the M–X and M–Solv bonds in solution, as well as the degree of solvation of the reactants: i.e. it determines the energy and entropy components of the free energy of activation of reaction (1). Berëzin and Smirnova[41,56–62] measured the rates of this reaction with copper(II) and zinc(II) salts in various types of organic solvents—alcohols, ketones, ethers, amides, nitrogen-containing heterocycles, and aliphatic acids—and found a thousandfold variation in the rate of formation of metal analogues of chlorophyll depending on the nature of the solvent (Table 4). The rate is maximal in glacial acetic acid, and minimal in pyridine. The effect of the solvent on the kinetics of reaction (1) was explained[56–62] by variation in the stability of the solvent coordination sphere of the salt MX_2Solv_{n-2}, i.e. in ease of rupture of the M–Solv bond, and by spatial factors, in particular steric hindrance by solvent molecules in the coordination sphere of the activated salt impeding entry of the large flat phaeophytin molecule.

Table 4. Kinetic parameters of the reaction

$$Cu(OAc)_2 + H_2\Phi \rightarrow Cu\Phi + 2HAc$$

in various solvents at 25°C.

Solvent	$10^3c^0_{Cu(OAc)_2}$, M	10^3k_v, M^{-1} h^{-1}	E, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.
C_2H_5OH	0.130	5.91	10.6	−26
CH_3OH	0.150	29.7	14.8	− 4
n-$C_5H_{11}OH$	0.240	1.99	27.1	31
$(CH_3)_2CO$	0.280	3.26	11.1	−16
$O(CH_2—CH_2)_2O$	0.300	0.165	17.2	− 6
CH_3COOH	0.160	95.0	11.2	−14
$HCON(CH_3)_2$	0.900	0.131	18.9	− 2
C_5H_5N	0.900	0.0331	22.9	9
C_9H_7N	0.900	0.101	24.1	15

Table 5. Kinetics of formation of copper phaeophytinate in ethanol–glycerol media at 25°C.

Glycerol / ethanol	Viscosity (discharge time)	$10^{-3}k_v$, M^{-1} h^{-1}	E, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.
0:100	4 s	3.42	10.6	22.7
20:80	10 s	1.81	10.8	23.4
50:50	1 min	1.46	11.9	20.0
80:20	7 min	0.44	12.8	19.4

Table 4 indicates that the reaction velocity of (1) decreases and the activation energy increases with increase in the volume occupied by the solvent in the immediate vicinity of the cation[63,64]. This is characteristic of dioxan, pyridine, quinoline, dimethylformamide, and n-pentanol. It is significant that merely strengthening the coordinate link (ethanol → methanol) does not diminish the rate, although it increases the activation energy appreciably. Another extremely interesting aspect is that change in the state of phaeophytin molecule $H_2\Phi$ has hardly any effect on the reaction velocity. Thus in glacial acetic acid, which forms a strong hydrogen bond with nitrogen atoms in the reaction centre of phaeophytin, the rate exceeds that in ethanol by a factor of 15; the latter solvent slightly blocks the nitrogen atoms. Interaction of π–π type between the aromatic rings of phaeophytin and nitrogen heterocycles (pyridine, quinoline) also has no appreciable effect on the reactivity of phaeophytin. Thus the rates of (1) in quinoline and in dimethylformamide are roughly the same. An analogous effect of nature of solvent on reactivity was established with phaeophytin and zinc salts[41,56–61]. Neither the displacement of the keto–enol equilibrium of phaeophytin-a occurring in ethanol–glycerol

solutions nor the increase in viscosity of the medium (Table 5) has a significant effect on the rate of reaction (1).[62] It was suggested that the enolic form nevertheless possesses a higher kinetic coordinating power than does the ketonic form.

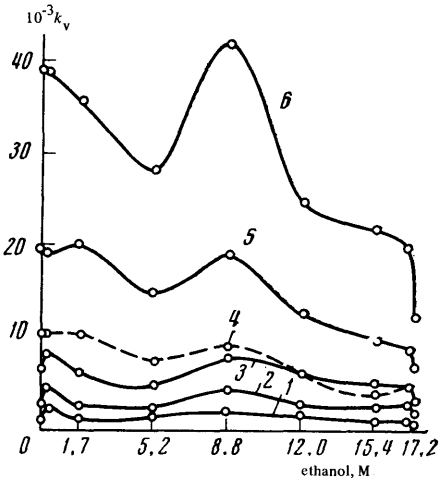


Figure 3. Dependence of rate constant of formation of CuΦ on composition of ethanolic acetic acid for different approximate $Cu(OAc)_2$ concentrations (M) at different temperatures (°C): 1) 0.0025 at 15°; 2) 0.0025 at 25°; 3) 0.0025 at 35°; 4) 0.00025 at 15°; 5) 0.00025 at 25°; 6) 0.00025 at 35°.

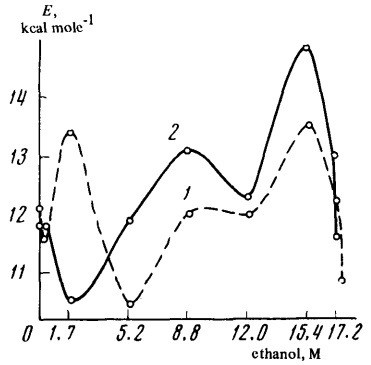


Figure 4. Dependence of activation energy of CuΦ on composition of solvent for different approximate concentrations (M) of $Cu(OAc)_2$: 1) 0.0025; 2) 0.00025.

Berëzin and Klopova[65-67] found several extremal points n the variation of rate, activation energy, and entropy of ıctivation of reaction (1) with solvent composition in ethanoic acetic acid (Figs. 3–5). The extrema were attributed[66] o resolvation, on passing from acetic acid to alcoholic nedia, of the solvate complex $[M(OAc)_2(HOAc)_{n-2}]$ through $M(OAc)_2(HOAc)_{n-2-m}(C_2H_5OH)_m]$ to $[M(OAc)_2(C_2H_5OH)_{n-2}]$; hey were attributed also to formation of an association complex $CH_3COOH...C_2H_5OH$ with a stable hydrogen bond; and in some measure to resolvation of the reaction centre of phaeophytin from >N...HOCOCH₃ to >N...HOC_2H_5 and >NH...O(H)–C_2H_5. Rearrangement of the structure of the pure solvent produced by small additions of another solvent, in particular stabilisation of the structure of methanol, is probably quite an important factor[68].

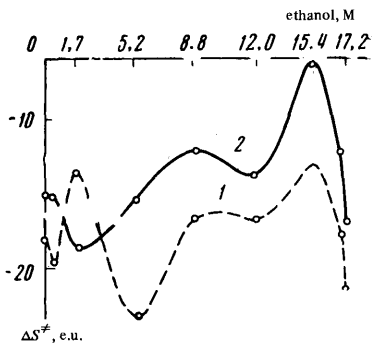


Figure 5. Dependence of entropy of CuΦ on composition of solvent for different approximate concentrations (M) of $Cu(OAc)_2$: 1) 0.0025; 2) 0.00025.

Phillips and others[69] found that the nature of the solvent had a very strong effect on the rate of formation of other metal porphyrins. Cobalt(II) salts react rapidly with porphyrins in dry acetone even at 25°C. Addition of a small quantity of water greatly retards the reaction. A still more interesting observation, which cannot yet be interpreted, was made on nickel salts: nickel(II) reacts very rapidly when the reaction is conducted in higher alcohols (butanol, pentanol) or in phenol, but very slowly in methanol, ethanol, or water. The reasons for such behaviour are now being studied in detail on complexes of cobalt(II) with chlorophyllic acid[70].

2. Formation of Complex Compounds—Structural Analogues of Chlorophyll

Quantitative investigation of the formation of porphyrin complexes—structural analogues of chlorophyll—began comparatively recently[71]. The need for their study arose from the importance and great biological activity not only of chlorophyll but also of other metal porphyrins, possessing a different system of side-chains and different central metal atoms. The selective action of metal porphyrins is probably governed precisely by the nature and range of substituents. These change the σ- and π-acceptor and the donor properties of the conjugated macrocycle, as well as the ability of the central metal atom to coordinate additional ligands involved in particular biological acts (photosynthesis, respiration, oxidation, decomposition, etc.). It is therefore a very urgent task to investigate kinetic and equilibrium aspects of the formation of metal porphyrins as a function of the nature and number of side-chains in porphin.

Choi, Fleischer, et al.[71,72] studied complex formation by αβγδ-tetrapyridylporphin (H_2TPP) with copper(II), cobalt(II), manganese(II), and nickel(II) salts in glacial and aqueous

acetic acid. This porphin possesses good solubility in proton-donating solvents, including aqueous media. The reaction, probably represented by the equation

$$H_2TPP + M^{2+}_{Solv} \xrightarrow{k_v} MTPP + 2H^+_{Solv} \quad (3)$$

has the first order with respect both to the porphin and to the metal. Unfortunately, the reaction velocity was measured only at a single concentration (~ 0.004 M) of the metal salt, and the unjustified assumption was made that copper(II) acetate is present in glacial acetic acid as Cu^{2+}. Calculation based on the second-order equation (2) gave for the rate constants of reaction (3) involving copper, cobalt, manganese, and nickel diacetates the respective values 1400, 310, 210, and 87 M^{-1} h^{-1} at 25°. The reaction takes place considerably more slowly than with chlorophyllic acid (cf. Table 4).

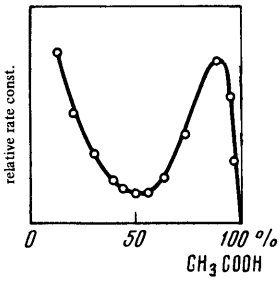


Figure 6. Dependence of rate of formation of CuTPP on acetic-acid concentration.

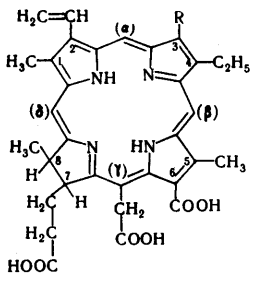
The formation (3) of copper and zinc complexes from the perchlorates in 8.3% aqueous acetic acid containing 0.01 M perchloric acid has rate constants at 25°C of 63 and 22 M^{-1} h^{-1}. Replacement of acetic acid by water molecules in the coordination sphere lowers the rate by 50–67%. The rate of reaction (1) in aqueous solution is inversely proportional[71,72] to the hydrogen-ion concentration, but in aqueous acetic acid it passes through a maximum in the 90% acid (Fig. 6). However, these facts were left unexplained[71]. It may be supposed that protonation of the pyridine residues accelerates the reaction (in concentrated aqueous acetic acid) owing to increased protonation of the pyrrole nitrogen–hydrogen bonds, while protonation of the reaction centre, i.e. of the pyrrole nitrogen atoms (aqueous perchloric acid) lowers the reaction velocity. Competition between the two processes may produce the observed variation (Fig. 6). The fact that cadmium, lead, and mercury complexes of tetrapyridylporphin are not formed under the given conditions[71] causes no surprise, since these complexes are unstable in proton-donating media.

Brisbin and Balanura[73] studied the kinetics of the reaction between manganese(II) and haematoporphyrin in glacial acetic acid, and suggested a reaction mechanism which was subjected to an impartial critique[74]. The effect of the pH of the medium on the rate of coordination of sulphonated deuteroporphyrin IX by Cu^{2+} ions was studied by Weaver and Hambright[75]; and the catalytic action of nitrogen-containing solvents on the reaction of zinc(II) with water-soluble porphyrins was investigated by Stein and Plane[76]. We shall not discuss these papers, since their results introduce nothing significantly novel into the kinetics and the mechanism of the reactions of metal salts with porphyrins.

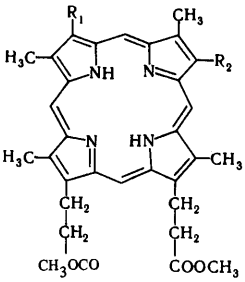
A most interesting paper by Baum and Plane[77] deals with the direct introduction of magnesium into a porphyrin from a solution of a salt in an ordinary organic solvent (acetone, methanol). The rate of incorporation of magnesium into the dimethyl ester of deuteroporphyrin IX is given by the kinetic equation

$$\frac{d[MP]}{dt} = k_1\frac{[PH_2]}{[H^+]} + k_2\frac{[PH_2][Mg^{2+}][Py]}{[H^+]} \quad (4)$$

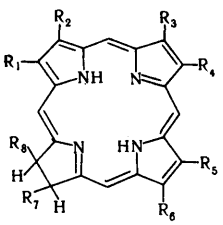
in which the rate constants of the uncatalysed reaction and of the reaction catalysed by pyridine or other nitrogen-containing solvent are respectively $k_1 = 4.7 \times 10^{-4}$ and $k_2 = 3.6$ M^{-1} h^{-1}, the corresponding activation energies being $E_1 = 36.5$ and $E_2 = 15.8$ kcal $mole^{-1}$. Comparison with Table 1 indicates that the rate of coordination of magnesium by porphyrins from solution is vanishingly small, but the catalytic effect of nitrogen-containing compounds is so intense that the rate of incorporation of magnesium approaches those for cobalt from the dichloride and the diacetate in ethanolic solution. These results encourage the hope of the direct introduction of magnesium into chlorophyllic acid, and also a fresh look at the formation of chlorophyll in the living cell[78].



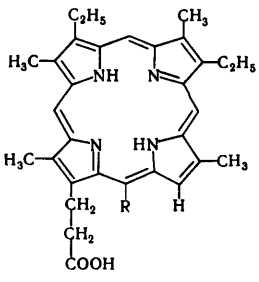
(II) chlorin-e_6 R = CH_3
(III) *rhodin*-g_7 R = CHO



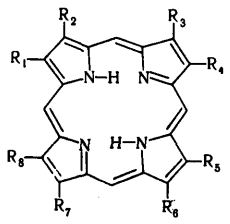
(IV) mesoporphyrin IX: dme: $R_1 = R_2 = C_2H_5$
(V) protoporphyrin IX: dme: $R_1 = R_2 = CH = CH_2$



(VI) chlorin:
$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = R_7 = R_8 = H$
(VII) acetiochlorin II:
$R_1 = R_4 = R_5 = R_8 = CH_3$
$R_2 = R_3 = R_6 = R_7 = C_2H_5$



(VIII) pyrroporphyrin XV: R = H
(IX) phylloporphyrin XV: R = CH_3



(X) porphin:
$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = R_7 = R_8 = H$
(XI) acetioporphorin I:
$R_1 = R_3 = R_5 = R_7 = CH_3$; $R_2 = R_4 = R_6 = R_8 = C_2H_5$
(XII) aetioporphorin II:
$R_1 = R_4 = R_5 = R_8 = CH_3$; $R_2 = R_3 = R_6 = R_7 = C_2H_5$

Berëzin and Koifman have reported[79-86] systematic investigations of the effect of structural units of the porphyrin molecule on the kinetics of the formation of metal porphyrins (see Table 6). To facilitate discussion of the results we give here the structural formulae of the natural and synthetic porphyrins investigated. Opening the cyclopentanone ring (ring E in structure I), i.e. the conversion of phaeophorbide-a into chlorin-e_6 (II), doubles the reaction velocity, while the activation energy and entropy remain almost unchanged. The explanation given[80] was that the substitution of carboxyl for -CO.R at $C_{(6)}$ in chlorin-e_6 changes the inductive effect exerted by the substituent on the nitrogen atoms of the macrocycle. The carboxy-group, while possessing about the same conjugation effect as the group it replaces, probably exerts a greater inductive effect, so that the nitrogen–hydrogen bond in the chlorin may become strongly protonated, with a tendency to accelerate the reaction

$$H_2P + MX_2 \rightarrow MP + 2HX. \qquad (5)$$

The suggestion that the state of the nitrogen–hydrogen bond in porphin greatly influences the coordinating power of the compound is supported[79] by a comparison of chlorophyllic-a and -b acids (structure I). Conversion of $H_2\Phi$-a into $H_2\Phi$-b is accompanied by a decrease in the rate of coordination of the Cu^{2+} ion roughly to one-seventh, with an appreciable increase in activation energy, associated with an increase in electron density on the nitrogen–hydrogen bond under the influence of the positive conjugation effect (+C-effect) of the 3-formyl group (structure I). The greater stability of chlorophyll-b in solution finally provides convincing evidence that the above hypothesis[74,79] is correct. An adverse effect of the 3-formyl group on the rate of formation of complexes in solution has been established also in a comparison[81] of chlorin-e_6 (II) with rhodin-g_7 (III), which have the same structural relationship as chlorophyllic-a and -b acids.

Table 6. Kinetic parameters of formation of copper complexes of natural and synthetic porphyrins in ethanol at 25°C.

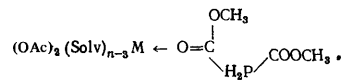
Porphyrin	$10^4 c^0_{Cu(OAc)_2}$, M	$10^{-3}k_{V_1}$, $M^{-1}\,h^{-1}$	E, kcal mole^{-1}	$\Delta S^{\neq}$; e.u.
Chlorophyllic-a acid	3.75	5.91	11.8	−17
Chlorophyllic-b acid	4.50	0.18	14.0	−17
Phaeophorbide-a	3.75	4.75	7.5	−28
Chlorin-e_6	4.50	8.20	6.5	−34
Rhodin-g7	2.70	1.70	6.4	−38
Synthetic chlorin	5.50	2.20	11.2	−21
Porphin	4.45	2.00	13.2	−16
Mesoporphyrin IX dme*	2.50	6.70	7.5	−31
Protoporphyrin IX dme*	2.50	3.60	8.8	−29
Pyrroporphyrin XV	2.64	15.50	7.0	−32
Phylloporphyrin XV	0.90	48.50	10.0	−18
Aetioporphyrin I	2.30	7.00	13.4	−12
Aetioporphyrin II	2.30	6.90	12.8	−14
Aetiochlorin II	2.30	7.50	11.3	−18

*dme = dimethyl ester.

The conversion of chlorin-e_6 (II) into mesoporphyrin (IV), involving disappearance of one carboxyl conjugated with the macro-ring at $C_{(6)}$, and of the 2-vinyl group, produces hardly any change in the kinetic parameters[84] (Table 6). Here similar electron-accepting substituents (COOH and $CH:CH_2$) have been replaced by similar alkyl and "pseudo-alkyl" substituents (C_2H_5 and $CH_2.CH_2.COOH$). The rate constants remain unchanged probably because the 2- and 6-substituents have opposite effects.

Protoporphyrin coordinates copper salts at half the rate observed with mesoporphyrin[84]. Conversion of the latter (IV) into the former (V) involves replacement of the two alkyl substituents at $C_{(2)}$ and $C_{(4)}$ by vinyl groups, which possess an analogous but weaker +C-effect than that of the formyl group. This leads to a diminution in the protonation of the nitrogen–hydrogen bond and a lower reaction velocity.

Completely unexpected results were obtained[82] for the coordinating properties of porphin (X) and synthetic chlorin (VI), and their comparison with the aetioporphyrins (XI) and (XII).[85] Porphin and synthetic chlorin do not differ in the kinetic parameters of coordination (Table 6). Hence the hydrogenation of one "semi-isolated" double bond of a pyrrole ring has no appreciable effect on the state of the N–H bond and the reactivity of the macro-ring. Nevertheless, porphin and synthetic chlorin coordinate copper salts at one-quarter the rate observed with chlorin-e_6 or mesoporphyrin. The favourable effect of residues of propionic acid was explained[84] by primary coordination of the metal salt on them:



Because of favourable arrangement of methoxycarbonyl groups relative to the main coordinating centre (the four nitrogen atoms of the macrocycle), primary coordination probably favours the enclosure of both reaction centres in a solvent "cage", which will increase the rate and lower the activation energy. The entropy of activation will also diminish in conformity with the compensation effect characteristic[74,83] of reaction (5). The aetioporphyrins (XI) and (XII), in which the propionic-acid residues have been replaced by alkyl groups, possess double the activation energy with the same rates of coordination. A similar result appears on comparing aetiochlorin (VII) with chlorin-e_6 (II). The high rates of reaction (5) with aetioporphyrin and aetiochlorin, relative to those with porphin (X) and chlorin (VI), are explained by the presence of a factor counterbalancing the energy factor in the coordination of porphyrins[85]. This factor is universal solvation, which is probably less favourable to alkylated than to unsubstituted pyrrole rings in porphyrins. The solvation factor is especially strongly developed when the symmetry of the porphyrin molecule and also that of the π-electron system of the macro-ring are destroyed. Pyrroporphyrin XV (VIII), which contains no 6-substituent, coordinates at double the rate observed with mesoporphyrin (Table 6). Finally, phylloporphyrin XV (IX), which unlike pyrroporphyrin has a γ-alkyl group, exhibits the maximum rate of coordination of metal salts[86]: its rate of reaction with copper(II) acetate exceeds that of phaeophytin-b by a factor of 270.

Falk's monograph[8] gives the relative rates of formation of copper(II) complexes with mesoporphyrin, protoporphyrin, and 2,4-diacetyldeuteroporphyrin in aqueous solutions of sodium dodecyl sulphate as 7 : 1.5 : 1.0. These agree well with the above results[78-85], and support the main conclusions reached.

Thus by now not only has the strong effect of structural features of the porphyrin molecule on its coordinating reactivity been established but the influence of energetic factors (variation in state of nitrogen–hydrogen bond produced by substituents), solvation factors, and primary coordination on the kinetic parameters has also been shown.

All the conclusions reached[79-85] for reaction (5) with copper(II) salts have been found to hold also for zinc(II) salts[74].

3. Mechanism of Formation of Metal Analogues of Chlorophyll and Other Metal Porphyrins

The formation of complex compounds with large planar molecules having continuous peripheral conjugation exhibits several features distinguishing such reactions from the formation of complexes (often termed ligand substitution) with simple ligands[87,88]. Several factors are responsible for such distinguishing features: (i) the ligand possesses low mobility in solution, and is a target for the more mobile reactant—the salt molecule (or ions); (ii) the ligands are acidic, and are usually extremely difficult to convert to the anionic state ($H_2P \rightarrow 2H^+ + P^{2-}$); (iii) the continuous π-cloud of the conjugated macrocyclic system (structures I–XII) shields the reaction centre of the ligand, including the four inner nitrogen atoms; and (iv) solvation of the ligand involves complicated phenomena, as the ligand carries multifarious centres of solvation.

The main feature of the formation of metal porphyrins is its slowness in comparison with the coordination of other ligands. Systematic investigations of the formation of metal analogues of chlorophyll[48-51,56-62] indicated, for organic solvents possessing no appreciable ionising power, the stoichiometric equation

$$M(Solv)_{n-m}X_m + H_2\Phi(Solv)_p \rightarrow M\Phi(Solv)_q + 2HX(Solv)_s + (n-m+p-q-2s)\,Solv \quad (6)$$

which conforms to the second-order kinetic equation (2).

Reaction (6) probably takes place in a single stage in most of the solvents studied, since intermediate compounds were not detected, either kinetically or spectroscopically[48,49]. In several cases, however, formation of an intermediate complex of type $H_2\Phi.MX_2$ was a possibility[57,89,90]. Such complexes are formed in glacial acetic acid when reaction (6) is conducted with zinc(II) chloride, cobalt(II) chloride, cobalt(II) acetate, iron(II) chloride, palladium(II) chloride, and mercury(II) acetate in ethanol. They are distinguished from a phaeophytinate by a hypsochromic shift of the first two bands and a strong bathochromic shift of the other three bands in the electronic absorption spectrum. An exception is $H_2\Phi.Hg(OAc)_2$.[91] The intermediate complexes are far less stable than complexes of the bivalent metal with pyridine and with alcohols. They are converted into the corresponding phaeophytinates either at room temperature ($H_2\Phi.Co(OAc)_2$) or when the solutions are boiled ($H_2\Phi.FeCl_2$).

The stoichiometric mechanism (using Langford and Gray's classification[87]) of the formation of metal porphyrins is most probably covered by two possibilities (written here in simplified form)—(*a*) in a single bimolecular stage

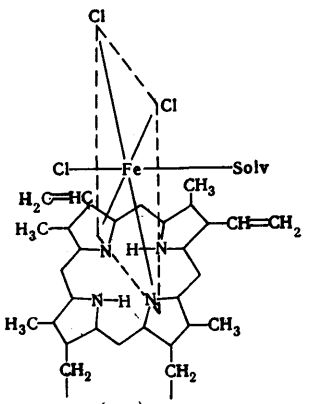
$$H_2P + MX_2 \rightarrow [MX_2 \cdot H_2P]^{\ddagger} \rightarrow MP + 2HX \quad (6a)$$

(*b*) in two stages with preliminary formation of an intermediate

$$H_2P + MX_2 \underset{\text{(stage I)}}{\overset{\text{rapid}}{\rightleftharpoons}} MX_2 \cdot H_2P \xrightarrow[\text{(stage II)}]{\text{slow}} [MX_2 \cdot H_2P]^{\ddagger} \rightarrow MP + 2HX. \quad (6b)$$

The two reaction paths undoubtedly cross different forms of potential barrier, but the shape and height of the final peak in the potential curve, determined by the structure of the transition state $[MX_2.H_2P]\dagger\dagger$, are the same, since the latter has the same structure in reactions (6a) and (6b). According to existing schemes of classification[86,88,92,93] the stoichiometric mechanism of reactions (6a) can be regarded either as associative bimolecular S_E2[93] or as a concerted process with associative activation[87]. The mechanism of reactions (6b) can be denoted dissociative unimolecular S_E1 in Ingold's classification[92].

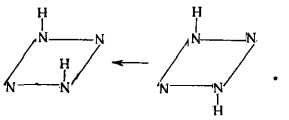
It is of interest to examine data on the detailed mechanism of the elementary stage of the coordination of porphyrins by metal salts. These data also deepen and refine information on the stoichiometric mechanism. It was first established[37] that the dimethyl ester of protoporphyrin in acetone, chloroform, and other weakly solvating solvents forms with iron(II), iron(III), cobalt(II), platinum(IV), tin(II), and zinc(II) salts initially a complex whose spectrum is closely similar to that of the diprotonated porphyrin $H_2PH_2^{2+}$. On this basis the structure



(XIII)

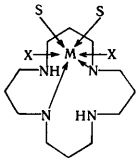
was assigned to the complex, and is probably closest to reality. This structure is supported by the results of infrared spectroscopy[37]: the vibrations of the nitrogen–hydrogen bond were shown to change in character.

In strongly solvating media, such as water, alcohols, pyridine, etc., the above cations gave metal porphyrins without forming intermediates. No intermediate complexes are formed when the cations Ni^{2+}, Cu^{2+}, Hg^{2+}, and Cd^{2+} react with the dimethyl ester of protoporphyrin in acetone. In the reaction with chlorophyllic acid the formation of intermediate complexes was only rarely observed in polar solvents, including acetone[57,89,90]. Such complexes are generally produced in glacial acetic acid, since the metal–solvent bond in the solvate coordination spheres of the salt MX_2Solv_{n-2} is not very stable. It follows from these observations that the elementary act, both in reactions (6a) and in stage (I) of reactions (6b), involves the detachment of one or two solvent molecules from the inner sphere of the salt, i.e. its activation to MX_2Solv_{n-3} or MX_2Solv_{n-4} and activation of the porphyrin, which evidently entails conversion of the *trans*-form of H_2P into the *cis*-form and its partial resolvation[50]:



The reacting system (6a) forms an activated complex (transition state $[H_2P.MX_2]\dagger\dagger$), but the reacting system (6b) forms a complex of type $H_2P.MX_2$. There is no

special reason to doubt that these two structures are the same (XIV).



(XIV)

The reacting system (6a), having reached the summit of the potential barrier, readily splits off $2H^+$, $2X^-$, and perhaps some of the solvent molecules from the inner sphere to give the metal porphyrin (MP). The reactant system (6b) remains in the potential well at the summit of the barrier, since detachment of the anions X^- and perhaps also H^+ is difficult in a weakly solvating medium, in which alone are intermediates formed. Addition of a more polar solvent leads to the displacement of H_2P molecules from the intermediate complex, and the reacting system (6b) returns to the initial state. This indicates that the intermediate is a very unstable complex. In spite of this, the second stage of reaction (6b) is difficult and is accomplished only on prolonged heating. The reason is that, as had been suggested[90], the formation of metal porphyrins in this case involves breakdown of the intermediate complex into the starting materials, which react by scheme (6a).

Thus it is highly probable[90] that metal porphyrins are not formed at all by scheme (6b). This view is supported by the analogous behaviour of the MX_2-H_2P system in strongly proton-donating solvents, in which the species $H_2PH_2^{2+}$ is formed, resembling the intermediate $H_2P.MX_2$ in properties. The rate constant for the formation of CuΦ in 95% formic acid at 25°C (6.5 M^{-1} h^{-1}) is 0.03% of its value in glacial acetic acid. The activation energy has increased from 10.5 to 29 kcal: i.e. it includes the activation energy for the breakdown of $H_2PH_2^{2+}$ to H_2P and the energy of activation of MX_2 and H_2P in reaction (6a).

Falk in his monograph[8], on the basis of results obtained by Phillips et al.,[69] concludes that the formation of metal porphyrins, like that of complexes of chlorophyllic acid, occurs predominantly by scheme (6a): i.e. it has a bimolecular mechanism¶. Some interesting results were obtained[94,95] on the detailed mechanism of reaction (6): complex formation between copper(II) and mesoporphyrin is accelerated by the presence of hydroxyquinoline (OX^-) at a concentration corresponding to formation of $CuOX^+$, after which the rate drops sharply when $Cu(OX)_2$ is formed. Thus a chelating ligand added to the MX_2-H_2P system may act either as an activator or as an inhibitor. The authors[94,95] were unable to give the true reasons for such behaviour of foreign ligands. The conclusion is suggested by data[48-51,56-62] on the complexes of chlorophyllic acid (Tables 2–4). When the reactant salt MX_2Solv_{n-2} contains the anion X^- in the inner sphere, as occurs with hydroxyquinoline, the number of coordinated solvent molecules diminishes from 4 to 0, and their bonding with the cation becomes weaker. This weakening favours the reaction, increasing the rate and lowering the activation energy. Decrease in the number of solvent molecules in the inner sphere acts in the opposite direction, and when $n - 2 = 0$ reaction may cease, as in the case of $Cu(OX)_2$.[94,95] The above considerations readily explain facts established by one of us[48-53,56-62]—that reaction (6) is not retarded by such chelating additives as malonate, succinate, citrate, and alanine (Table 2), which occupy no more than 2–4 coordination sites in the inner sphere of Cu^{2+}, leaving 2 solvent molecules in it; that reaction (6) occurs at very high rates with the very stable complex salts $HgCl_2$ and HgI_2 (Table 3); and that rates are lower in solvents having bulky molecules, such as dioxan, pentanol, dimethylformamide, pyridine, etc. (Table 4).

Nevertheless, the formation of metal porphyrins with $HgCl_4^{2-}$ and HgI_4^{2-} and the absence of reaction[53,63,64] with $[Co(NH_3)_6]^{3+}$, $[CoCl(NH_3)_5]^{2+}$, $[Co(HCOO)_2(NH_3)_4]^+$, $[Fe(CN)_6]^{4-}$, and $[Fe(CN)_5NO]^{2-}$ salts indicate a second possible detailed mechanism for reaction (6a)—displacement of ligands from their positions in the course of interaction between the porphyrin and the complex salt[51]—which is possible with HgX_4^{2-} but impossible with $[CoL_6]^{n+}$ and $[FeA_6]^{n-}$. Porphyrins can react by this mechanism with salts containing no solvent molecules in the inner sphere, provided that such salts can be distorted with contraction of the coordination sphere and the freeing of two sites for the development of interaction with two nitrogen atoms in the reaction centre of the porphyrin.

Investigation of the coordination of porphyrins (6) raises the question whether the kinetic parameters will be affected if reaction occurs with the cation of the dissociated salt:

$$M^{2+} + H_2P \rightarrow MP + 2H^+ \qquad (7)$$

a form in which the stoichiometric equation has been written[8,33,35,37]. Such a crude representation of the reaction suggests that the salt MX_2Solv_{n-2} is completely or almost completely dissociated, and is present either in the form $MSolv_n^{2+} + 2X^-$ or else as the ion-pair $[MSolv_n]X_2$. Such a state of the salt is possible with strongly solvating solvents only when weak M–X coordination interaction is present in solution (MX_2 has a high instability constant). All the results obtained for the coordination of chlorophyllic acid indicate that the kinetic parameters are little affected by change in state of the salt from $[MX_2Solv_{n-2}]$ to $[MSolv_n]X_2$ or even to $[MSolv_n]^{2+} + 2X^-$. This conclusion is based on experiment and is easily explained by the reaction mechanism (6a).

In order to understand the detailed mechanism it is necessary to know how the state of the porphyrin molecule—in particular that of the N–H bond—changes during activation. Several results tending to answer this question will be found in Refs. 50, 79, and 86. In organic solvents porphyrin undergoes the elementary act as H_2P, not as $H_2PH_2^{2+}$, PH^-, or P^{2-}.[50,90] The slight dependence of the rate of reaction (1) on the nature of the salt cation under identical experimental conditions indicates that the major component of the total activation energy resides in the stretching of the N–H bond. Investigation of the effect of structural changes in the porphyrin molecule[79-86] on the rate and on the energy and entropy of activation of reaction (6) has not only confirmed this conclusion but also established that polarisation (protonation) of the N–H bond favours the reaction.

III. DISSOCIATION OF CHLOROPHYLL, ITS METAL ANALOGUES, AND OTHER METAL PORPHYRINS IN SOLUTION

In this Section we shall discuss the heterolytic breakdown or solvolytic dissociation of porphyrin complexes,

¶ These authors[8,69] write the mechanism S_N2, not S_E2: i.e. they take porphyrin to be the reagent, which on the above considerations cannot be regarded as reasonable.

which occurs only in proton-donating media. Dissociation of the complexes into ions

$$MP + mn\,Solv \rightleftarrows M(Solv)_n^{2+} + P^{2-}(Solv)_m \quad (8)$$

is not observed owing to the very slight acidity of H_2P and the very great stability of metal–porphyrin complexes MP in solution. Appreciable dissociation begins to develop in media containing solvated protons H^+_{Solv} or molecules of strong acids. It occurs as protolytic dissociation

$$MP + 2H^+_{Solv} + 2X^- \rightleftarrows MX_2 + H_2P \quad (9)$$

but in media of high acidity

$$MP + 4H^+_{Solv} + 2X^- \rightleftarrows MX_{2(Solv)} + H_2PH^{2+}_{2(Solv)}. \quad (9a)$$

1. Dissociation of Chlorophyll and its Labile Metal Analogues

The first attempt at a quantitative kinetic study of the dissociation of chlorophyll was made by Mackinney and Joslin[30-32], who examined the reaction

$$Mg\Phi + 2HX \rightarrow Mg^{2+} + H_2\Phi + 2X^- \quad (9b)$$

in 90% aqueous acetone, using oxalic, sulphurous, sulphuric, and hydrochloric acids. The reaction was presumably of the first order with respect to the acid, but the order with respect to chlorophyll was not established, and no reliable kinetic characteristics were obtained. The failure of these experiments is explained by the choice of an unsuitable proton-donating solvent, in which partial protonation of $H_2\Phi$ to $H_2\Phi H_2^{2+}$, aggregation of $H_2\Phi$, etc. were possible. An important result[30-32] was that chlorophyll-a dissociates seven times as rapidly as chlorophyll-b†.

The kinetic experiments on the dissociation of chlorophyll and its derivatives have since been repeated by Schanderl et al.,[96] who used 80% aqueous acetone with additions of 10^{-4} M hydrochloric acid. Under the given conditions chlorophyll-a was found to dissociate more rapidly than chlorophyll-b by a factor of 5.5, while the activation energy was the same at 10.5 kcal mole^{-1}. Replacement of the phytyl residue ($C_{20}H_{39}$) in the chlorophylls by ethyl, methyl, and hydrogen, i.e. conversion of the chlorophylls into the ethylphaeophorbides, methylphaeophorbides, and phaeophorbides, produces slight acceleration of dissociation (the experimental rate constants for the a-compounds at 25°C are respectively 0.0103, 0.0127, 0.0156, and 0.0171 min^{-1}) without affecting the activation energy. The investigations provided no information on the mechanism of reaction (9) or the nature of the bond between magnesium and the porphyrin. The dissociation of chlorophyll and its analogues has therefore been studied under comparable conditions by Berëzin and Drobysheva[89,91,97-105]. The dissociation of chlorophyll-a and of cadmium and mercury phaeophytinates was examined[102] in absolute ethanol with small additions of glacial acetic acid, between 20° and 60°C. The results[102] are given in Table 7.

The dissociation of chlorophyll in ethanolic acetic acid occurs irreversibly in conformity with Eqn. (9), is strictly of the first order with respect to chlorophyll, has the activation energy $E = 13.7 \pm 0.5$ kcal mole^{-1} and the entropy of activation $\Delta S\dagger\dagger = -37 \pm 1$ e.u., and is very strongly dependent on (varies more rapidly than the fourth power of) the total concentration of acetic acid. Dissociation of the cadmium analogue of chlorophyll is reversible and of the first order with respect to the complex, with zero activation energy. Fig. 7 illustrates the dependence of the effective dissociation rate constants of chlorophyll and its cadmium analogue on the square of the total acetic-acid concentration. Dissociation of the cadmium complex is of the second order with respect to acetic acid and of the fourth order with respect to the solvated proton, whose concentration is calculated on the assumption that it is the attacking species in the act of dissociation of the complex.

† Chlorophyll-b is the magnesium complex of chlorophyllic-b acid—see structure (I).

Table 7. Dissociation of Mg, Cd, and Hg phaeophytinates in ethanolic acetic acid.

Complex	HOAc in ethanol, M	Temp., °C	k_{eff}, h^{-1}	Complex	HOAc in ethanol, M	Temp., °C	k_{eff}, h^{-1}
MgΦ	2.0	25	0.013*	CdΦ	0.02	25	0.68
		40	0.038			35	0.64
		50	0.076			45	0.62
		60	0.142		0.04	25	1.86
	4.0	25	0.34		0.06	25	3.80
	8.0	25	3.30		0.10	25	13.8
	10.0	25	41.5		0.20	25	83.0
				HgΦ	0.02	25	very rapid

*Calculated by means of the Arrhenius equation.

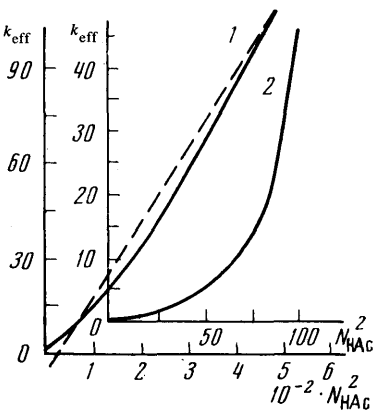


Figure 7. Dependence of effective dissociation rate constant on acidity of medium for: 1) CdΦ; 2) MgΦ.

The explanation offered[91,102] for such an unusual dependence was that not only $C_2H_5OH_2^+$ but also others, in particular CH_3COOH, may function as active protogenic species with not too stable metal porphyrins (the magnesium, cadmium, and mercury(II) complexes). Probably changes in the structure and properties of the solvent (ethanol) with increasing concentration of acetic acid should also be taken into account. These changes may have a large kinetic effect[65-67]. Since the nature of the reagent species in the act of dissociation of chlorophyll and its analogues is an important question, efforts must be directed to finding a proton-donating solvent in which one type of proton-donor would predominate, and its concentration could be calculated exactly. The Reviewers are making a search for such media in the laboratory.

Table 7 indicates an unusually large variation in the kinetic stability of the magnesium, cadmium, and mercury complexes. The mercury complex HgΦ is surprisingly unstable: in the presence of traces of acetic acid in ethanol it dissociates instantaneously. The cadmium complex is several orders of magnitude more stable. Chlorophyll is the most stable among these labile phaeophytinates. This stability is a not unimportant factor in Nature's choice as the principal complex for effecting photosynthesis.

2. Dissociation of Stable Complexes of Chlorophyllic Acid and Other Porphyrins

The stability of porphyrin complexes is of great interest for biochemistry, so that qualitative observations of this most important property were made long ago, and the results have been summarised [8,33,36]. The first quantitative data on the rates of dissociation of copper aetioporphyrin (XII) were published by Caughey and Corwin [36]. The dissociation was studied in glacial acetic acid with additions of sulphuric acid monohydrate. The results are given in Table 8.

Table 8. Rates of dissociation of copper aetioporphyrin at 30°C.

H_2SO_4, M	H_0	Expt. rate constant $10^{-6}k_{obs}$, h^{-1}
0.216	−2.02	0.715
0.267	−2.13	2.05
0.287	−2.17	2.83
0.312	−1 22	4.41
0.328	−0.328	5.00

The reaction velocity is described by the kinetic equation [36]

$$-\frac{d[\mathrm{CuAeP}]}{dt} = k\,[\mathrm{CuAeP}]^2 \cdot h_0^4 . \qquad (10)$$

The interpretation of the results [36] was subsequently criticised [37,108,107], and has not found support in investigations on other porphyrins.

Table 9. Kinetic parameters of dissociation of MΦ-a in glacial acetic acid at 25°C.

Complex	Added H_2SO_4, mole	E, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.	k_{eff}, h^{-1}
AcOFeΦ	0.500	17.30	−29	$8.95\cdot10^{-4}$
NiΦ	0.500	16.50	−28	$1.20\cdot10^{-3}$
	1.00	17.00	−26	$1.67\cdot10^{-3}$
CuΦ	0.200	16.40	−28	$1.23\cdot10^{-3}$
	0.500	15.30	−31	$1.92\cdot10^{-3}$
PdΦ	1.00	17.10	−29	$2.18\cdot10^{-3}$
CoΦ		12.80	−44	$1.61\cdot10^{-3}$
NiΦ		27.40	−11	$1.3\cdot10^{-5}$
CuΦ		19.00	−29	$9.8\cdot10^{-5}$
ZnΦ		10.10	−40	0.976
AgΦ		19.60	−16	$2.25\cdot10^{-3}$

Rates of dissociation of stable complexes of chlorophyllic acid (a-series) have been measured [97–103] by a spectrophotometric method. The iron(III), [80] nickel(II), [100] copper(II), [97,100] and palladium(II) [100] complexes dissociate at a measurable rate in strongly proton-donating media (sulphuric acid monohydrate in glacial acetic acid), but the zinc(II), [98] cobalt(II), [89] and silver(II) [101] complexes are decomposed even in weakly proton-donating media (glacial acetic acid and its mixtures with ethanol). At high temperatures the rates of dissociation of the nickel and copper complexes could also be measured in glacial acetic acid. The phaeophytinates-a of iron, zinc, and silver, like those of magnesium, cadmium, and mercury, dissociate according to Eqn. (9) or (9a). Dissociation of the copper, palladium, nickel, and cobalt phaeophytinates-a is accompanied by degradation of the phaeophytin molecule $H_2\Phi$-a to slightly coloured products. It was assumed [97] that detachment of the metal ion may yield an active form of the $H_2\Phi$-a molecule, which breaks down rapidly:

$$\mathrm{M\Phi} + 2\mathrm{HAc} \xrightarrow[\text{slow}]{} \mathrm{H_2\Phi^*} + \mathrm{MAc_2}\,, \qquad (11)$$

$$\mathrm{H_2\Phi^*} \xrightarrow[\text{rapid}]{} n\,\mathrm{A}\,. \qquad (12)$$

Reaction (12) involves no change in the side-chains, but a fundamental breakdown of conjugation occurs in the macrocycle, which is impossible without preliminary detachment of the metal by reaction (11) and freeing of the reaction centre. Conditions for the mechanism of dissociation by processes (11) and (12) are at present under investigation [105]. It is favoured by a strong metal–nitrogen covalent bond in the dissociating complex, except in the iron(III) complex [91]. The occurrence of reactions according to scheme (9) or (11) and (12) depends greatly on the temperature and on the solvent. Figs. 8 and 9 illustrate the variation in the absorption spectra [91] for these reactions.

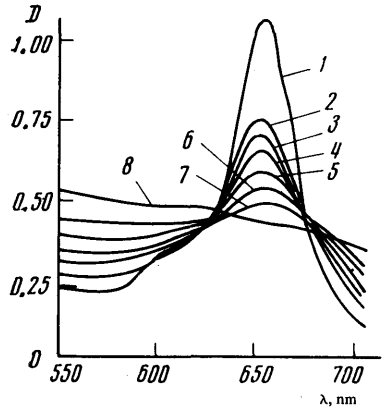


Figure 8. Dissociation of CuΦ in glacial HOAc + 0.5 M H_2SO_4 at 70°C (l = 1 cm): 1) initial CuΦ in acid mixture at 25°C; 2) initial CuΦ under experimental conditions; and after different periods of time (h): 3) 0.25; 4) 0.75; 5) 1.25; 6) 2.25; 7) 3.25; 8) 5.0.

Table 9 lists the kinetic parameters of dissociation for the stable complexes of phaeophytin-a. [91,100,108] Dissociation of stable complexes of chlorophyllic-a acid is very slow, with mean activation energies of 10–12 kcal (with the exception of the nickel complex in glacial acetic acid) and strongly negative entropies of activation, caused by the

high polarity of the transition state and the active participation of the solvent in the act of dissociation. Tables 7 and 9 indicate that the sequence of kinetic stability is

$$AcOFe\Phi \rhd Pd\Phi > Ni\Phi > Cu\Phi > Co\Phi > Ag\Phi > Zn\Phi \gg Mg\Phi > Cd\Phi > Hg\Phi.$$

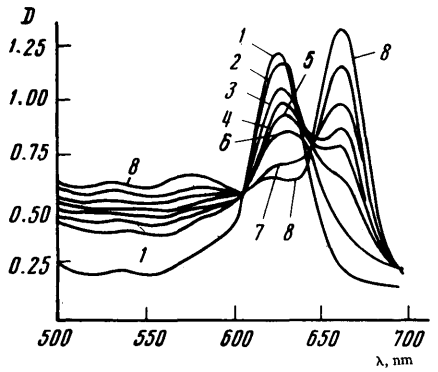


Figure 9. Dissociation of AcOFeΦ in mixture of glacial HOAc + 1.0 M H_2SO_4 at 50°C (l = 1 cm): 1) initial complex in glacial acetic acid; 2) complex under experimental conditions; and after different intervals of time (h): 3) 1; 4) 2; 5) 3; 6) 5; 7) 10; 8) 20.

Interesting investigations have recently been made[104] on the kinetic and the thermodynamic stability of complexes of chlorophyllic-b acid with copper and zinc. Table 10 compares the kinetic stability of metal analogues of chlorophyll-a and -b. The rates of dissociation of complexes of chlorophyllic-b acid are lower than those of the a-derivatives by factors of 25–300, and their rates of formation are also lower by factors of 10–10^2. These differences are attributed[104] to the influence of the formyl group in changing the electron density on the nitrogen atoms of the reaction centre. The retarding effect of this group on the rates of formation and dissociation of the complexes is eliminated in the equilibrium constants. Therefore the a- and b-complexes differ only threefold in thermodynamic stability.

Table 10. Dissociation of complexes of chlorophyllic acid in glacial acetic acid.

Complex	k_{eff}, h^{-1}	E, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.	K_{eq}
CuΦ-b	$0.38\cdot10^{-5}$	23.4	−25	$1.6\cdot10^{-9}$
CuΦ-a	$9.8\cdot10^{-5}$	19.0	−29	$5.1\cdot10^{-9}$
ZnΦ-b	$3.1\cdot10^{-3}$	10.9	−49	$2.4\cdot10^{-5}$
ZnΦ-a	0.976	10.1	−40	$7.3\cdot10^{-5}$

Iron(III) protoporphyrin (haemin) and the corresponding complex of chlorophyllic-a acid show similar kinetic stability in glacial acetic acid with additions of sulphuric acid (cf. Tables 9 and 11).

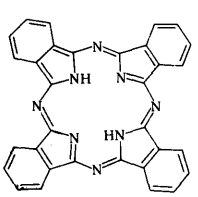
3. Mechanism of the Dissociation of Metal Porphyrins in Proton-donating Media

The first hypotheses on the mechanism of the protolytic dissociation of metal porphyrins were put forward in Ref. 36. The kinetic equation (10), showing the second order with respect to the porphyrin, was interpreted on the assumption of the improbable transition state $(MP.2H^+)_2$††. A combination of two porphyrin molecules in true solution, in which the relatively immobile "target" aetioporphyrin molecules, having no active peripheral substituents, are attacked by a proton-donating species, can hardly be taken seriously. The improbability of such a mechanism has been pointed out[97,107]. The first order of the reaction with respect to the porphyrin has since been shown convincingly[97–102,104] for the dissociation of complexes of chlorophyllic acids and also of iron protoporphyrin[105]. It follows from this that the transition state contains one molecule of the porphyrin complex.

Table 11. Dissociation of iron(III) protoporphyrin (haemin) in glacial acetic acid.

Added H_2SO_4	Temp., °C	k_{eff}, h^{-1}	E, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.
2.0	25	0.00177		
2.0	70	0.056		
2.0	80	0.103	15.9	−34
2.0	90	0.200		
5.0	25	0.00845		
5.0	60	0.205		
5.0	70	0.455		
5.0	80	1.04	18.0	−24
5.0	90	1.88		

The general applicability of this principle to all complexes of tetrapyrrole ligands is supported by kinetic data on the dissociation of phthalocyanine complexes. Phthalocyanine



(XV)

is a close structural analogue of the porphyrins, and is widely used as a simple model thereof[1,3–10,14–16,110]. The complexes (MPc) dissociate in conformity with the third-order kinetic equation

$$\frac{dc_{MPc}}{dt} = -k \cdot c_{MPc} c^2_{H_3O^+}. \qquad (13)$$

Several facts have shown convincingly[109] that a termolecular mechanism is most probable. In concentrated sulphuric acid, in which a metal phthalocyanine generally dissociates at a measurable rate only at 100°C, the attacking species is not H_2SO_4 but H_3O^+. In the transition state $[MPc.2H_3O^+]$†† are two N–H bonds resulting from acid–base interaction, two coordinate links $M\leftarrow OH_3^+$ appear, and two M←N bonds are deformed and become weaker. The mechanism of dissociation can be represented by the scheme

$$MPcH^+ + H^+_{Solv} \underset{I}{\overset{k_1}{\rightleftarrows}} HN \cdots \overset{\overset{N}{\downarrow}}{M} \overset{\overset{Solv\ N}{\nearrow\ \uparrow}}{} \leftarrow N + H^+_{Solv} \underset{II}{\overset{k_2}{\rightleftarrows}} HN \cdots \overset{\overset{Solv\ N}{\searrow\ \downarrow}}{M} \overset{\overset{N\quad Solv}{\uparrow\ \nwarrow}}{} \cdots NH \xrightarrow{\overset{H^+_{Solv}}{k_3}} H_2PcH^+ + M^{2+}_{Solv}. \qquad (14)$$

With stable phthalocyanines processes I and II take place in a single stage.

The close structural analogy between phthalocyanine and porphyrins suggested[100,110] that mechanism (14) applied also to stable complexes of the latter. Experimental examination of the kinetic order of the dissociation of stable complexes of chlorophyllic acid with respect to the proton-donating species has not yet given general support to this hypothesis. An unambiguous result has so far been obtained[89] only for iron(III) phaeophytinate, whose rate of dissociation in glacial acetic acid is proportional to the total concentration of sulphuric acid. In weakly ionising media such as acetic acid we have $[H_2SO_4]_{total} \simeq [H^+_{Solv}]$, which confirms the validity of Eqn. (13) for AcFeΦ and of the mechanism (14).

On the basis of the general theoretical concepts of coordination chemistry it may be predicted that it will be sufficient to break one M–N bond and convert it into M⁺...NH in the case of labile metal phthalocyanines and metal porphyrins, in which the metal–ligand bond is predominantly ionic. After the metal has been displaced from the plane of the macrocycle, subsequent rupture of the remaining bonds and transition to the structure (XIV) will take place readily. For these complexes we may not only expect the first order with respect to $[H^+_{Solv}]$ but also postulate the H_2SO_4 molecule and even HOAc as active protogenic species. This makes it clear why labile complexes dissociate instantly on the addition of traces of sulphuric acid to their acetic-acid solutions and show a high order with respect to the total concentration of acetic acid[91,100,102]. Chlorophyll itself can be included in this category: it is assumed that $k_1 \gg k_2$ in process (14).

IV. THERMODYNAMIC AND PHOTOCHEMICAL STABILITY OF CHLOROPHYLL AND ITS METAL ANALOGUES IN SOLUTION

The first paper on the thermodynamic stability of the zinc complex of the dimethyl ester of mesoporphyrin (ZnMP) appeared in 1961.[111] The instability constant in aqueous hexadecyltrimethylammonium bromide was found to be 10^{-29}. In conformity with critical comments[112] this value must be regarded as a very crude approximation. In spite of this, however, it clearly demonstrates the extraordinary stability of porphyrin complexes. In fact, zinc complexes with an instability constant of 10^{-16} are formed by one of the most strongly chelating ligands, ethylenediaminetetra-acetate[55]. Such great stability of porphyrin complexes is due to their very low rates of formation and dissociation, resulting from π-electron shielding of the four nitrogen atoms constituting the coordination centre. The first investigations in this field were made by Kukhtevich on the equilibrium formation of metal analogues of chlorophyll using an extraction method[34,35,113,114]. He studied the formation equilibria

$$M^{2+}_w + H_2\Phi_{org} \rightleftarrows M\Phi_{org} + 2H^+_w \qquad (15)$$

of bivalent zinc, cadmium, copper, and cobalt phaeophytinates by then partitioning them between the aqueous phase and an organic solvent (butanol). Kukhtevich calculated the equilibrium constants of (15) and the so called "extraction" constants

$$\frac{[M^{2+}]_w[\Phi^{2-}]_w}{[M\Phi]_{org}} = K_{M\Phi_{org/w}} \qquad (16)$$

obtaining values of 2×10^{-23}, 5.2×10^{-20}, 5×10^{-20}, and 1.7×10^{-11} for CuΦ, CoΦ, ZnΦ, and CdΦ respectively. Complexes of chlorophyllic-a and -b acids had identical constants.

Kukhtevich also reported[35] so called "extraction" constants for both stages of the acid ionisation of phaeophytin:

$$K_1 = \frac{[H^+]_w \cdot [\Phi H^-]_w}{[H_2\Phi]_{org}} = 2.3 \cdot 10^{-11},$$

$$K_{1,2} = \frac{[H^+]^2_w \cdot [\Phi^{2-}]_w}{[H_2\Phi]_{org}} = 10^{-20}.$$

Data on the dissociation of phaeophytin differ sharply from the preliminary results reported by McEwen[115] for aetioporphyrin ($K_1 \simeq 10^{-16}$ and $K_{1,2} \simeq 10^{-32}$). Ionisation constants differing by a factor of 10^{12} cannot be explained in terms of molecular structure. The exact values of the acid dissociation constants of porphyrins, which are necessary for calculating the instability constants of their complexes, remain unknown, and their determination is an urgent problem in the physical chemistry of porphyrins. "Extraction" constants give only a crude indication of the order of stability of porphyrin complexes. However, these constants have correctly revealed the very great stability of the complexes, the great difference between the zinc and cadmium complexes in this respect, and the feebly developed acidic properties of chlorophyllic acid. Significant defects of the extraction method have been pointed out[116], and mention made of our ignorance of existing extraction equilibria and the absence of clarity concerning the mechanism of complex formation in a two-layer system comprising water and an organic solvent.

The difficulties associated with the direct measurement of equilibria involving porphyrin complexes led to the successful use[91,108,112] of two forms of kinetic method. The first procedure entailed calculating equilibrium constants for metal porphyrins (MP) from their known dissociation and formation rate constants obtained under identical conditions (temperature, solvent, anionic composition of the medium, etc.). The principle of detailed balancing was used[108], according to which the formation and dissociation stages of these compounds have the same transition state (Sections II and III). Dissociation equilibrium constants were found in this way for zinc, cobalt, copper, and nickel phaeophytinates in glacial acetic acid[91]. The second variant of the kinetic method was used to calculate dissociation equilibrium constants for the palladium(II), iron(II), and silver(II) phaeophytinates, since their formation rate constants could not be obtained under conditions of dissociation. This utilises the slight dependence of the formation rate constants of MΦ on the nature of the metal, i.e. that k_v^{form} is almost constant. We can then write the relation

$$\frac{K^0_{MP}}{K'_{M'P}} = \frac{k^0_v}{k'_v} \qquad (17)$$

for a complex adopted as standard and for the ith complex MP to be compared with it. If the equilibrium constant for the standard K^0_{MP} is taken to be unity, the relative equilibrium constant of M'P will be the ratio of the dissociation rate constants of the ith complex and the standard under comparable conditions:

$$K^i_{M'P} = k^i_v/k^0_v. \qquad (18)$$

Equilibrium constants were found in this way for the palladium(II), iron(III), and silver(II) complexes relative to copper(II) phaeophytinate as standard. The known true equilibrium constant of the standard enabled true constants to be obtained for PdΦ, AcOFeΦ, and AgΦ. Values obtained by both forms of the kinetic method are given in Table 12.[91]

The very great difference in stability between zinc and cadmium phaeophytinates makes it impossible to determine

their equilibrium constants in the same proton-donating medium. The constants of the cadmium complex were measured in ethanol with small additions of acetic acid, and those of the zinc complex in glacial acetic acid with small additions of ethanol. The results were then extrapolated to 50% ethanolic acetic acid. The rough values thus obtained were $K_{eq}^{Cd\Phi} \simeq 0.5$ and $K_{eq}^{Zn\Phi} \simeq 5 \times 10^{-7}$. Thus under identical conditions the complexes $Cd\Phi$ and $Zn\Phi$ would differ in stability by factors of about 10^6. Published data enable a crude estimate to be made of the dissociation equilibrium constant of chlorophyll—from the dissociation rate constant of chlorophyll measured[102] in ethanol containing 2 M acetic acid, and from the formation rate constant of magnesium mesoporphyrin, converted by means of the data in Tables 4 and 6 into the formation rate constant of chlorophyll in ethanol $k_v^{form} = 3.6 \times 10^{-5}$ M^{-1} h^{-1}—as

$$K_{eq} \approx \frac{0.013}{3.6 \cdot 10^{-6}} \approx 360$$

in ethanol–acetic acid medium. An analogous estimate of the equilibrium constant in 10 M ethanolic acetic acid yields 1.2×10^6, which exceeds the constant for zinc phaeophytinate by a factor of 10^{12}, and that for the cadmium complex by more than 10^6.

Table 12. Equilibrium constants for the dissociation of stable phaeophytinates in glacial acetic acid at 25°C.

Complex	$K_{eq} = \frac{[MOAc_2]}{[HOAc]^2} \cdot \frac{[H_2\Phi]}{[M\Phi]}$
$Zn\Phi$	$7.32 \cdot 10^{-5}$
$Co\Phi$	10^{-5}
$Ag\Phi$	$2.3 \cdot 10^{-7}$
$Ni\Phi$	$3 \cdot 10^{-8}$
$Cu\Phi$	10^{-9}
$Pd\Phi$	$8 \cdot 10^{-11}$
$AcOFe\Phi$	$5 \cdot 10^{-11}$

Several conclusions follow from the above values. Firstly, the positions of metal analogues of chlorophyll in the kinetic stability sequence (see above) and in the thermodynamic stability sequence

$$AcOFe\Phi > Pd\Phi > Cu\Phi > Ni\Phi > Ag\Phi > Co\Phi > Zn\Phi > Cd\Phi > Mg\Phi,\ Hg\Phi$$

do not coincide in those cases in which the rates of formation exhibit anomalies. The rate of formation of chlorophyll ($Mg\Phi$) exceeds those of its metal analogues by factors of 10^7–10^8. Therefore, while possessing far higher kinetic stability than cadmium phaeophytinate, chlorophyll is markedly inferior in thermodynamic stability. Certain anomalies in the rates of formation of the nickel complex make it thermodynamically less stable than the copper complex, although the kinetic stability of the former is rather greater. The same applies to cobalt(II) and silver(II) phaeophytinates: the former is kinetically the more stable, whereas the silver complex exhibits the greater thermodynamic stability. In this connection, the numerous attempts to make deductions as to thermodynamic stability from the rates of dissociation of porphyrin complexes, which have been widely undertaken both abroad[8,33,36] and in the Soviet Union[112], must be regarded as a first, very rough approximation.

Secondly, the position of a complex in the kinetic stability sequence is determined predominantly by the covalency of the metal–porphyrin bond. Kinetic stability in solution is probably a quite reliable criterion of the type of bond. The magnesium–porphyrin bond is far more covalent than the corresponding bonds with cadmium and mercury(II). This covalency is responsible for the adequate stability of chlorophyll in the plant cell. Nevertheless, chlorophyll is far less covalent than the zinc complex, one of the least stable members of the group of stable phaeophytinates. This intermediate position of chlorophyll in the covalency sequence ensures that the magnesium shall carry a sufficient effective charge to favour coordination of the various molecules forming part of the complicated photosynthetic apparatus[2].

Thirdly, the position of a metal porphyrin in the thermodynamic stability sequence is largely determined by specific aspects of its formation in solution. Consideration of the mechanism and the kinetic parameters of the formation of metal porphyrins (Section II) shows that the stability (covalency) of the complex makes no significant contribution to its rate of formation. For this reason the thermodynamic stability sequence of metal porphyrins does not reflect their covalency.

The only serious rivals to metal porphyrins in their extraordinary stability are the phthalocyanine complexes[108]. Under very severe conditions (concentrated sulphuric acid) stable metal phthalocyanines dissociate at vanishingly low rates; metal porphyrins eliminate the cation instantly under these conditions. Such a substantial difference in stability between these close structural analogues has been explained by differences in the molecular structures of the ligands[110,117,118], by differences in their electron-donating and electron-accepting powers. It must be added that probably the most significant reasons why metal porphyrins are less stable than metal phthalocyanines are some departure of the molecules from planarity[8] and the absence from the molecular periphery of nitrogen atoms, which buffer the electron density in antibonding π-orbitals of the macrocycle. Coordination of a metal with phthalocyanine removes four pairs of electrons from such orbitals of the ligand. The resulting deficiency of π-electron density is immediately filled by the lone pairs of the outer nitrogen atoms[119]. Such a possibility is not available to a porphyrin molecule.

An important problem in the chemistry of porphyrin complexes is their photochemical stability in solution and its relation to their kinetic and thermodynamic stability. The lack of work in this field is acutely felt at the present time. A parallelism between photochemical and thermodynamic stability of phaeophytin complexes was reported[120] on the basis of qualitative and semi-quantitative experiments. The general conclusion was reached that phaeophytinates of the b-series are more resistant to fading than are those of the a-series.

Detailed quantitative investigations of the photochemical stability of chlorophylls-a and -b, chlorophyllic acids, and their complexes in ethanol and glacial acetic acid[99] have enabled these conclusions to be refined. Rate constants calculated for photochemical degradation over the range 20–60°C showed that the rate is little influenced by temperature but is strongly affected by the solvent. Photochemical fading is more rapid in acetic acid than in ethanol. However, the opposite effect is observed with cadmium phaeophytinate. Phaeophytins-a and -b have the same rates of fading in ethanol; cadmium phaeophytinate-a is twice as fast to light as the b-complex. In glacial acetic acid phaeophytin-b is four times as fast as phaeophytin-a.

No correlation between photochemical and thermodynamic stability is observed in either solvent. Thus in ethanol mercury(II) phaeophytinate is more stable to light than the zinc complex, whereas the magnesium and cadmium complexes are equally fast. In glacial acetic acid cobalt(II) phaeophytinate is more stable than the palladium and copper complexes. The sequence of diminishing photochemical stability in glacial acetic acid was found[99] to be

$$AcOFe\Phi > Ni\Phi > Co\Phi > Pd\Phi > Cu\Phi.$$

This sequence does not correspond to those of kinetic and thermodynamic stability. The lack of parallelism between light fastness and resistance to ionic dissociation is not unexpected, since there is no similarity in the mechanisms of the two processes[99].

Summing up the above account, we must note an acute lack of data on several aspects, despite the substantial progress made during the past decade in investigating the conditions and mechanism of the formation and decomposition of chlorophyll and its structural analogues. This applies primarily to the fine mechanism of dissociation of the complexes and directly to measurement of the formation equilibria of metal porphyrins. The main efforts of research workers in such an important and interesting branch of chemistry should be directed to solving these problems.

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